Keynote Address Program
100 Mouse Models of Autism to Discover Causes and Develop Treatments
Speaker: J. N. Crawley *National Institute of Mental Health, National Institutes of Health*

Searching for the causes and cures for autism depends on strong animal models. As candidate genes linked to 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 DNA methylation, neuroanatomical abnormalities, immune dysfunctions, diets, environmental toxins, and other proposed causes of autism.

The key to successful translational applications is robust, highly replicable functional assays. Our laboratory has generated a constellation of mouse behavioral paradigms with conceptual analogies to the three diagnostic symptoms of autism. This presentation will focus on behavioral tests for mice that offer reasonable face validity to the defining symptoms of autism. The core deficit in reciprocal social interactions is modeled longitudinally across developmental stages with juvenile and adult reciprocal social interaction scoring and automated social approach paradigms. Communication in mice is investigated with measures of the emission, detection, and responses to olfactory and auditory social cues. Motor stereotypies, repetitive behaviors, insistence on sameness, and narrow restricted interests are analyzed in mice by quantitating spontaneous stereotyped motor behaviors, repetitive self-grooming, perseveration during the reversal phase of T-maze and Morris water maze spatial tasks, and restricted exploration of complex environments.

Behavioral assays relevant to the associated symptoms of autism, including anxiety, seizures, sleep disruption, low IQ, and hyperreactivity to sensory stimuli, may provide further insights into the phenotypes of a mouse model of autism spectrum disorders. Comprehensive control tests for general health, motor functions, and sensory abilities are conducted, to detect potential confounds due to physical defects, thus avoiding overinterpretations of artifacts.

Both forward genetics and reverse mouse genetics are employed in our laboratory to understand the genetic basis of social, communication, and repetitive behaviors. Results from knockout mice with targeted mutations in candidate genes for autism will be described. BTBR T+tf/J, an inbred strain that displays autism-like traits on many of these tasks, will be used to illustrate phenotypes of a robust mouse model of autism.

Targeted gene mutations and inbred strains of mice that incorporate traits with face validity to the diagnostic and associated symptoms of autism offer attractive model systems to evaluate potential treatments. Early preclinical results will be presented on drug treatments and environmental interventions that reverse components of the autism-relevant behavioral phenotypes in the BTBR mouse model of autis

Invited Educational Symposium Program
101 Neuroimaging Genetics: Bridging Disciplines
Moderator: L. Davis *University of Iowa*

Efforts to integrate neuroimaging and genetics are well underway in the study of schizophrenia and ADHD and are gaining momentum in the study of autism. While imaging genetics is of very high interest to many investigators, methods and best practices in this young field are still undefined. The current lack of cohesive best practices makes neuroimaging studies both daunting to initiate and difficult to interpret for new investigators. The session will introduce the attendee to neuroimaging genetics by reviewing the state of the field and identifying current gaps in knowledge. Speakers will clarify some of the practical and theoretical issues surrounding the integration of these two fields and finally, data from current studies of neuroimaging genetics will be presented. The session will consist of three 30 min lectures with 10 minutes following each for questions and discussion.

101.001 Imaging Genetics: Translating Genetic Association Into Neural Mechanisms of Illness. D. Weinberger*, *National Institutes of Health*

The discovery of statistical association of genes with complex behavioral disorders such as autism and schizophrenia raises important new challenges for understanding the mechanisms in brain of these statistical relationships. One approach that has emerged over the past decade as a strategy to bridge this gap involves the application of neuroimaging to map gene effects in brain. This talk will describe the principles and some of the practices that characterize this novel strategy, including effects of several potential psychosis susceptibility genes in brain, such as CACNA1, GAD1 and GRM3, and approaches for understanding their biologic interactions.

101.002 Neural systems approaches to the neurogenetics of autism spectrum disorder?. J. Piggot*, *University of California, Los Angeles*

Despite more than several decades of genetic study, the etiology of autism remains unknown, largely due to the genetic and phenotypic diversity, or heterogeneity, of this disorder, and the lack of biologically based classification systems. At the same time, in the neuroimaging literature, the body of research identifying candidate neural systems underlying aspects of autistic impairment has grown considerably, fuelled by the advent of technologies such as functional magnetic resonance imaging (fMRI). With the increasing recognition that there may be different "autisms" (Geschwind and Levitt, 2007) with unique neural mechanisms, would the incorporation of neural systems approaches allow for the identification of more biologically informative phenotypes for genetic studies of autism and neuroimaging markers for "neurogenetic" studies of the disorder?

101.003 Genetic Variation of the Serotonin System and Cortical Enlargement in Autism. T. Wassink*, *University of Iowa*

Identifying the genetic basis of the cortical abnormalities in autism may help elucidate the genetic basis of autism itself. But while the volume of both genotyping and brain imaging data in autism is rapidly expanding, studies integrating these modalities are still modest in size, necessitating careful selection of genetic variants for study. We examined the effect of variation in two serotonin genes (*SERT* and *MAOA*) on brain size in children with autism and found that, in both genes, polymorphisms associated with diminished serotonin metabolism were associated with increased cortical size. Strengths and limitations of this type of research approach, as well as challenges faced by the attempt to integrate genetic with brain imaging data, will be discussed.

Cognition Program
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102.001 A Multilevel Analysis of Response Monitoring in Higher Functioning Children with Autism. H. A. Henderson*[1], L. Mohapatra[1], C. Hileman[1], K. E. Ono[1], C. Schwartz[2], N. Kojkowski[1], M. Jaime[1] and P. C. Mundy[3], (1)*University of Miami*, (2)*Yale University*, (3)*UC Davis*

Background: Response monitoring, or the ability to recognize and spontaneously self-correct errors in ongoing behavior, relies on the coordinated functioning of the anterior cingulate cortex and related regions. There is evidence that children with autism display behavioral impairments in response monitoring, yet there is conflicting evidence from imaging and electrophysiological studies regarding the integrity of ACC functioning during response monitoring tasks.
Objectives: The goals of the current study are (1) to examine the associations between physiological and behavioral indices of response monitoring, and (2) to examine the mediating role of self-perceived locus of control in the association.

Methods: Preliminary data are presented on 37 (32 male) higher functioning (IQ> 70) children with autism (9 – 16 years) and a comparison sample of 34 age-, IQ-, and gender-matched typically-developing children. EEG was collected continuously from 22 scalp sites as children completed a modified version of the Eriksen Flanker Task. Electrophysiological measures of response monitoring were measured at midline sites as the most negative peak 25 to 150 ms following error (ERN) versus correct (CRN) responses. Post-error slowing (RT on trial after error – RT on trial after correct) served as a behavioral index of response monitoring. Self-perceived Locus of Control was assessed using the Behavior Assessment

System for Children – Self Version (BASC-2). Results: A 2 (diagnostic group: HFA vs. comparison) x 4 (cortical site: Fz, FCz, Cz, Pz) x 2 (response type: error vs. correct) repeated measures ANCOVA controlling for error rates revealed that all participants had larger amplitude responses on error versus correct trials. This effect was generalized across all midline sites in the HFA sample, but localized to frontal sites (Fz, FCz) in the comparison sample, $F(3, 204) = 3.31$, $p = .02$. Within the comparison sample, enhanced amplitude ERN responses predicted more post-error slowing, $r(33) = -.40$, $p = .02$. In contrast, ERN amplitude did not predict post-error slowing in the HFA sample, $r(37) = -.02$, ns. Diagnostic group differences in the associations between physiological and behavioral measures of response monitoring appeared to be partially accounted for by differences in self-perceived locus of control. For the comparison sample an enhanced amplitude ERN was associated with a more internal locus of control, $r(32) = .61$, $p < .001$, whereas for children in the HFA sample an enhanced amplitude ERN was associated with a more external locus on control, $r(37) = -.40$, $p = .02$.

Conclusions: These results suggest that children with autism may have less well developed response monitoring tendencies as indicated by a lack of frontally-localized ERN responses. Unlike children in the comparison sample, enhanced physiological reactions to errors did not predict more behavioral compensation for errors. For children with autism, enhanced physiological reactions to errors in conjunction with feelings of a lack of personal control over their environment, may lead to behavioral and attentional disengagement in the context of errors. These results will be discussed in terms of the importance of using multi-method approaches to further integrate existing neurobiological and psychological models of autism.

102.002 Distinguishing Gaze Aversion From Gaze Indifference in Two-Year-Olds with Autism. J. M. Moriuchi*[1], A. Klin[1] and W. Jones[2], (1)*Yale University School of Medicine*, (2)*Yale School of Medicine*

Background: Atypical eye contact is among the most prominent and early-emerging symptoms of autism spectrum disorders (ASD). Eye-tracking studies of individuals with ASD during viewing of dynamic social stimuli and some instances of static stimuli have found reduced fixation on the eyes as well as increased fixation on both the mouth and background objects relative to typically developing (TD) controls. However, the underlying cause of this difference in visual attention remains controversial. One hypothesis is that children with ASD purposefully shift visual attention away from the eyes because the eyes have negative emotional saliency (e.g., leading to hyperarousal). Alternately, children with ASD may show reduced fixation on the eyes because they are indifferent to the significant social cues conveyed by the eyes. In other words, one hypothesis suggests an active avoidance with implicit awareness of the social significance of eye contact, while the other suggests insensitivity to the underlying social signal.

Objectives: The current study seeks to determine whether reduced visual fixation on eyes in toddlers with ASD reflects an aversion or indifference to direct gaze.

Methods: Eye-tracking data were collected while two-year-olds with ASD and matched TD peers viewed video clips of actresses portraying caregivers engaged in naturalistic, child-directed interaction. During interstimulus intervals between each video scene, visual attention was directed towards a centering cue so that all viewers began viewing of the scenes by fixating at the same locations. The position of the actresses within the video frame was systematically adjusted between scenes so that the location of the centering cue would prime a viewer to fixate on either the actress' eyes or mouth when the cue disappeared and the video began. Measures of the directionality of initial saccades and duration of fixations were compared between conditions. In addition, a novel computational method of quantifying visual scanning patterns through time was used to determine periods within the clips when the eyes were most salient to TD viewers. If children with ASD find eye gaze aversive, they

would be more likely to shift attention away from the eyes during these time periods; on the other hand, if children with ASD were insensitive to social cues from the eyes, their tendency to look towards or away from the eyes would be unchanged during these periods.

Results: Preliminary analyses suggest that when primed to orient towards the eyes, children with ASD exhibit increased attention to the eyes as compared to cases when they are primed to orient towards the mouth. Across conditions, children with ASD did not specifically redirect their scanning away from the eyes when the eyes conveyed the most salient social cues.

Conclusions: The reduced eye fixations observed in the viewing patterns of children with ASD indicate insensitivity to social cues conveyed by another's eyes rather than an aversion to gaze.

102.003 Eye-Blinking as An Index of Perceived Stimulus Relevance in Toddlers with Autism Spectrum Disorder. S. Shultz*[1], W. Jones[1] and A. Klin[2], (1)*Yale School of Medicine*, (2)*Yale University School of Medicine*

Background:

Many studies have now demonstrated that individuals with autism attend to their visual environment in ways that differ from typically-developing peers: individuals with autism look less at people in general and less at people's eyes in particular. While these altered patterns of looking evidence basic differences in attention to social adaptive information, few studies have directly measured how individuals, on a moment-by-moment basis, perceive the relevance of what they are looking at. In order to directly measure the perceived task relevance of visual content, during a natural viewing task, we measured the probability of blinking and blink inhibition while collecting eye-tracking data. While eye-blink data are often discarded as noise, a small research literature links blinking to visual information processing in a variety of cognitive tasks. That research demonstrates that blinking is inhibited during moments in which a viewer perceives that he or she will be processing important task-relevant visual information. Here we measure blink inhibition to index perceived stimulus relevance during natural viewing.

Objectives:

Our objectives were (1) to test whether the ongoing probability of blink inhibition during natural viewing might quantify the perception of task-relevant, salient information in typically-developing children; (2) to determine whether children with autism differed from typically-developing children in their blinking behavior; and (3) to measure whether between-group differences in timing of blink inhibition and in content of visual fixations during blink inhibition might reveal information about the perceived task-relevance of visual stimuli in children with autism relative to typically-developing peers.

Methods:

Eye-tracking data were collected from 2-year-olds with autism (n = 41) and matched, typically-developing peers (n=52) while watching movies of social interaction. Differences in physiological properties of eye-blinking were tested by measures of individual blink rate (mean blinks per minute) and expected positive correlation between age and blink rate. Movies were selected for their range in affective content, varying from low emotional valence to highly charged exchanges; affective valence was rated by 10 adult viewers naïve to experimental aims.

Results:

Children with autism and their typically-developing peers differed significantly in their timing of blink inhibition relative to scene content. Control measures—blinks per minute and correlation of blink rate with chronological age—were not significantly different. A repeated-measures ANOVA revealed a significant interaction between diagnosis and affective scene content during blink inhibition. Typically-developing toddlers inhibited their blinking during scenes with greater affective content, while blink inhibition in toddlers with autism was unrelated to affect.

Conclusions:

While physiological properties of eye-blinking were equivalent between groups, and both groups inhibited their blinking more than expected by chance, only typically-developing 2-year-olds inhibited their blinking selectively during scenes of high affective valence. These results demonstrate that patterns of blink inhibition index perceived task relevance of visual stimuli and also that they quantify reactions to, and expectations of, emotional content during natural viewing. Together these results reveal what information is missed—in the blink of an eye—by children with autism.

102.004 Post-Decision Wagering Shows That ASD Subjects Appear to Be Unusually Confident in Their Choices During a Motion Discrimination Task. R. J. Krauzlis* and N. Dill, *Salk Institute for Biological Studies*

Background: Several studies have found that individuals with autism spectrum disorder (ASD) exhibit impairments in discriminating the direction of motion in a visual display. Last year, we reported similar results, but also showed that ASD subjects performed as well as typically developing (TD) subjects when required to delay their response. These findings challenged the idea that the impairments in motion processing of ASD-diagnosed individuals are due to abnormalities in the early stages of visual processing, and instead suggest that the impairments are related to abnormalities in the decision process underlying the behavioral response. Objectives: To investigate this alternative explanation, we have now designed a task that probes the subjects' confidence in their judgments by asking them to wager on their choices in the motion discrimination task. Methods: Subjects (ASD and TD children, aged 10 to 18) performed a 2-AFC visual motion discrimination task with post-decision wagering. On each trial, subjects viewed a stochastic motion stimulus for 750 ms (8º diameter patch, 8º above a fixated spot, variable strength rightward or leftward motion), and indicated their motion direction judgment by pressing either the left or right button on a response pad. They then were asked to place a bet, either high or low, on the correctness of their choice, by pressing either the upper or lower button on the same response pad. We ran two versions of the task that were identical in all respects except that the payoff values were adjusted so that the optimal betting strategy changed. In one version, the best strategy was to always wager high, whereas in the second version, the best strategy was to bet low when the correct answer was uncertain. Subjects received visual and auditory feedback about their choices after each trial and received a monetary reward for total points won. Results: As we found previously, ASD and TD subjects had similar thresholds for discriminating the direction of motion when required to delay their response. However, their betting strategies were very different. TD subjects tended to bet high when the motion coherence was high and bet low when the motion coherence was low, possibly reflecting a tendency to be risk averse. AD subjects, in contrast, tended to bet high regardless of motion coherence, and thus tended to not take the quality of the sensory stimulus into account when setting their wager. Moreover, when the payoff values were changed in the second version of the task, TD subjects modified their betting strategy as expected, increasing their frequency of low bets. ASD subjects wagered the same way in both versions of the task. Conclusions: These results show that ASD subjects appear to be unusually confident in their choices, even when the sensory evidence is weak and the correct choice is uncertain. These findings support the idea that impairments in sensory discrimination observed in ASD are due, at least in part, to abnormalities in the decision-making process, perhaps reflecting an inability to accurately monitor the quality of signals prior to generating a behavioral response.

102.005 The Effects of Social Context On Perception of Audiovisual Synchrony in Infants with Autism. J. B. Northrup*[1], J. Xu[1], G. Ramsay[1], A. Klin[2] and W. Jones[1], (1)*Yale School of Medicine*, (2)*Yale University School of Medicine*

Background: In recent research, we found that two-year-olds with autism failed to give preferential attention to point-light displays of human biological motion. Instead, they oriented towards non-social, physical

contingencies—contingencies that were disregarded by control children in favor of preferential attention to biological motion. These results showed that a skill present in two-day-old, typically-developing infants, as well as in chronologically-, verbally-, and nonverbally-matched control children, was derailed in young children with autism. In its place, toddlers with autism demonstrated intact processing of a physical contingency: audiovisual synchrony.

Objectives: The goal of the current project is to understand how attention to audiovisual synchrony is modified by the social context in which stimuli are perceived. Our aims are (1) to assess baseline sensitivity to audiovisual synchrony in both infants with ASD and in control children; and (2) to measure, in the same children, the effect of varying social context upon preferential looking to 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. 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. Infants' looking was measured by eye-tracking.

Results: Results show that infants with autism and typically-developing peers do not differ in their baseline sensitivity to audiovisual synchrony. However, audiovisual synchrony detection in infants with autism was less influenced by accompanying social context: while the introduction of biasing social context altered the preferential viewing patterns of TD and DD controls—who showed a strong preference for synchronous faces—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, the perception of physical contingencies is not altered by accompanying social context. This gives insight into a way of learning about the world in which sensory stimuli are experienced as coincident patterns of light and sound, unmoored from their social adaptive context. Future investigations will benefit from studies, starting still earlier in life, of the developmental unfolding of this process. 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.

102.006 Age Trends in the Allocation of Voluntary Attention in Typical Development and Autism. N. Sasson*[1], J. T. Elison[2], L. Turner-Brown[3] and J. W. Bodfish[4], (1)*University of Texas at Dallas*, (2)*University of North Carolina at Chapel Hill*, (3)*UNC-Chapel Hill*, (4)*University of North Carolina - Chapel Hill*

Background: Flexibly attending to and efficiently processing salient information in the visual environment is necessary to navigate the dynamics of social interaction. The nature by which toddlers, school-aged children, and adolescents explore complex visual scenes remains a compelling assay for these attentional and information processing capacities. We have developed a passive viewing Visual Exploration Task that consists of complex visual arrays balanced for social and nonsocial content. Past research has shown that children with autism spectrum disorders (ASD) demonstrate reduced exploratory visual behavior, increased perseverative attention and a more detail-oriented perceptual profile relative to typically-developing (TD) children. How these attentional operations and information processing strategies change over the course of childhood in both TD children and children with ASD is not yet known.

Objectives: To examine age-related trends across childhood in the allocation of voluntary attention in TD and ASD using the Visual Exploration Task.

Methods: The eye movements of 51 children with ASD (M age, 9.29 years; range, 2.67 – 17.25 years) and 43 TD children (M age, 8.20 years; range, 2.08 – 16.17) were tracked as they passively viewed a series of 12 arrays consisting of pictures of people and objects. Dependent measures included exploration (the number of images fixated), perseveration (fixation time per image viewed) and detail orientation (the average number of fixations per image viewed).

Results: Across the entire task, all three dependent measures correlated strongly with age for both TD and ASD children. Both groups exhibited greater visual exploration with age (TD: $r(43)=.77$, $p < .001$; ASD: $r(51)=.54$, $p < .001$), less perseveration (TD: $r(43)=-.47$, $p = .001$; ASD: $r(51)=-.39$, $p = .004$) and less of a detail-orientation (TD: $r(43)=-.63$, $p < .001$; ASD: $r(51)=-.39$, $p = .005$).

Conclusions: The presence of strong developmental trends in the data across the TD and ASD groups indicates that as children age, they demonstrate increasing attentional flexibility and processing efficiency, regardless of clinical status. Older children explore more items, exhibit fewer discreet fixations and spend less time processing the images explored. While children with ASD continue to demonstrate reduced visual exploration and increased perseverative attention relative to their TD counterparts from toddlerhood through adolescence, they nevertheless follow the normative developmental pattern of increasing visual exploration and decreasing perseveration across the course of childhood. While the slopes of the developmental effect appear similar for both the TD and the ASD groups, identifying the age at which the intercepts may differentiate remains an enduring challenge, and may potentially represent early markers for an autism diagnosis. Future directions include differentiating between flexible distribution of attention and efficiently processing information, and characterizing how these subcomponents contribute to voluntary and reflexive visual attention proper.

102.007 Driving Hazard Perception in Autism: An Eye Tracking Study. E. Sheppard*[1], D. Ropar[2], G. Underwood[2] and E. Van Loon[2], (1)*University of Nottingham Malaysia Campus*, (2)*University of Nottingham*

Background: Klin, Jones, Schultz and Volkmar (2003) identify driving as a 'challenging task' for individuals with ASD. However, an increasing number of individuals with ASD have been applying for driving licenses. Hazard perception is a component of driving that may pose particular problems for people with ASD, as many hazards involve the perception or anticipation of another person's intentions and movements. In a previous study we found that participants with ASD were less accurate at detecting hazards that were social in nature i.e. contained a visible human figure (Sheppard, Ropar, Underwood & Van Loon, in press). Participants with ASD had longer response times for both kinds of hazard, but it was unclear whether this was due to slowness in perceiving the hazard or difficulties in making the response itself.

Objectives: This study used eye tracking to elucidate reasons for the slowness of those with ASD during a driving hazard perception task by determining when the hazardous object was first fixated by participants with and without ASD.

Methods: Eighteen males with HFA or AS, and 17 matched comparison participants viewed 20 video clips containing driving hazards. In half of the clips the cause of the hazard was a visible person (social), whilst in the other half the cause was a car (non-social). Participants were instructed to respond with a button-press as soon as they saw a hazard developing. They then identified the hazard verbally. Accuracy and timing of the responses was recorded. Participants' eye movements were recorded using a tobii portable eye-tracker.

Results: Participants with ASD correctly responded to as many hazards as comparison participants. However, they were less likely to anticipate the driving hazards, by responding prior to their onset ($U=91.5$, $N=35$, $p<.05$). Also, number of anticipatory responses correlated negatively with AQ score (Kendall's $tau\_b=-.45$, $N=35$, $p<.0005$).

Results of the eye tracking analyses will also be reported.

Conclusions: The results here support the notion that people with ASD have difficulty perceiving and detecting driving hazards, and that this difficulty may relate to strength of autistic traits (self-reported). Implications of the results of the eye tracking analyses will also be discussed. _

102.008 Self-Referential Gaze Judgements Are Impaired in Autism. M. McWhirr*[1], J. H. G. Williams[1], D. I. Perrett[2] and J. S. Lobmaier[3], (1)*University of Aberdeen*, (2)*University of St Andrews*, (3)*Universität Bern*

Background: Impaired social cue processing is characteristic of autism. Gaze direction is a vital social cue that can serve several purposes; direct gaze may signal communicative intent, whilst averted gaze directs an observer's attention to an object of mutual interest. Direct and averted gaze may be processed differently and one hypothesis is that impairment in gaze processing in autism is limited to direct gaze judgements. In typical development judgements of gaze direction are also influenced by the emotional expression of the face, such that happy faces are more likely to be judged as looking at the observer. This effect has not previously been tested in children with autism.

Objectives: This study disambiguated accuracy for geometric gaze discrimination from self-referential gaze discrimination in children with autism and assessed the influence of emotion expression on these judgements.

Methods: Participants were 22 children with autism and 21 age and IQ matched control children. Experiment 1 presented emotional face photographs at 2°, 4° and 6° deviations from direct gaze and required participants to judge if the face was averted to the left or right (geometric gaze judgement). Experiment 2 presented emotional face photographs at 0° (direct gaze) and 4° and required that participants judge if the face was 'looking at them' (self-referential gaze judgement).

Results:

Experiment 1: The main effect of gaze angle was statistically significant (F= 52.22, p< .01, ___=.56) indicating that as gaze angle increases, accuracy of gaze judgments also increase. A significant interaction between gaze angle and emotional expression was also present (F= 5.75, p< .01, ___=.12). No other main effects or interactions were significant, critically there was no main effect of Group, nor did Group interact with any of the within participant measures (all p>.05).

Experiment 2: The main effect of Group was statistically significant (F= 4.46, p<.05, ___= .10), and indicates that participants with autism made more errors than controls. The main effect of angle was also significant (F= 14.13, p<.01, ___= .26), however, this was qualified by a small but statistically significant interaction between emotional expression and gaze angle (F=3.18, p<.05, ___=.07). The interaction was investigated by testing the difference in accuracy between direct and averted gaze for each emotion. This was greater for happy emotional expressions than neutral emotional expressions (t=2.623, p<.05), and also shows a trend to be greater than fearful expressions (t=3.933, p= .06). There was no difference between neutral and fearful expressions (t=.06, p =.95).

Conclusions: Judgement of gaze direction is impaired in autism but this impairment is limited to self-referential gaze judgments and cannot be explained by a general weakness in gaze discrimination abilities. Furthermore, children with autism are equally as sensitive as controls to the affect of emotional expression on gaze direction judgements. We suggest that this impairment may be related to atypical development of the cognitive processes determining egocentrism in autism.

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103.001 Head Circumference Across the First Year of Life Correlates with a Positive Screen for Autism at Age 36 Months. M. Hornig*[1], M. Bresnahan[1], D. Hirtz[2] and A. B.C. Study Group[3], (1)*Columbia University*, (2)*National Institutes of Health*, (3)*Columbia University and Norwegian Institute of Public Health*

Background: Abnormal head size and growth patterns in early life are associated with a later diagnosis of autism or other neurodevelopmental disorders in some, but not all, studies. Accelerated growth of head circumference (HC), beginning after birth and plateauing before three years of age, is reported to be more common in autistic disorder, particularly in males, or in genetic overgrowth syndromes; however, microcephaly is also relatively frequent in subsets with other dysmorphic features, mental retardation and less male-predominant sex ratios. Although micro- and macrocephaly at birth are well-established harbingers of poor central nervous system outcomes, the clinical significance of abnormal head growth trajectories is less clear.

Objectives: Determine whether accelerated HC growth across the first year of life predicts screen-positivity at 36 months of age on the Social Communication Questionnaire (SCQ), an autism screening tool. Methods: The Autism Birth Cohort (ABC) is a subsample of a prospective pregnancy birth cohort in Norway (MoBa). Data for 29,093 children were available for this analysis. The SCQ was given at 36 months; scores ≥ 12 were defined as positive. The HC obtained at well-baby clinics at 6 weeks and 12 months of age were used to derive the first-year HC growth rate, defined as the difference between the two HC measures. HC growth rate was categorized as: slow (≤ 20^{th} percentile), normal (20^{th} through 80^{th} percentile), or accelerated (≥ 80^{th} percentile). Micro- and macrocephaly were defined as values ≤ or ≥ 2 SD of the ABC population mean at age 6 weeks or 12 months. We examined the relationship of early and late infancy HC abnormalities as well as first-year change in HC to SCQ-positivity using chi-square analyses.

Results: 1.1% screened positive on the SCQ. Average HC growth was 8.21 ± 1.1 cm. Microcephaly was more common in girls than boys at both measurement ages (6 weeks: 3.3 vs. 1.5%; 12 months: 2.6 vs 0.3%; both $p<0.0001$); macrocephaly showed a male-predominant pattern at both measurement points (6 weeks: 0.3% of girls vs 3.3% of boys; 12 months: 0.4 vs 4.8%; both $p<0.0001$). Neonatal microcephaly was more highly associated with SCQ-positivity at 36 months than macrocephaly in all children ($p<0.0001$); by 12 months of age, this pattern remained significant for boys ($p=0.003$) with a trend in the same direction for girls ($p=0.074$). None of the SCQ33-positive girls were macrocephalic at either measurement age. Accelerated HC growth predicted SCQ-positive scores in all children (1.2% of accelerated growth, vs. 0.9% of normal and 0.6% of slow growth children, $p=0.017$).

Conclusions: Head size and HC growth may be markers for autism risk. Pediatricians should carefully record values and screen at age 3 when indicated. Delineation of the mechanisms underlying abnormal head growth trajectories may also improve understanding of the pathogenesis of autism and related neurodevelopmental disorders.

Acknowledgments: Members of the ABC Study group include W. Ian Lipkin, Camilla Stoltenberg, Ezra Susser, Per Magnus, Deborah Hirtz, Mady Hornig, Michaeline Bresnahan, Synnve Schølberg, Ted Reichborn-Kjennerud and Pål Surén.

103.002 Association Between Ovulation Inducing Drug Use, Infertility, and Autism Spectrum Disorders in the Nurses' Health Study II. K. Lyall*[1], D. L. Pauls[2], S. L. Santangelo[2], D. Spiegelman[1] and A. Ascherio[1], (1)*Harvard School of Public Health*, (2)*Massachusetts General Hospital*

Background: An increasing number of women are utilizing fertility treatments, and the safety of these therapies has been studied with regard to a number of perinatal outcomes. However, the relationship between infertility, fertility treatments, and autism spectrum disorders remains understudied.

Objectives: To determine whether infertility and use of ovulation-inducing drugs are associated with risk of having a child with an autism spectrum disorder. Methods: We conducted a cohort study of participants from the Nurses Health Study II, a cohort of U.S. female nurses initiated to assess risk of cancer and other major diseases. Participants have reported their reproductive and medical history since 1989, and

disorders in their children in 2005. 3,985 cohort participants who had their first child between 1993 and 2003 and completed a questionnaire including information on autism spectrum disorder in 2005 were included in our analyses. Logistic regression was used to obtain odds ratios for having a child with autism spectrum disorder according to self-reported history of infertility and use of ovulation inducing drugs.

Results: The 111 mothers who reported a child with autism spectrum disorder reported both use of ovulation inducing drugs (34.2%) and infertility (46.8%) more commonly than the 3,874 comparison mothers (23.8 % and 32.6% respectively). After adjustment for pregnancy complications, maternal age, and other possible autism risk factors, the odds ratio comparing women reporting infertility and use of ovulation inducing drugs to those who reported neither was 1.91 (95% CI 1.20, 3.05; p =0.007). History of infertility was also significantly associated with autism spectrum disorders (OR=1.81, 95% CI 1.20, 2.72, p=0.005), though not when accounting for ovulation-inducing drug use (OR=1.58, 95% CI 0.89, 2.82). The odds ratio for autism spectrum disorder increased with the number of reports of use of ovulation inducing drugs (p for trend = 0.008).

Conclusions: These preliminary results suggest that maternal use of ovulation inducing drugs should be considered as a potential risk factor for autism spectrum disorders in future studies.

103.003 Diagnostic Prevalence of ASD in An Older Low Birth Weight Cohort. J. Pinto-Martin*[1], S. E. Levy[2], J. Feldman[3], A. Whitaker[3], J. Lorenz[3] and N. Paneth[4], (1)*University of Pennsylvania*, (2)*Children's Hospital of Philadelphia*, (3)*Columbia University Medical Center*, (4)*Michigan State University*

Background: Recent reports indicate that very young low birth weight (LBW) survivors are at higher risk of screening positive for ASD. Thus far, however, there have been no reports of the diagnostic prevalence of ASD in LBW populations. This presentation is a preliminary report of screening and diagnostic findings for ASD in a large LBW cohort assessed in adolescence and young adulthood.

Objectives: To determine the diagnostic prevalence of ASD in adult survivors of LBW .

Methods: 623 surviving members of a regional LBW cohort (<2000g; n = 1,105 births) , were screened for ASD at age 16 using the Social Communications Questionnaire (SCQ), the Autism Spectrum Screening Questionnaire (ASSQ), and parental report of professionals' diagnosis. Liberal cut-points on the SCQ (9) and ASSQ (12) were employed to maximize sensitivity 117 (18.8%) screened positive on at least one of the three screens.

201 of the screened participants were evaluated as young adults (mean age = 21.4) with the Autism Diagnostic Observation Schedule (ADOS) and/or Autism Diagnostic Interview-Revised (ADI-R) by research staff trained and certified on both instruments.

We were able to assess 65.8% (77/117) of young adults who had screened positive at 16 and 24.5% (124/506) of the negative screens. The two groups were comparable in gender distribution both at age 16 and in young adulthood.

Results: Of the 77 screen positives , 11 had ASD ; of the 124 screen negatives, 3 had ASD

To estimate the prevalence of ASD in the original sample of 16-year-olds (n= 623), the numbers of screen positives and negatives at 16 were weighted by the proportions of screen positives and negatives evaluated as young adults who were found to have ASD as shown in the table below:

ESTIMATED PREVALENCE OF ASD IN
BASED ON FINDINGS IN 201 SUBJECTS WITH DI

	ASD prevalence in young adults by screening status	Screening prevalence cohort
Screen positive	14.3% (11/77)	18.8% (11
Screen negative	2.4% (3/124)	71.2% (50
TOTAL	7.0% (14/201)	

Thus, the best estimate of the prevalence of ASD in this LBW population is 29/623 or 4.7%.

Conclusions: The diagnostic prevalence of ASD in this young adult LBW cohort is nearly five times the highest reported prevalence for the US general population . Previous

suggestions of increased risk for ASD in the LBW population were based either on case-control studies or prospective studies of ASD symptoms (not diagnoses) in very early childhood.

103.004 In Vitro Fertilization and Prematurity Are Prenatal Risk Factors Associated with Autism Spectrum Disorder but Not with Autism Severity. D. A. Zachor*[1], E. Lahat[1] and E. Ben Itzchak[2], (1)*Tel Aviv University / Assaf Harofeh Medical Center*, (2)*Ariel University Center of Samaria*

Background:

Little is understood about the causal mechanisms underlying autism spectrum disorders (ASD). Prenatal risk factors, including maternal obstetric characteristics, labor and delivery complications, and neonatal problems have all been associated significantly with autism.

Objectives:

1. To define the prevalence rates of in vitro fertilization (IVF) and prematurity in a cohort with ASD and compare them to the general Israeli population rates

2. To examine possible relationships between prenatal IVF and prematurity to autism severity, adaptive skills and developmental trajectories (regression/no regression)

Methods:

The study included 564 children who came to a tertiary autism center in Israel for a comprehensive evaluation. A pediatric neurologist obtained birth and developmental histories and performed a neurological examination. Evaluations of autism severity and of adaptive skills were performed using standardized tests [Autism Diagnosis Interview (ADI-R), Autism Diagnosis Observation Schedule (ADOS, the new ADOS severity scale and Vineland Adaptive Behavior Scales].

Results:

Of the 564 participants, 461 (81%) children, (M=39.8 months, SD=26.3) were diagnosed with ASD. IVF was present in 10.2% (47/438) which was significantly higher than the rate in the general Israeli population (3.5%) ($\_^2$=73.5, p<0.001). Maternal age (M=32.6y, SD=4.8) in the IVF group was significantly higher than in the non-IVF group (M=30.8y, SD=5.6) [F(1,425)=4.9, p<.05, h^2=.011]. Paternal ages in the two groups were not significantly different. There were no significant differences between the IVF and the non-IVF groups in mean age (months) at evaluation (M=43 vs 40), ADOS mean severity score (M=7.6, SD=1.7 vs 7.5, SD=2.1), mean Vineland composite scores (M=71.8, SD=11.2 vs M=71.9, SD=15.3), and history of regression [8/47 (17%) vs 99/381 (26%)].

Prematurity: Of the ASD cohort, the birthweight of 17/354 (4.8%) was below 1500 gr. (low birthweight=LBW), which was significantly higher than the 1% in the general Israeli population ($\_^2$= 37.3, p<0.001). There was no difference in the ADOS severity score between the LBW group (M=7.3, SD=2) and the >1500 gr. group (M=7.5, SD=2). The LBW group had significantly lower adaptive composite scores (M=62.3, SD=18.7) than the >1500 gr. group (M=72.1, SD=14) [F(1,264)=4.4, p<.05, h^2=.016]. When looking at the Vineland specific domains, the LBW group had significantly lower scores than the >1500 gr. group in daily living skills (DLS), socialization and motor scores (p<0.5).

Gestational age: Of 417 participants, 16 (3.8%) had gestational age (GA) <32 weeks. There was no difference in the ADOS severity score between GA <32 w (7.1, SD=1.9) and GA >32 w (M=7.5, SD=2.1). However, the GA <32 w had significantly lower adaptive composite scores (M=55.0, DS=1.9) than the GA >32 w (M=67.0, SD=9.6) [F(1,277)=12.9, p<.001, h^2=.044]. Specifically, the GA <32 w group had lower DLS and motor skills scores than the GA >32 w (p<0.01) but did not significantly differ in communication and socialization scores.

Conclusions:

Prevalence rates of IVF and LBW were significantly higher in the ASD cohort than in the general population, adding to previous reports on birth risk factors in autism. These

birth risk factors are not associated with autism severity and do not suggest a specific clinical subtype, but add to the severity of the child's general functioning.

103.005 The Sex-Specific Risk of Autism Spectrum Disorders Following Low Birth Weight. L. Hjort*[1], M. B. Lauritsen[2], P. Thorsen[3] and E. Parner[1], (1)*University of Aarhus*, (2)*Regional Centre for Child and Adolescent Psychiatry, Aarhus University Hospital*, (3)*Atlanta*

Background: In large epidemiological studies preterm birth, low birth weight (<2500g, LBW), and very low birth weight (<1500g, VLBW) have been associated with increased risks of autism. Recently, the risks of autism associated with preterm birth and LBW were shown to differ in autism subgroups defined by sex and the presence of other developmental disabilities. Objectives: To study the sex-specific risk of ASD in LBW groups in a population-based cohort study. Methods: From the Danish Medical Birth Register all live born children in Denmark from 1990 through 2003 were identified as the study population comprising a total of 931,770 children. Through linkage with the Danish Civil Registration System information on autism spectrum disorder (ASD) diagnoses (F84.0, F84.1, F84.5, F84.8, and F84.9 according to ICD-10) was retrieved from The Danish Psychiatric Central Register. By December 31, 2008, 7,536 children (6,138 boys and 1,398 girls) from the study population were diagnosed with ASD. Information on birth weight (BW) and important covariates were retrieved from the Danish Medical Birth Register. We assessed the sex-specific hazard ratios (HRs) of ASD in a low-normal BW group (2500g-2999g) and LBW groups (2000g-2499g,1500g-1999g, and <1500g) when compared to a reference BW group (3000g-3999g) using Cox regression. The HRs can be interpreted as relative risks, and is abbreviated RRs in the following. Results: Preliminary analyses stratified on sex show statistically significant increased RRs of ASD for the low-normal BW group (2500g-2999g) and the LBW groups (2000g-2499g,1500g-1999g, and <1500g) when compared to the reference BW group (3000g-3999g) for girls, with estimated RRs of 1.53 (95%CI 1.20, 1.94), 1.96 (95%CI 1.31, 2.91), 2.27 (95%CI 1.17, 4.44), and 2,51 (95%CI 1.11, 5.67) respectively. The trend of RRs increasing with decreasing BW for girls is highly statistically significant (p<0.001). Corresponding RRs of ASD for the low-normal BW group (2500g-2999g) and the LBW groups (2000g-2499g,1500g-1999g, and <1500g) when compared to the reference BW group (3000g-3999g) for boys were lower than for girls: 1.19 (95%CI 1.03, 1.36), 1.19 (95%CI 0.91, 1.55), 1.35 (95%CI 0.87, 2.10), and 1.93 (95%CI 1.10, 3.37), respectively. There was no statistically significant trend of increasing RRs with decreasing BW for boys (p=0.189). The provided estimates are adjusted for gestational age, apgar score, parity, multiples and birth year. Conclusions: VLBW is documented as a risk factor for ASD in both sexes, but for the other LBW groups (2000g-2499g,1500g-1999g) the estimated RRs for ASD are statistically significant for girls only. Further, a highly significant trend of increasing RRs of ASD with decreasing BW is documented in girls but not in boys.

103.006 Testing the Fractionable Autism Triad Hypothesis Further: Evidence From a General Population Twin Sample at Age 12. E. Robinson*[1], K. Koenen[1], M. McCormick[1], K. Munir[2], V. Hallett[3], F. Happe[3], R. Plomin[3] and A. Ronald[4], (1)*Harvard School of Public Health*, (2)*Children's Hospital Boston*, (3)*Institute of Psychiatry, King's College London*, (4)*Birkbeck College, University of London*

Background: Autism spectrum disorders (ASD) are highly heritable neurodevelopmental disorders. Twin studies have previously reported that autistic-like behaviors display high heritability in the general population. Moreover, recent evidence suggests that the core symptoms that define ASD: social impairments, communication impairments and restricted repetitive behaviors and interests (RRBIs), are caused by largely non-overlapping genetic influences. This study expanded upon previous research conducted using the Twin Early Development Study (TEDS), a longitudinal study of twins in the United Kingdom, to investigate these research questions in 12-year-old children.

Objectives: This study investigated for the first time the extent to which autistic-like traits in the general population are explained by genetic and environmental influences in

12-year-olds. The second set of analyses explored the etiological overlap between specific autistic traits (social impairments, communication impairments, and RRBIs) in extreme scoring individuals at age 12.

Methods: Parents of 5,900 12-year-old twin pairs completed the Childhood Asperger Syndrome Test (CAST), a population-based screening tool for autism spectrum disorders. Structural equation model fitting was conducted in the full sample to examine the extent to which genes and environment influence variation in autistic traits at age 12. DeFries-Fulker (DF) regression analysis was employed to examine the heritability of the total scale and subscales at the impaired extremes. A bivariate extension of DF analysis was used to analyze the degree of shared genetic etiology between specific autistic traits.

Results: In the full sample analysis, high heritability for autistic traits was found: 76% for males (95% CI 0.69-0.79) and 52% (95% CI 0.43-0.61) for females. The influence of the shared environment was significantly greater in females (26%, 95% CI 0.18-0.34) than in males (2%, 95% CI 0.005-0.09). In the extremes analyses, high heritability was found for the total scale and the individual subscales (0.67-0.80). Estimates of bivariate heritability (shared genetic influences between specific autistic traits) were modest overall, ranging from 0.31-0.53 for males and 0.10-0.28 for females.

Conclusions: Parent-rated autistic-like traits showed high heritability and modest shared environmental effects at age 12. Specific autistic-like traits -- social impairments, communication impairments, and RRBIs -- had partly non-overlapping genetic influences, which concurs with previous studies of younger children. These data support the notion that the autistic triad is largely fractionable and there may be symptom-specific causal influences underlying autistic traits. These findings also concur with recent molecular genetic findings that have related specific genes to specific aspects of the autism phenotype, and support further research into symptom-specific causal pathways relevant to ASD.

103.007 Maternal Infection During Pregnancy and Risk of Autism Spectrum Disorders. L. A. Croen* and Y. Qian, *Kaiser Permanente*

Background: Converging evidence points towards an immunologic component in an unknown proportion of children with autism. An initiating role for immune factors during the critical period of neurodevelopment has been suggested. Gestational exposure to viral infections has been associated with higher autism risk in a few previous studies.
Objectives: To investigate the association between maternal infection 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 in Kaiser Permanente Northern California (KPNC) hospitals. Cases (n=407) were children with an ASD diagnosis recorded in KPNC outpatient databases; controls (n=2075) were children without an ASD diagnosis, randomly sampled at a 5:1 ratio and frequency-matched to cases on sex, birth year, and birth hospital. Information on maternal infection during pregnancy was ascertained from KPNC clinical databases which document all diagnoses recorded by health care providers at every inpatient and outpatient encounter. Multivariable unconditional logistic regression analysis was conducted to estimate the risk of ASD associated with maternal infection during pregnancy. Separate models were run for all infections combined, and organism-specific infections (bacterial, viral, parasitic, and mycosal). For each exposure definition, we examined ASD risk associated with trimester of exposure. Risks associated with infections documented only during hospitalizations were also examined. Women with no inpatient or outpatient infection diagnoses for the entire pregnancy period were considered unexposed for all analyses.
Results: Nearly 50% of both case and control mothers had at least one diagnosed infection at some point during pregnancy (48.9% vs. 46.6%, P=0.4). After controlling for covariates (maternal race, age, education, parity, and plurality), the risk of delivering a child later diagnosed with an ASD was

somewhat higher for women with diagnosed bacterial infections (inpatient or outpatient) in the 2nd trimester (6.3% vs. 3.4%, P=0.04; OR_{adj}=1.9, 95% CI 1.0-3.7), and 3rd trimester (16.5% vs. 12.3%, P=0.07; OR_{adj}=1.5, 95% CI 1.0-2.2) of pregnancy. Mycosal infections during pregnancy were also associated with a borderline increased risk (13.3% vs. 9.5%, P=0.07; OR=1.5, 95% CI 1.0-2.3). The frequency of maternal viral infections anytime during pregnancy did not differ between cases and controls (17.1% vs. 14.9%, P=0.4; OR_{adj}=1.1, 95% CI 0.8-1.6). Women who were diagnosed with an infection during a hospitalization (inpatient only) in the 2nd trimester of pregnancy had a significantly increased risk of delivering a child who was subsequently diagnosed with an ASD (2.8% vs. 1%, P=0.03; OR=3.7, 95% CI 1.3-10.5). Inpatient diagnoses of maternal bacterial infections in the 2nd trimester occurred more often among cases than controls, but the difference was not statistically significant.
Conclusions: These results suggest that maternal infection in the second half of pregnancy, particularly bacterial infection, is associated with a modest increase in risk of having a child with an autism spectrum disorder. Possible pathogenic mechanisms include direct trans-placental infection of the fetus, hyperthermia, medications used to treat the infection, or the maternal inflammatory response. Additional studies are needed to clarify the underlying biology accounting for this observed association.

103.008 Maternal Smoking During Pregnancy and Prevalence of Autism Spectrum Disorders. A. E. Kalkbrenner*[1], J. L. Daniels[1], J. M. Braun[1], C. M. Cunniff[2], M. Durkin[3], L. C. Lee[4], J. Nicholas[5] and S. Pettygrove[6], (1)*University of North Carolina*, (2)*University of Arizona College of Medicine*, (3)*University of Wisconsin-Madison*, (4)*Johns Hopkins Bloomberg School of Public Health*, (5)*Medical University of South Carolina*, (6)*University of Arizona*

Background: *In utero* tobacco exposure has been associated with neurodevelopmental deficits such as behavior problems and intellectual disabilities and may therefore exert neurotoxic effects that contribute to the development of autism. Several European cohort studies have found an elevated prevalence of autism in children whose mothers smoked during pregnancy.
Objectives: We estimated the association between maternal smoking during pregnancy and prevalence of autism spectrum disorders (ASD) at age 8, using a large, population-based case-cohort design.
Methods: The study cohort included all children who resided at the time of birth in a county subsequently under surveillance for autism through the Autism and Developmental Disabilities Monitoring (ADDM) network. This included children born in 1992, 1994, 1996, and 1998 from select counties in Alabama, Arkansas, Colorado, Georgia, Illinois, Maryland, Missouri, New Jersey, North Carolina, Pennsylvania, South Carolina, and Wisconsin. Variables for this base population were obtained from publicly available natality files from the National Center for Health Statistics. All children from less populous counties (< 100,000) were excluded because vital statistics records for these counties lack geographic identifiers needed to select the cohort. Cases were defined as children from the base population who were identified by the ADDM surveillance network as having ASD in these same counties at age 8 years. ADDM is a multiple-source, active, records-based surveillance network that relies on documented behavioral symptoms in developmental records to determine whether a child meets standardized criteria for ASD based on the DSM-IV-TR. Information on maternal smoking during pregnancy was obtained from birth certificates. We estimated prevalence ratios of maternal smoking and ASD using logistic regression, adjusting for maternal age, race, education, and marital status.
Results: Of 591,639 total birth records meeting inclusion criteria with complete covariate data, 2663 were later identified as meeting ADDM criteria for ASD. About 13% of the total sample and 11% of ASD cases had a report of maternal smoking in pregnancy. We estimated an adjusted prevalence ratio of 0.9 with 95% confidence limits of 0.8-1.0.
Conclusions: Unlike previous reports, we did not find an association between maternal smoking in pregnancy and subsequent ASD. Strengths of this study include its large sample size using a population-based birth cohort, use of standard ASD diagnostic criteria, and ascertainment of maternal smoking prior to ASD diagnosis. Limitations include under ascertainment of maternal

smoking due to reliance on information from birth certificates, potential residual confounding due to social class, and inability to remove from the cohort denominator individuals who moved out of the study area after birth. Such children could not be identified as cases, introducing a potential selection bias if residential mobility is related to tobacco use. Further research is needed to determine the extent to which these limitations have contributed to the estimated lack of association between maternal smoking and ASD observed in this study or alternatively, whether maternal smoking during pregnancy does not contribute to ASD.

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104.001 A Randomized Trial: Group Cognitive Behavior Therapy for Children with High-Functioning Autism Spectrum Disorders and Anxiety. J. Reaven*[1], A. Blakeley-Smith[2], K. Culhane-Shelburne[2] and S. Hepburn[1], (1)*University of Colorado Denver School of Medicine*, (2)*JFK Partners, University of Colorado Denver School of Medicine*

Background: Children with high-functioning autism spectrum disorders (ASD) are at high risk for developing significant anxiety symptoms (Brereton et al. 2006). Anxiety problems can be especially "debilitating" for individuals with ASD (Greig & MacKay, 2005) by adversely impacting school performance, peer relationships, family functioning, and further exacerbating the core-deficits of ASD (Bellini, 2004; Sze & Wood, 2007). Cognitive-behavioral therapies (CBT) are frequently used for children with anxiety symptoms with good success (Walkup et al. 2008). In spite of the high co-occurrence between ASD and anxiety, most clinical trials examining the efficacy of CBT for children with anxiety, exclude children with pervasive developmental disorders (Barrett, Healy-Farrell, & March, 2004; Cobham, Dadds, & Spence, 1998; Walkup et al. 2008). However, recent treatment studies have demonstrated reductions in anxiety symptoms for children with ASD, following modified CBT interventions delivered in groups (Chalfant, Rapee, & Carroll, 2006; Reaven, et al., 2009) and individually (Wood, et al., 2008).
Objectives: To conduct a randomized trial of the treatment package by comparing Treatment As Usual (TAU) with parent and child participation in the 12 week CBT intervention specifically developed for children with ASD. Impact of the treatment package was primarily assessed by examining the reduction in severity of anxiety symptoms in children.
Methods: Forty-seven children ages 8-14 (and their parents) participated in the study and met the following inclusion criteria: 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; Silverman & Albano, 1998)), and 5) Verbal IQ of 80 or higher. Children and their parents were randomly assigned to either Active Treatment (AT) (N=22) or TAU (N=25). Key elements of the 12 week treatment included teaching cognitive strategies, somatic management of physical symptoms and use of graded exposure. An Independent Clinical Evaluator, blind to condition completed pre and post-assessments. Multiple outcome measures were used including the Clinical Global Impressions-Improvement Scale (CGI-I) derived from the ADIS-P and the Screen for Child Anxiety Related Disorders (SCARED; Birmaher et al. 1999). There were no pre-treatment differences on measures of IQ, age, autism severity and clinical anxiety symptoms.
Results: Child participants in both the TAU and AT groups presented with multiple psychiatric diagnoses in addition to their diagnosis of ASD. The number of co-morbid psychiatric diagnoses ranged from 2-8 (M = 5.13 and SD=1.48). Preliminary findings indicated that 75% of participants in the AT group demonstrated improvement in anxiety symptoms according to the CGI-I (e.g., a positive change in diagnostic status for 1 or more anxiety disorders) compared with 30.8% of children in the TAU group.
Conclusions: Initial results from this rigorously designed treatment study, suggests that a group CBT intervention specifically developed for children with ASD and complex psychopathology, may be effective in decreasing children's anxiety

symptoms. Limitations of this study include small sample size, as well as the lack of an attention control group.

104.002 Effectiveness of Cognitive-Behavioral Therapy for Children with Autism Spectrum Disorder and Anxiety. R. McNally Keehn*[1], M. Brown[1], D. Chavira[2] and A. J. Lincoln[1], (1)*Alliant International University*, (2)*University of California San Diego*

Background: Approximately 47 to 84 percent of children with autism spectrum disorder (ASD) experience clinically significant levels of anxiety (Gillott, Furniss, & Walter, 2001; Muris, Steerneman, Merckelbach, Holdrinet, & Meesters, 1998). Children with ASD may be at a greater risk for developing anxiety due to inhibited temperament, physiological hyperarousal (Bellini, 2006), and information processing biases (Happe & Frith, 2006). Despite the clear need for effective treatments for individuals with ASD and anxiety, few empirical studies exist. Cognitive-behavioral therapy (CBT) has been deemed the treatment of choice for typically developing children with anxiety disorders (Ollendick & King, 1998). Kendall and Hedtke's (2006) Coping Cat CBT program is among the most empirically supported and widely disseminated treatment programs for anxiety disorders in youth and has garnered the distinction of "probably efficacious" (Ollendick & King, 1998). A small body of literature has demonstrated growing support for the use of CBT to treat anxiety in children with ASD (e.g., Chalfant, Rapee, & Caroll, 2007; Sofronoff, Attwood, & Hinton, 2005) though no studies to date have evaluated the effectiveness of this treatment package for reducing anxious symptoms in children with ASD.

Objectives: The aim of this study was to evaluate the effectiveness of an empirically supported, individually-based cognitive-behavioral treatment for reducing anxious symptoms in children with ASD using a randomized controlled trial design.

Methods: Participants to date are twenty-two 7 – 14 year-old children with a diagnosis of ASD and clinically significant anxiety difficulties consistent with Separation Anxiety Disorder, Generalized Anxiety Disorder, or Social Phobia. ASD diagnoses were confirmed by the ADOS and ADI-R. Anxiety disorder classifications were confirmed using the Anxiety Disorders Interview Schedule – Parent Version (ADIS-P). All participants scored ≥ 70 on measures of intellectual and language abilities. Participants were randomly assigned to either 16 sessions of CBT (n=12) or a 16-week waitlist (n=10). Kendall and Hedke's (2006) sixteen-session Coping Cat program for anxious children was employed as the primary intervention. Outcome measures included ADIS-P Clinician Severity Ratings (CSR) made by independent evaluators blind to treatment condition, as well as parent and child ratings on the Multidimensional Anxiety Scale for Children (MASC) and Spence Children's Anxiety Scale (SCAS).

Results: Preliminary findings suggest that some children who completed a 16-session CBT program evidenced clinically significant reductions in anxiety symptoms as measured by diagnostic outcomes and parent and child ratings of anxiety symptoms. Reductions in specific symptoms of anxiety such as subjective physiological arousal, catastrophic thinking, and avoidance of feared stimuli were found in children who completed CBT treatment. Individual differences contributed to considerable variability in responses to the intervention. Comparative outcomes for participants in the CBT and waitlist groups will be presented.

Conclusions: Preliminary evidence suggests that the Coping Cat CBT program may be an effective treatment for reducing anxious symptoms in some children with ASD and anxiety. Specific adaptations for applying a manualized cognitive-behavioral treatment to children with ASD will be discussed.

104.003 Improving Social Responsivity and Friendship Skills for Adolescents with Autism Spectrum Disorders: A Review of the UCLA PEERS Program. E. Laugeson*[1], F. Frankel[1], A. Gantman[1], C. Mogil[1] and A. R. Dillon[2], (1)*UCLA Semel Institute for Neuroscience & Human Behavior*, (2)*Pacific Graduate School of Psychology*

Background:

Lack of social responsivity and impaired social skills have long been known to negatively impact the social functioning of adolescents with Autism Spectrum Disorders

(ASD), making it difficult for many of these youth to develop close reciprocal friendships. Yet very few evidence-based social skills interventions have been developed and tested to improve friendship skills for teens with ASD, representing a large gap in the ASD treatment literature.

Objectives:

This study examines change in social responsivity and social functioning following the implementation of an evidence-based parent-assisted social skills intervention known as PEERS. Change in skills related to developing friendships were measured for high-functioning middle school and high school adolescents with ASD. Maintenance of treatment gains at a 14-week follow-up assessment were also examined.

Methods:

Using a matched convenience sample, 28 participants were assigned to a treatment with follow-up or delayed treatment control condition. Participants attended weekly 90-minute small group sessions over a 14-week period. Skills were taught through didactic instruction using concrete rules and steps of social etiquette in conjunction with role-play demonstrations. Teens practiced newly learned skills during behavioral rehearsal exercises and parent-assisted weekly socialization homework assignments. Targeted friendship skills included: verbal and nonverbal communication; electronic communication and online safety; appropriate use of humor; expanding and developing friendship networks; peer entry and exiting strategies; good host/guest behavior during get-togethers with friends; good sportsmanship; methods for resolving peer conflict, including strategies for handling arguments and rumors/gossip; and strategies for handling rejection, including how to change a bad reputation and how to handle verbal teasing, physical bullying, or cyber bullying.

Results:

Major findings reveal that treatment participants, in comparison to delayed treatment control participants, significantly improved their social responsivity as measured by the Social Responsiveness Scale (SRS; $p < 0.01$) following the intervention. Increases in social awareness ($p < 0.05$), social cognition ($p < 0.05$), and social communication ($p < 0.01$) were observed. Results further suggest improved overall social skills on the Social Skills Rating System (SSRS; $p < 0.01$) following treatment. Improvements in cooperation ($p < 0.01$), assertion ($p < 0.05$), and responsibility ($p < 0.01$) were found. Data obtained at a 14-week follow-up assessment reveal that treatment gains were maintained on the SRS ($p < 0.01$) and the SSRS ($p < 0.01$), with further improvements in the areas of decreased problem behaviors ($p < 0.01$), decreased externalizing ($p < 0.01$), and increased self-control ($p < 0.01$).

Conclusions:

This research represents one of the few treatment intervention studies aimed at improving the friendship skills of adolescents with ASD. Findings suggest that PEERS, a parent-assisted manualized social skills intervention, is efficacious in improving the social responsivity and overall social skills needed to develop and enhance friendships for teens with ASD. Possibly due to active participation of parents in the intervention, treatment gains were maintained at a 14-week follow-up assessment, and in some areas were further improved.

104.004 Social Inclusion of Children with ASD at School: Effects of a Randomized Controlled Treatment Study. C. Kasari*, *University of California, Los Angeles*

Background: Positive peer interactions and friendships remain elusive or problematic for most children with ASD. Children with ASD are often observed as isolated or on the periphery of social networks in their school environment. While many children are in social skills groups, these are often off campus or in a clinic. Few interventions are conducted in the child's natural environment of school. Objectives: The main objective of this study was to compare the intervention effects of four child conditions (child- or peer-mediated, combined, or no intervention) on the peer relationships and social networks of

children with autism at school. A secondary objective was to examine the maintenance effects of the intervention over 3 months. Methods: Participants included 60 fully-included high functioning and ethnically diverse children with autism (54 male, 6 female) 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 and once again at a 12-week follow-up 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. Results: Children with autism who received the combined treatment group had the most improvement in their social network salience and these effects were maintained at follow-up for 36 children who did not switch classrooms, $F(1,28) = 0.24$, $p = 0.63$. In addition, there was a significant main effect of peer treatments, $F(1, 52) = 4.03$, $p<.05$ after controlling for baseline scores. Pairwise comparisons revealed that children with autism who received a treatment with a peer -mediated component had significantly higher social network salience (0.49 ± 0.04) compared to children with autism who did not receive a treatment with a peer-mediated component (0.34 ± 0.04). 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.

104.005 The Secret Agent Society: A Multimedia Curriculum for Enhancing the Social Skills of Children with Asperger's Disorder. R. B. Beaumont* and K. V. Sofronoff, *University of Queensland*

Background:

Social skill deficits lie at the heart of Asperger's Disorder and often contribute to peer rejection, academic underachievement, emotional disorders and a limited capacity for employment and independent living in adulthood. Despite the profound impact that social difficulties have on the lives of children with Asperger's Disorder, few evidence-based social skills programs have been developed for this population.

Objectives:

This study aimed to evaluate the efficacy of The Secret Agent Society: a new multi-systemic social skills program for children with Asperger's Disorder.

Methods:

Forty-nine child participants with Asperger's Disorder aged 7 _ to 11 years were randomly assigned to a treatment (n=26) or wait-list control (n=23) condition. Treatment participants attended weekly two hour group sessions over a seven week period and a booster session at six-week follow-up. Parents attended concurrent parent training sessions and teachers were forwarded weekly handouts.

Child sessions typically began with children playing a computer game that taught them skills in emotion recognition, emotion regulation and social interaction. In the game, the player assumes the role of a Junior Detective who completes a three-level course to become a mind-reading specialist. In level one, the player decodes how suspects feel from their facial expressions, body postures and voice tones. In level two, they calibrate scales to show how their own body signals the nature and intensity of their feelings. In level three, the user completes virtual reality missions that require detecting how characters feel in social scenarios such as being bullied, playing with others and trying a new activity, and choosing how to respond appropriately. The game teaches children about simple and complex emotions (e.g. embarrassment, teasing) and includes animated and human characters.

Participants spent the remainder of the child session time doing role-play activities to help them apply and extend on the skills they learned in the computer game. After each session, children were asked to do 'home missions' to practise using their social skills in real life. They recorded their progress on these missions in a computerised 'Secret Agent Journal' for review in the next session. Concurrent parent training sessions and weekly teacher handouts helped parents and teachers to support children in using their social skills in real life.

Results:

Relative to wait-list controls, program participants showed significantly greater improvements in social skills, as indicated by parent-report measures. Teacher-report data also suggested that treatment participants made significant improvements in social functioning from pre- to post-treatment. Child-based competency measures indicated that children in the treatment group knew more appropriate emotion-regulation strategies at post-intervention than at pre-intervention, whereas children in the control group did not. Parent-report data suggested that treatment gains were maintained at 5-months follow-up, with 76% of children improving from the clinical to normal range of social functioning.

Conclusions:

These results support the use of a multi-systemic approach to social skills training for children with Asperger's Disorder. Future research is needed to determine the effectiveness of the program in improving children's observable peer-interaction skills and peer relationships.

104.006 Learning through Interaction. D. Casenhiser*, S. Shanker and J. Stieben, *York Univeristy*

Background:
Behaviorist methods of treating autism which often focus on manipulating the contingencies of behaviors using so-called artificial reinforcers have lead some researchers and parents to criticize their inflexibility and one-size-fits-all approach to intervention (e.g., Fay, W.H. 1980, Prizant, Barry 1982).

Objectives:
We present a **randomized control trial** of the effectiveness of a therapy program based on the Developmental Individualized Relationship-Based (DIR) model of autism intervention that is distinguished from typical behaviorist programs by (1) employing no artificial reinforcement, and (2) solely using play-based social interaction as a vehicle for treatment.

Methods:
56 children ages 2;0 – 4;11 were recruited from the Toronto area. Children were previously diagnosed with an ASD and the diagnoses were confirmed via ADOS and ADI-r. Children were randomly selected for either treatment through the DIR-based program (DTx) or a community-based treatment program (CTx). Children in the DTx group met with therapists for 2 hours each week to receive hands-on training in the DIR-based method. Participants were assessed both prior to the onset of treatment and 12 months post treatment using a modified version of the Child Behavior Rating Scale (*m*CBRS) video-taped rating scale of 5 behaviors thought to be pivotal for development including attention to activity, enjoyment in interaction, cooperation, involvement, and initiation of joint attention (Mahoney, 1998). In addition, a standard language assessment was also administered to participants to determine whether the increase in social interaction skills was accompanied by an increase in language skills.

Results:
The results indicate that children in the DTx group displayed significantly more of the sorts of pivotal interaction behaviors that are associated with healthy development than did the community treatment group. Moreover, analysis of the scores obtained from the language assessments also revealed that the DTx group made significantly greater gains in the standardized language scores over the course of 12 months than did the CTx group. The associated effect sizes are clinically significant or near clinically significant (Wolf

1986) ranging from .47 to 1.01. These results are encouraging since they suggest that children are improving not only in basic interaction behaviors, but also in language skills as measured by standard language assessments. Finally, a regression analysis confirms the hypothesis that performance on the mCBRS was a significant predictor of change in language scores for this group of children diagnosed with an ASD.

Conclusions:
Children in the DTx group showed significantly greater enjoyment in interactions with their parents, were significantly more attentive and involved in interactions with their parents, initiated more joint attentional frames, and made significantly greater language gains. Along with the regression analysis, which suggests that children's performance on the *m*CBRS is a significant predictor of language change, these results support the hypothesis that children with autism can in fact learn through play-based social interaction (as do typical children) without the apparent need for so-called artificial reinforcers.

104.007 Type, Function, and Complexity of Language Gains in Young Children with Autism Spectrum Disorder Following Behavioral Intervention. C. Hoffman*[1], S. Dufek[2], M. Rocha[2], L. Schreibman[2], A. Stahmer[3], R. L. Koegel[4] and L. K. Koegel[4], (1)*UCSD Autism Research Program*, (2)*University of California, San Diego*, (3)*Rady Children's Hospital*, (4)*University of California, Santa Barbara*

Background: Qualitative impairment in communication is a hallmark feature of autism spectrum disorder (ASD; APA, 2000). Research has shown that behavioral intervention can improve communication ability for individuals with ASD, especially when given as part of an early intervention program (Rogers & Vismara, 2008). Two such behavioral interventions are the Picture Exchange Communication System (PECS) and Pivotal Response Training (PRT).

Objectives: This study was designed to examine the type, function, and complexity of language gains in young children with ASD following an early intervention program consisting of PECS and PRT.

Methods: Thirty-eight children diagnosed with ASD (aged 20-45 months) were randomly assigned to one of two treatment conditions (PECS or PRT). All children had fewer than 10 functional words at intake. All children received 258 hours of intervention across approximately 6 months. A 25-minute Structured Laboratory Observation (SLO) was administered at pre-and post-treatment, consisting of a semi-structured play session where the primary caregiver tried to elicit different child behaviors, one of which was language. Trained undergraduate research assistants blind to the study purpose coded the SLOs for child language behaviors. The Type (spontaneous, cued, or imitated), Function (request, comment, question/answer, or other), and Complexity (vocalization, one-word, or word combination) of language used by the children at pre- and post-treatment were coded.

Results: To date, fourteen children have been coded for preliminary analyses. Paired-sample t-tests were utilized to examine change from pre- to post- treatment for all language behaviors. All Types of Language significantly increased from pre- to post-treatment: spontaneous (pre M = 0.86, post M = 10.00; t = -2.34, p = 0.04), cued (pre M = 17.71, post M = 37.57; t = -3.20, p = 0.01), and imitated (pre M = 0.79, post M = 12.36; t = -3.79, p = 0.00). Regarding Function of Language used: requesting significantly increased from pre- to post-treatment (pre M = 16.07, post M = 45.79; t = -5.05, p = 0.00). Commenting, question/answer, and other increased from pre- to post-treatment but these changes were not significant. All Complexities of Language significantly increased from pre- to post-treatment: vocalizations (pre M = 18.64, post M = 34.57; t = -2.43, p = 0.03), one-words (pre M = 0.79, post M = 19.50; t = -2.55, p = 0.02), and word combinations (pre M = 0.07, post M = 5.71; t = -2.24, p = 0.04).

Conclusions: Early intervention programs targeting communication are helpful at increasing spontaneous, cued, and imitated language skills in children with risk for autism. In addition, children can be expected to increase the complexity of their language

use. However, the communication skills the children gained were primarily used to request items or activities rather than to share information through commenting or responding to questions. This highlights the need to focus on social aspect of language development in early intervention. In addition, language gains varied greatly among participants. Heterogeneity in language gains will be discussed and recommendations to address language skills that did not change will be provided.

104.008 Using the Tools of the Trade: The ADOS as a Measure of Treatment Change. S. Dufek*[1], C. Corsello[2], N. Akshoomoff[1], L. Schreibman[1], A. Stahmer[3], R. L. Koegel[4] and L. K. Koegel[4], (1)*University of California, San Diego*, (2)*Rady Children's Hospital - San Diego*, (3)*Rady Children's Hospital*, (4)*University of California, Santa Barbara*

Background: One of the most complicated issues involved in autism intervention research is how to measure outcome. The majority of studies measure outcome by changes in scores on intelligence tests, educational placement and services, adaptive scores, or language abilities (Rogers & Vismara, 2008; Legoff & Sherman, 2006; Kasari et al., 2008). Relatively few studies address changes in autism specific behaviors (Wolery & Garfinkle, 2002). Some have looked at changes in overall scores on standardized diagnostic measures, most often the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000; Aldred et al., 2004; Owley et al., 2001; Gutstein et al., 2007). However, research on how well these instruments measure change has not yet been undertaken.

Objectives: This study was designed to evaluate whether ADOS scores could be used as a measure of change in young children with autism following a behavioral intervention.

Methods: Thirty-two nonverbal children diagnosed with autism were randomly assigned to one of two treatment conditions (PECS or PRT). Each child had a comprehensive evaluation prior to and following treatment that included Module 1 of the ADOS, the Mullen Scales of Early Learning (Mullen, 1995) and the Vineland Adaptive Behavior Scales (Sparrow et al., 1984). All ADOS videotapes were coded by one of the authors of this study after establishing inter-rater agreement of 80% or better including distinguishing between codes of '2' and '3'.

Results: Repeated measures univariate analyses of variance revealed that revised algorithm total scores decreased pre (M=21.28) to post treatment (M=19.03), with a small effect size (eta squared = .25). However, severity scores did not show a significant change pre to post treatment, with only six children showing a reduction in score of more than one and only one child moving to a less severe diagnostic classification. Adjusted total scores that included all ADOS items as well as codes of '3' and the substitution of a '4' in place of '8' resulted in a significant difference from pre (M= 50.81) to post treatment (M= 40.81), with a moderate effect size (eta = .5). There were significant differences between pre and post-treatment adjusted scores for the communication, social, and play domains. There was no difference in adjusted total scores between treatment conditions. Six items in Module 1 of the ADOS, distributed among the domains, demonstrated significant changes in scores from pre to post treatment. Three of these items were from the social domain (Giving, Response to Joint Attention, and Quality of Social Overtures) one from the communication domain (Use of other's body to communicate) and one was from the play domain (Imagination/creativity).

Conclusions: ADOS scores are a possible measure of treatment change; however, diagnostic classification scores including algorithm totals and severity scores may not be the best measure of treatment change. Scores that allow for a greater range that include more items and more score possibilities within items may lead to a more robust measure of change. Items that showed change may provide information on how to improve the ADOS as a measure of treatment change.

105 Autism Symptoms

105.001 1 Exploration of the Activities of Others Predicts Social and Cognitive Deficits in Toddlers with ASD. F. Shic*[1], J.

Bradshaw[1], A. Klin[1], B. Scassellati[2] and K. Chawarska[1], (1)*Yale University School of Medicine*, (2)*Yale University*

Background: Monitoring the activities of others is an early-developing skill crucial for learning by observation. Previous work in our lab has shown that toddlers with ASD monitor the activities of others to a lesser extent than chronologically age-matched typically-developing (TD) toddlers. However, the nature of this limited attention towards activities in terms of social and cognitive factors, as well as the relationship of activity monitoring to social dynamics more generally, are not fully understood.
Objectives: In this study we link atypical activity monitoring with social and cognitive deficits in toddlers with ASD and, by comparison with a cognitively matched group of children with developmental delays (DD), show that the results are not completely described by cognitive deficits. We further examine dynamic changes in scanning patterns in response to the ongoing social exchange in order to clarify the nature of limited attention to activities.
Methods: Subjects were toddlers with ASD (N=28, M=20.7 months), other developmental delays (DD) (N=16, M=19.3 months), and typical development (TD) (N=34, M=19.6 months). Participants were presented with a 30s video of an adult-child play interaction which centered on the assembly of a puzzle. Eye-tracking was used to measure attention towards activities (the area of shared focus of people in the scene), people, and the background (room elements as well as scattered toys).
Results: ASD toddlers monitored activities (M=35.5%, SD=21.8%) less than both DD (M=50.5%, SD=24.7%) and TD controls (M=54.6%, SD=13.8%), $F(2,77)=7.8$, $p< .01$, diverting their attention towards the background (ASD: M=29.8%, SD=20.9%; DD: M=17.2%, SD=10.6%; TD: M=16.7%, SD=9.6%; $F(2,77)=6.9$, $p<.01$). No differences in looking at people were found. In ASD, more activity monitoring was associated with less severe social impairment ($r=-.39$, $p<.05$) and higher verbal ($r=.56$, $p<.01$) and nonverbal ($r=.63$, $p<.001$) functioning. A temporal analysis examining attention to the scene in three consecutive temporal sections found that DD and TD toddlers modulated attention towards activities in response to changing scene content ($p<.05$, $p<.01$ respectively), whereas ASD toddlers did not ($p=.93$). A measure of the responsiveness of ASD toddlers to these dynamics correlated with social deficits independent of both verbal and nonverbal cognitive functioning ($r=-.44$, $p<.05$).
Conclusions: Infants with ASD show less attention towards the activities of others, limiting their ability to learn about and participate in typical social play. In addition, both TD and DD toddlers respond to the subtle evolution of the social exchange by modulating their attention to scene components, whereas ASD toddlers did not. These results suggest that, from an early age, children with ASD visually explore the social activities of others in an atypical fashion, and that the extent of these atypicalities may either reflect or contribute to the emergence of autism-specific psychopathology. Furthermore, limited attention towards the activities of others in ASD may be linked to decreased exploration induced by limited response to the social dynamics of the interactions of others.

105.002 2 Relationship Between Sensory Over-Responsivity and Anxiety in Young Children with Autism Spectrum Disorders:.
S. A. Green*[1], A. Ben-Sasson[2] and A. S. Carter[3], (1)*University of California, Los Angeles*, (2)*University of Haifa*, (3)*University of Massachusetts Boston*

Background: Anxiety disorders are extremely common in children with autism spectrum disorders (ASD), and can increase the functional impairment of these children (Lainhart, 1999), with rates two to three times as high as in the general population (Sukhodolsky et al., 2008). Sensory over-responsivity (SOR) is another common, and impairing feature found in more than half of children with ASD, and SOR has been linked to anxiety in children with ASD (Ben-Sasson, Cermak, Orsmond, Tager-Flusberg, Kadlec, & Carter, 2008; Liss, Saulnier, Fein, & Kinsborne, 2006; Pfeiffer, Kinnealey, & Herzberg, 2005). While there is some evidence that anxiety and SOR are associated in children with ASD, it is unclear what reciprocal patterns of influence (if any) exist between the two. A greater understanding of patterns of influence over time has direct implications for etiological

study and intervention choices in this population.

Objectives: The purpose of this investigation was to gain a better understanding of associations between anxiety and SOR in children with ASD by examining the extent to which anxiety predicted changes in SOR and vice versa in young children with ASD.

Methods: Participants were 149 toddlers with an ASD diagnosis who were between 18 and 33 months at initial assessment, and between 28 and 50 months at a follow-up assessment approximately 1 year later. Anxiety and sensory sensitivity (SOR) were assessed by mother's report on the Infant-Toddler Social and Emotional Assessment (ITSEA) at both time points. Autism symptoms were assessed at time 1 using a combined social-communication score on the Autism Diagnostic Observation Schedule (ADOS).

Results: Anxiety and SOR were significantly correlated at time 1 ($r=.52$, $p<.001$) and time 2 ($r=.60$, $p<.001$). Mean anxiety scores increased from time 1 ($M=.31$, $SD=.24$) to time 2 ($M=.35$, $SD=.30$), $t(148) = -3.00$, $p=.003$. However, mean SOR scores were stable from time 1 ($M=.53$, $SD=.43$) to time 2 ($M=.57$, $SD=.43$), $t(148) = -1.10$, $p=.275$. Cross-lagged panel analyses were conducted in Mplus to compare the two pathways (SOR to anxiety and vice versa) controlling for the autocorrelation within measure. Time 1 child age and autism severity as measured by the ADOS social-communication score were entered as covariates. Results indicated a significant cross-lagged effect between time 1 SOR and time 2 anxiety after controlling for time 1 anxiety, child age, and autism severity ($B=0.13$, $SE = .05$, $p=.01$). The reciprocal cross-lagged effect from time 1 anxiety to time 2 SOR was not significant ($B=.19$, $SE=.14$, $p=.18$).

Conclusions: The presence of SOR appears to contribute to changes in anxiety, which overall increased in this group of children with ASD. In contrast, the early presence of anxiety does not appear to contribute to changes in SOR, which was quite stable. These results support SOR as a possible contributor to anxiety in children with ASD. Implications for further study of the etiology of affective disorders and intervention choices in this population will be discussed.

105.004 4 Effect of Context On Face Exploration in 12-Month-Old Infants Later Diagnosed with ASD. K. Chawarska* and F. Shic, *Yale University School of Medicine*

Background: A recent study suggests that 2- and 4-year-old children with ASD show atypical distribution of attention to facial features and that their scanning pattern becomes more abnormal with age (Chawarska & Shic, 2009). In response to novel static faces children with ASD show a restricted scanning pattern, which appears to hamper their ability to effectively encode facial identity information. Moreover, older children with ASD show a decline in attention to key facial features compared to younger affected children, which suggests that face processing might become more abnormal with age. It is not clear, however, when the atypical scanning patterns begin to manifest in ASD.
Objectives: We examined (1) whether face scanning abnormalities are present in 12-month old infants later diagnosed with ASD; and (2) whether the infants are sensitive to the context in which faces are presented and adjust their scanning strategies accordingly.
Methods: We compared performance on face scanning tasks of 10 infants later diagnosed with ASD with 26 typically developing (TD) infants. All infants participated in a prospective study of children at high and low genetic risk for ASD. They were tested at 12 months ($M=12.29$, $SD=.40$) and their provisional diagnostic status was ascertained at 24 months. Infants were presented with three 20s clips: (1) a static image of a neutral face (Static); (2) a video of a person smiling (Affect); (3) a video of a person reciting a nursery rhyme (Speech). Scanning patterns were recorded with an eye-tracker.
Results: Infants in both groups modulated their attention to eye and mouth regions depending on context, spending more time looking at the eyes in the Static and Affect conditions than in the Speech condition. This pattern was reversed for the mouth region. No significant differences between groups were found in Static and Affect conditions; however, in the Speech condition, infants

later diagnosed with ASD exhibited enhanced attention to the mouth ($F(1, 33) = 5.88$, $p<.021$), and marginally suppressed attention to the eyes ($F(1, 33) = 3.39$, $p < .075$) compared to typical peers. Conclusions: Preliminary analysis suggests that 12-month-old infants later diagnosed with ASD show elementary sensitivity to the context in which faces are presented and adjust their scanning strategy accordingly. That is, they spent more time looking at the eyes in the conditions when faces are either static or dynamic/affective but devoid of speech. However, when viewing face of a speaker, their pattern of scanning becomes exaggerated compared to TD controls and they monitor the mouth more frequently. Proportional decrease in attention to eyes was also noted but was not statistically significant. The pattern of results in the Speech condition replicates and extends findings reported by Jones, Carr, & Klin, 2009 in 2-year-olds with ASD, suggesting that excessive focus on the mouth is condition specific. Factors that might contribute to the enhanced attention to mouth in the speech condition might include increased sensitivity to audiovisual contingencies (Klin, et al., 2009) or employment of a compensatory lip reading strategy in children with difficulties in language acquisition.

105.005 5 Improving Motivation During Academics in Young Children with Autism. A. K. Singh*, *University of California, Santa Barbara*

Background: Active participation in academics is important. However, many children with ASD show little interest in academic tasks and exhibit disruptive behavior when tasks are presented. Previous research demonstrates, incorporating motivational components (e.g., choice, interspersal of maintenance tasks, and natural reinforcers) in interventions leads to improvements in symptoms of autism. These motivational strategies may also be effective in improving academic performance.

Objectives: The purpose of this study was to assess whether motivational variables could be employed to improve performance in academic tasks. Specifically, we assessed whether these variables would improve writing and math performance, interest in academic activities, and decrease disruptive behavior.

Methods: Four children (4 to 7 years old) with ASD were selected for participation in this study. A non-concurrent multiple baseline across participants and behaviors design was used. During the intervention, the adult presented a writing or math activity and asked the child to complete the task in order to earn a child chosen reinforcer. Additionally, the adult provided choices of the materials that could be used and the choice of the setting where the task could be carried out. The reinforcer was embedded within the task to provide a natural reward, and easy tasks were interspersed with more difficult tasks. For example, in the writing intervention, the adult could offer a choice between writing implements (e.g., pen or pencil) and/or where to sit (e.g., floor or table). After the child made choices, the adult presented the demand paired with the contingency for natural reinforcement (e.g., "Write some sentences about playing outside, and after you're done, you can play outside.")

Results: For all participants, the latency to complete academic demands decreased following intervention and remained low during follow-up. Similarly, all participants had low rates of academic task completion during baseline but showed increases during intervention. Finally, each child engaged in high levels of disruptive behavior during all academic tasks in baseline and, following intervention, disruptive behavior decreased immediately and remained low through follow-up. Effect size (Cohen's d) was calculated for all dependent measures for all children using the standard mean difference method. The results for all children on all academic tasks yielded large effect sizes.

Conclusions: Results indicated that the intervention decreased the children's latency to begin academic tasks, improved their rate of performance and interest, and decreased their disruptive behavior. Theoretical and applied implications are discussed.

105.006 6 Sensory Modulation and Affective Disorders in Children with Asperger's Disorder. B. Pfeiffer*, *Temple University*

Background: Sensory processing issues have been identified by numerous researchers as prevalent in individuals with Asperger's Disorder (Baranek & Berkson, 1994; Dawson & Lewy, 1989)). In particular, individuals with Asperger's Disorder frequently demonstrate sensory modulation disorders resulting in hypo or hypersensitive responses to sensory stimuli (Ornitz, 1989). Affective disorders such as depression and anxiety have been theorized to have a relationship with sensory hyposensitivity and hypersensitivity. (Johnson, 1975; Neal, Edelmann, & Glachan, 2002). Similar central nervous system arousal levels are associated with both sensory modulation and affective disorders. It is speculated that depression and sensory hyposensitivity are associated with low levels of arousal while anxiety and sensory defensiveness are associated with high levels of arousal (Johnson, 1975; Lane, 2002). Both depression and anxiety are considered comorbid conditions with Asperger's Disorder. Along with clarifying the relationships between sensory modulation and affective disorders in children and adolescents with Asperger's Disorder, understanding the impact of these relationships on adaptive behavior is essential for diagnosis, evaluation and intervention.

Objectives: The purpose of the study was to determine if there were significant relationships between dysfunction in sensory modulation, affective disorders, and adaptive behaviors in children and adolescents between the ages of 6 and 17.

Methods: Parents of 46 children and adolescents between the ages of 6 and 17 diagnosed with Asperger's Disorder based on the DSM-IV-TM criteria completed the a) Sensory Profile or the Adolescent/Adult Sensory Profile b) the Adaptive Behavior Assessment System c) Revised Children's Manifest Anxiety Scale (Adapted); and d) the Children's Depression Inventory (Adapted). Descriptive statistics and the Pearson product-moment coefficient of correlation calculations were used for data analysis.

Results: There were statistically significant positive correlations between anxiety and sensory defensiveness (r = .270, p = .035) in the total group and depression and sensory hyposensitivity in only the older group (r = .461, p = .024). There was an inverse significant relationship between depression and the total adaptive behaviors score (r = -.256, p = .043) and specific inverse relationships with the adaptive behaviors of functional academics, leisure and social skills. The relationship between anxiety and adaptive behaviors was not significant (r = -.121, p = .212) although there was a significant inverse relationship between sensory defensiveness and adaptive behaviors (r = -.254, p = .044). The relationship between hyposensitivity and adaptive behaviors approached significance (r = -.214, p = .077).

Conclusions: The data supports relationships between anxiety and sensory defensiveness in all age ranges and the relationship between depression and hyposensitivity in older children. A temporal relationship between anxiety and depression may explain the developmental nature of the results. Depression and sensory defensiveness demonstrated significant inverse relationships with overall adaptive behavior functioning. Evaluations and interventions need to address these relationships when treating children with Asperger Disorder.

105.007 7 Early Sensory Over-Responsivity and Affective Symptoms of Children with ASD and Later Family Impairment. A. Ben-Sasson*[1], F. Martínez-Pedraza[2] and A. S. Carter[2], (1)*University of Haifa*, (2)*University of Massachusetts Boston*

Background: Sensory over-responsivity (SOR) greatly influences family members by requiring them to adapt their routines, social activities, and home environment to meet their child's sensory needs (Werner-DeGrace, 2004). In addition, children with ASD often show internalizing and externalizing symptoms that impact parental emotional well-being as well (Davis & Carter, 2008; Hastings et al., 2005; Lecavalier, et al., 2006). Affective symptoms are often challenging to differentiate from SOR (Ben-Sasson et al., 2007). Identifying child factors that are associated with greater parental stress and family life restrictions is important

for service planning and in justifying early intervention to address such factors.

Objectives: Using family life as a measure of impairment, this study sought to examine the unique contribution of early SOR symptoms in children with ASD to later family life impairment above and beyond internalizing (i.e., anxiety and separation distress) and externalizing symptoms.

Methods: Findings are based on a longitudinal sample of young children with ASD (78% boys) with a mean age of 28 months at baseline, 40 months at 12-month follow-up (n = 156), and 53 months at 24-month follow-up (n = 88). Among other measures mothers completed the Infant Toddler Social Emotional Assessment (ITSEA; Carter & Briggs-Gowan, 2003), Infant Toddler Sensory Profile (ITSP; Dunn, 2002), Parenting Stress Index (PSI; Abidin, 1995), and the Family Life Impairment Scale (FLIS; Briggs-Gowan, 1997).

Results:

1. Children with (n=52) versus without (n=32) elevated SOR at baseline (more than 1*SD* above norms) showed higher family life impairment and parenting stress scores at both 12- and 24-month follow ups, which were not significantly influenced by child internalizing and externalizing symptoms at baseline.

2. In a model in which child social-communication symptom severity (step 1), and externalizing symptoms and internalizing symptoms (step 2) were entered, SOR at time 1 uniquely explained an additional 9% of the variance in family impairment at time 2 and 4% of the variance at time 3. Externalizing symptoms also significantly predicted family impairment at time 3.

3. SOR at time 1 also accounted for an additional 12% and 5% of the variance in parenting stress at times 2 and 3, respectively, after controlling for baseline scores on social-communication symptom severity (step 1), and child externalizing and internalizing symptoms (step 2). Affective symptoms did not predict parenting stress.

Conclusions: Findings support the independent impairing nature of SOR in the lives of children with ASD and their families over time above affective symptoms. This study suggests the need for early identification of SOR as a potential risk factor for family distress and for informing interventions that aim to minimize impairment in families of young children with ASD and SOR.

105.008 8 Intersensory Processing and Social Orienting in Children with Autism Spectrum Disorders: Integrating Typical and Atypical Development. J. T. Todd* and L. E. Bahrick, *Florida International University*

Background: Children with autism spectrum disorders (ASD) show altered intersensory processing and impairments in social orienting (Bebko et al., 2006; Dawson et al., 2004; Newell et al., 2007). Compared to nonsocial events, social events are more variable, complex, and provide an extraordinary amount of intersensory redundancy (e.g., synchrony, rhythm, and intensity changes invariant across the senses). Further, intersensory redundancy is highly salient and organizes the typical development of attention and perception in infancy (Bahrick & Lickliter, 2002). We hypothesize that the salience of intersensory redundancy plays a fundamental role in the emergence of social orienting across infancy and that an early disturbance of intersensory processing may lead to reduced social attention in ASD.

Objectives: Little is known about how social orienting emerges in typical development. Our aims are to investigate the emergence of social attention in typically developing (TD) infants, characterize atypical social attention in children with ASD, and evaluate the role of intersensory information. Our goal is to begin to bridge the gap between knowledge of typical and atypical development of social attention.

Methods: First, to examine the typical emergence of social orienting and the role of

intersensory redundancy, we evaluated cross-sectional data from 703 TD 2- to 8- month-old infants. We assessed attention maintenance and disengagement to films of social vs. nonsocial events providing intersensory redundancy (audiovisual synchrony) or no redundancy (unimodal visual, silent).

Second, to assess intersensory processing and attention in ASD, data from 2 to 5 year old children with ASD, developmental delays (DD), and TD were collected using our Behavioral Attention Assessment Protocol (BAAP; Newell et al., 2007). Children received trials of a central stimulus followed by two side-by-side peripheral events in blocks of social neutral, social positive, and nonsocial events. One peripheral event was synchronous with the natural soundtrack and the other was out of synchrony. Intersensory audiovisual matching, attention maintenance and disengagement were evaluated.

Results: TD infants showed a gradual emergence of enhanced attention to social events across infancy as a function of intersensory redundancy. Attention to audiovisual social events was maintained across age, while attention to all other events decreased with age.

Children with ASD showed impaired intersensory processing with no audiovisual matching for social or nonsocial events. In contrast, TD and DD children showed significant audiovisual matching for social events and TD children also matched nonsocial events. Further, children with ASD showed reduced attention maintenance and impaired disengagement to look to social events, but no difference for nonsocial events.

Conclusions: Collectively, these findings confirm growing reports of intersensory processing deficits and greater attention impairments for social than nonsocial events in ASD. Our findings also reveal new information indicating that social orienting emerges gradually across infancy as a function of intersensory redundancy. Together, these findings are consistent with the view that an intersensory processing disturbance in early infancy could lead to a failure of social events to become selectively salient and in turn to cascading effects across development including decreased social attention, impaired joint attention, language, and communication, consistent with impairments in ASD.

105 Communication

105.009 9 Autism and Music Therapy: Time, Rhythm and Music in Intersubiectivity Relationship. F. Suvini*, A. Narzisi, M. Innocenti, M. Venturi and U. Caselli, *AGRABAH - Associazione Genitori per l'Autismo*

Background: To explore the effect of music therapy in individuals with autism spectrum disorder

Objectives: This work aims to underline the relevance of the motivation to change which can be offered to the autistic children from the rhythmical and musical relationship in the context of the habilitation work.

Methods: At the Centre for Pervasive Disturbances of Development videos will be recorded during the individual setting of music therapy which will be then subject to microanalysis by expert personnel.

Results: Recent publications on mirror neurons and studies by the Infant Research highlight the difficulties experienced by autistic children when they are asked to make imitative processes or in understanding the intentions of people who interact with them. Studies investigating the dynamics of proto-conversations and music play with children clarify how music, rhythmic as well as prosodic elements may improve the expressive and emotional quality of the inter-subject relationship. Repetition in music is never repeating the same thing, it organizes variable and predictable dynamic moments. Heart beat and breathing are essentially a continuous repetition and variation: human beings base their existence biologically and psychologically on musical and rhythmical elements. Repetition and variation cause directionality in the perception of time, present time acquires a meaning because it is generated by a past which has just passed, instantly remembered, and which anticipates the forthcoming future. Repetitions and variations, considered from

the musical point of view, invite to play with time and sounds, remembering and anticipating: the pleasantness of coming back, the surprise of the unknown, the feeling that the future cannot be known and that the same moment can repeat itself or melt with another one. Therefore rhythm and repetition create moments of tension and relaxation connected to moments of waiting or frustration for un unfulfilled desire - which provoke an extremely intense and dynamic mental.

Conclusions: The music improvisation, the sonorous stimuli and vocal play may contribute to the understanding of the intentions and the shared significance.

105.010 10 Early Red Flags for Autism Spectrum Disorders in Toddlers in the Home Environment. L. Book*, D. McCoy and A. M. Wetherby, *Florida State University*

Background: Early detection of autism spectrum disorders (ASD) is crucial to optimizing child and family outcomes. Most research on early diagnostic features of ASD has been in clinical environments. Observation of behaviors of young children in their home environment is a possible way to assist in earlier diagnosis in a less time consuming, less stressful, and more cost-effective manner for families. Therefore there is a need for research on diagnostic features displayed in natural environments.

Objectives: The primary purpose of this study was to explore and quantify red flags for ASD in the behaviors of young children demonstrated in the home environment.

Methods: Participants were recruited from the ongoing longitudinal, prospective study of the FIRST WORDS® Project. The children in this study (N = 60) were between 17 and 36 months of age when a diagnosis of ASD (n = 45) or developmental delay in which ASD was ruled out (DD; n = 15) was made, based on a battery including the Autism Diagnostic Observation Schedule (ADOS; Lord, Rutter, DiLavore, & Risi, 2002). Measures on the Systematic Observation of Red Flags for Autism Spectrum Disorders in Young Children at Home (SORF-Home; Wetherby & Woods, 2009) were coded from video-recorded home observations of the child interacting with a parent or caregiver during everyday activities for up to sixty minutes.

Results: Overall, the results of this study demonstrated that early red flags of ASD were evident in the home environment. Seven of the red flags previously identified in the clinical environment were demonstrated by a majority of children during the home observations—lack of warm, joyful expression with directed gaze; lack of coordination of gaze, facial expression, gestures and sounds; lack of response to name; lack of communicative vocalizations with consonants; inappropriate eye gaze; lack of response to contextual cues; and lack of sharing interest or enjoyment. Examination of the relationship between the early red flags and developmental level revealed no significant correlations between the red flags and nonverbal cognitive developmental level and medium to large negative significant correlations between some red flags and verbal developmental level. Significant correlations were observed between many of the early red flags and composite scores on the ADOS. No significant correlations were observed between measures of parent report of red flags and the early red flags measured in the home environment.

Conclusions: The results of this exploratory study extend knowledge on the nature of red flags for ASD in young children to the home environment which adds valuable information for both practicing clinicians and families. The findings offer important implications for understanding how early red flags of ASD can vary across home and clinical environments and for building consensus with families on early signs of ASD.

105.011 11 Factor Analysis of the Social-Communication Items From the PIA-CV. J. H. Foss-Feig*[1], A. S. Nahmias[1], P. J. Yoder[1], A. S. Carter[2], D. S. Messinger[3] and W. L. Stone[4], (1)*Vanderbilt University*, (2)*University of Massachusetts Boston*, (3)*University of Miami*, (4)*Vanderbilt Kennedy Center*

Background: The Parent Interview for Autism-Clinical Version (PIA-CV) (Stone et al., 2003) was developed to obtain diagnostically relevant information from parents of young children for whom autism is

suspected. Interview and questionnaire versions are organized into conceptually-related, face-valid behavioral dimensions. However, psychometrically-defined factors have not yet been explored.

Objectives: The purpose of the present study was to factor analyze the 41 items comprising the four PIA-CV domains assessing social-communication development (i.e., Social Relating, Nonverbal Communication, Language Understanding, and Imitation) to examine the presence of an underlying factor structure.

Methods: An exploratory factor analysis was conducted on PIA-CV item scores from 223 children under age 48 months (mean CA=30.3mo, range=16.4–46.8mo) with or at risk for an autism diagnosis. Derived factors were then validated using data from 58 toddlers from the initial assessment of *A Multi-Site Clinical Randomized Trial of the Hanen More than Words Intervention* (mean CA=21.5 mo, range=15.5–25.0 mo) who met a predetermined cutoff on the Screening Tool for Autism in Two-Year-Olds (STAT) and had a clinical presentation consistent with ASD. A nomological network approach (Cronbach & Meehl, 1955) was utilized to assess the construct validity of proposed factors. Construct validity for individual factors was examined using the Mullen, Vineland, STAT, Infant/Toddler Social and Emotion Assessment (ITSEA), Early Social Communication Scales (ESCS), Parenting Stress Index (PSI) and Maternal Efficacy Scale (MES).

Results: Factor analysis yielded three factors, together accounting for 43% of the variance. Factor 1 contains 14 items (alpha=.89) representing language understanding, imitation, and joint attention. It was predicted to be associated with language (from the Mullen and Vineland, imitation (from the STAT and ITSEA), and directing attention (from the STAT and ESCS). Factor 2 contains 15 items (alpha=.88) reflecting instrumental communication and affection. It was predicted to be associated with requesting (from the STAT and ESCS). Factor 3 contains 11 items (alpha=.78) representing social engagement and enjoyment. It was predicted to be associated with social relatedness (from the ITSEA), interpersonal relationships (from the Vineland), parent child-interactions (from the PSI), and parenting efficacy (from the MES).

As predicted, Factor 1 correlated with language subscales on the Mullen (receptive r=.33, p=.02; expressive r=.39, p=.006) and Vineland (receptive r=.56, p<.001; expressive r=.48, p=.002). Factor 1 also correlated with the ITSEA imitation/play subscale (r=.69, p<.001) and with joint attention on the STAT (r=-.29, p=.04), but not with the ESCS. Correlations between Factor 2 and requesting measures were non-significant. Factor 3 was correlated with ITSEA social relatedness (r=.68, p<.001), Vineland interpersonal relationships (r=.64, p<.001), MES parenting efficacy (r=.72, p<.001), and PSI parent-child interactions (r=-.74, p<.001).

Conclusions: New PIA-CV factors show promise for assessing different domains of social-communicative development. Factors 1 and 3 were correlated with related constructs, as measured across observational, questionnaire, and interview methods. Future research will determine the utility of these factors for assessing response to the More Than Words intervention in young children with autism symptoms.

105.012 12 Identifying Relationships Between Parental Stress and Joint Attention Development in Infants at Risk for Autism. J. Johnson*, E. A. Koterba, M. V. Parladé, N. B. Leezenbaum and J. M. Iverson, *University of Pittsburgh*

Background: Infant siblings of children with autism, themselves at risk for developing the disorder (Zwaigenbaum et al., 2005, High Risk; HR), often experience delays in both initiating and responding to joint attention (e.g., Cassel et al., 2009). In children with ASD, joint attention improvements have been linked to better quality parent-child interaction (e.g., Siller et al., 2002). In typically developing samples, elevated parent-reported stress levels have been related to lower quality parent-child interaction (e.g., Fiore 2009). However, the relationship between parent stress, parent-child interaction, and joint attention

development has yet to be examined in a HR sample.
Objectives: (1) to describe the development of joint attention (JA) behaviors in HR infants from 12 to 18 months; (2) to explore the relationship between parental stress and parent-infant interaction; and (3) to identify links between parental stress and infant joint attention.
Methods: The Early Social Communication Scales (ESCS; Mundy et al., 2003) was administered to 19 HR infants (11 male) at 12-, 14-, and 18-months to assess high levels of responding to JA (HRJA) and initiating JA bids (HIJA). At 12-months, caregiver verbal utterances were coded during caregiver-infant toy play. These were classified as Redirecting (changing the object of infant attention) or Responding (addressing the object of infant attention) and according to success of caregiver's bid (e.g., whether the infant responded to bid). Caregivers completed the Parenting Stress Index (PSI; Abidin, 1983) at 12-months to assess stress from the caregiver/infant relationship on two subscales: Reinforce Parent (RE) and Attachment (AT). Infants were then classified according to caregiver stress: (a) low in both subscales (LS); (b) high in both subscales (HS); (c) mixed (high in one subscale; MXS); or (d) moderate (mid-range for both subscales; MOS).
Results: Although HIJA bids were infrequent in any group at 12 months, at 14 and 18 months the proportion of infants who produced HIJA bids was highest in the HS group (100% at 14 mo, 67% at 18 mo), followed by the MOS group (50% at 14 mo, 50% at 18 mo). The proportion of MXS and LS infants who exhibited HIJA bids was below 35% at all ages. Similar patterns were observed for HRJA; HS infants consistently scored 40% higher than any group; all other groups exhibited low HRJA scores (below 30%) at all age points. During toy play, caregivers of HS and MOS infants were slightly more successful than caregivers of MXS or LS infants when producing a Responding bid (H (3) = 6.949, p = .074). Additionally, caregivers of HS infants maintained their infants' attention longer than the other groups when responding to the infant's object of focus (H (3) = 10.309, p = .016).
Conclusions: The presence of higher or moderate stress levels in both subscales was *positively* associated with infant joint attention development. Caregivers who experienced greater stress tended to engage in more successful attention bids with their infants during toy play. Higher levels of stress may motivate parents to engage infants more frequently and more successfully, thus scaffolding joint attention development.

105.013 13 Joint Attention and Play of Nonverbal Children with Autism. K. A. S. Goods*[1], E. H. Ishijima[1], Y. C. Chang[2] and C. Kasari[1], (1)*University of California, Los Angeles*, (2)*UCLA Semel Institute for Neuroscience & Human Behavior*

Background:

Children with autism often demonstrate delays in both joint attention (Mundy & Newell, 2007) and play (Mundy, Sigman, Ungerer, & Sherman, 1986). Joint attention and symbolic play both have been linked to language (Toth, Munson, Meltzoff, & Dawson, 2006) . Furthermore it has been shown that interventions that target symbolic play and interventions that target joint attention both increase the expressive language of this population (Kasari, Paparella, Freeman, & Jahromi, 2008).

Objectives:

The current study seeks to research links between nonverbal communication and play abilities for young children with autism. The children attended a non-public school. In order to participate, each child had to have less than five spontaneous and functional words.

Methods:

Fourteen children diagnosed with autism participated in the study. All children were between the ages of three and five years old at entry. Participants completed assessments on their cognitive skills (Mullen Scales of Early Learning) as well as assessments of their spontaneous communication (Early Scales of Social Communication, or ESCS) and play abilities (Structured Play Assessment). Diagnoses of autism were confirmed by the Autism Diagnostic Observation Schedule.

The ESCS (Mundy, Hogan, & Doelring, 1996) was videotaped and later coded for spontaneous communication skills. These skills included gestures such as a give to request help and pointing to share distant objects. For this study, only unprompted skills were counted. Communication skills can include both requesting and sharing functions.

The Structured Play Assessment (Ungerer & Sigman, 1981)was also videotaped and coded for spontaneous play actions. The assessment provided opportunities for a range of play actions from functional play (e.g., completing shape sorters) to symbolic play (playing house with dolls and furniture). Only unprompted skills were included for this study. The present study focused on play types (different actions within a given play level) rather than frequency of play actions (how many shapes were put in a shape sorter). For example, completing a shape sorter would be counted as one type of play action and completing a puzzle would be a second type. They represent the same level of play, but are different examples.

Results:

A one-tailed correlation analysis revealed that children who exhibited more gesture communication skills on the ESCS also demonstrated more types of functional play skills in the Structured Play Assessment ($r = 0.5$, $p<0.05$). When self-stimulatory behaviors were excluded from the play skills, the same relationship was found ($r=0.48$, $p<0.05$). Gesture communication skill usage also significantly correlated with symbolic play type ($r = 0.55$, $p<0.05$).

Conclusions:

Results of this study indicate that spontaneous gesture use for communication is correlated with play abilities for nonverbal children with autism. This finding supports other research work targeting communication skills through play and vice-versa. Future studies should continue to develop interventions that target these skills to effects in other developmental skills among nonverbal children with autism.

105.014 14 Joint Attention Interventions for Young Children with Autism Spectrum Disorders: Caregiver and Child Actions and Transactions. A. K. Vo*[1], M. A. Conroy[1] and H. Schertz[2], (1)*Virginia Commonwealth University*, (2)*Indiana University*

Background: The development of joint attention behaviors is one of the central accomplishments of infancy and the early childhood period (Mundy & Newell, 2007). Joint attention has been linked theoretically and empirically to a number of other essential skill sets and developmental processes including language acquisition, affective sharing, social cognition, cultural learning, and the development of theory of mind (Adamson & McArthur, 1995; Baron-Cohen, Tager-Flusberg, Cohen, 1993; Carpenter, Nagell, & Tomasello, 1998; Kasari, Sigman, Mundy, & Yirmiya, 1990; Tomasello, 1995). Deficits in joint attention, characteristic of children with autism spectrum disorders (ASD), can have serious consequences for these children's functioning in multiple areas of development (Carpenter & Tomasello, 2000). As a result, it is essential that effective early interventions are used to target and ameliorate joint attention deficits in young children with ASD. Recent research on various interventions designed to promote joint attention in young children with ASD (e.g., Kasari, Freeman, Paparella, & Jahromi, 2008; Schertz & Odom, 2007; Whalen, Schreibman, & Ingersoll, 2006) shows promise, but is limited in two primary ways. First, most interventions fail to situate joint attention within the natural context of early caregiver-child relationships by involving caregivers in central roles. Second, the assessment of intervention outcomes is hampered by the absence of measurement systems capable of representing the changes that occur as a result of intervention in both child and caregiver actions and transactions. **Objectives:** Aim 1: To examine changes in the occurrence of child and caregiver joint attention actions across the course of a caregiver-mediated joint attention intervention for young children with autism spectrum disorders. Aim 2: To examine the sequential association between child and caregiver joint attention actions across the course of a caregiver-mediated joint attention intervention for young children with autism spectrum disorders. **Methods:** Participants

were six parent-child (two-years-of-age or below) dyads who had completed participation in a parent-implemented joint attention mediated learning intervention study conducted by Schertz, Odom, and Baggett (2007-2010). Extant digital video data from weekly parent-child interaction sessions was examined using a researcher-developed observational coding system (Caregiver-Child Joint Attention Coding System) supported by observational coding software. Aim 1 was addressed by using descriptive statistics and single-case design graphs to examine observational data resulting from the coding of digital video interaction sessions recorded throughout the course of the Schertz et al. (2007-2010) study. Aim 2 was addressed by using sequential analysis procedures to examine the relationship between temporally associated caregiver and child joint attention actions occurring in the coded observational data. **Results:** Data analyses to address both aims are currently being conducted. Preliminary findings indicate that caregiver actions and subsequent child joint attention actions are positively related to each other and reciprocal in nature. **Conclusions:** Data will be presented and discussed in terms of implications for intervention and the assessment of outcomes in future joint attention research.

105.015 15 Relationships Among Joint Attention, Imitation, Play and Language in Young Children with Autism Spectrum Disorders. C. C. Wu*[1] and C. H. Chiang[2], (1)*National Chung Cheng University*, (2)*National Chengchi University*

Background: The long-term outcome of the research in autism spectrum disorders (ASD) was an important issue until now. However, we did not really know what kinds of variables could predict long-term outcome of children with ASD. Previous studies had shown that one of the strongest predictor of long-term outcome for children with ASD was expressive language. And there were some early social communicative abilities (i.e. joint attention, imitation and play) associated with language in children with ASD above the age of three (Toth et al., 2006). However, there was no study to investigate the relationships between joint attention, imitation, play and language in young children with ASD under 36 months.

Objectives: The purpose of the study was to examine the relationships between joint attention, imitation, play and language in young children with ASD less than 36 months. We also further investigated which variable was the unique contribution to language in the ASD population.

Methods: The participants were thirty nine 29-month-old (range = 24-36 months) children with ASD, including 31 cases of typical autism and 8 cases of atypical autism. All of participants were recruited from one local hospital in southern Taiwan and diagnosed by multidisciplinary team with DSM-IV-TR (APA, 2000). A modified form, T-STAT copy of the STAT (Stone, et al., 2000, 2004), was used to measure the social communicative abilities, including initiating joint attention, responding joint attention, object imitation, manual imitation, and doll-directed play. Besides, the verbal abilities were assessed by Mullen Scales of Early Learning (MSEL, Mullen, 1995) and Macarthur Communicative Development Inventories (CDI, Fensen et al., 1993). Results: First, the correlations of all predictive variables were examined, and the results revealed that responding joint attention, object imitation, and doll-directed play were correlated with language of the young children with ASD. However, the study results could not support the relation between initiating joint attention and language in young ASD children. Next, we used multiple regression analyses to examine the stronger predictor for language. And the results revealed that object imitation could predict expressive language from MSEL and doll-directed play could predict vocabulary ability from CDI.
Conclusions: Results of this current study demonstrated that both object imitation and doll-directed play were the stronger predictors for expressive language in young children with ASD. Both object imitation and doll-directed play were that an agent performs an action involved an object. It provides salience via an action with an object for children with ASD to pay attention. It helped language development in children with ASD when they paid attention. The initiating joint attention could not predict the expressive language ability in young children with ASD. It was a surprising result. We suggested that maybe

the performance of initiating joint attention in young ASD children were rarely to be a reason. The development of the language in children with ASD was needed to discuss the spotlight effect of object action.

105.016 16 Sounds of Melody – Acoustic Features of Speech in Autism. M. Sharda* and N. Singh, *National Brain Research Centre*

Background:

Communicative dysfunction is a characteristic feature of Autism Spectrum Disorder (ASD). Despite the universal nature of the impairment, studies have failed to characterise vocalisations from ASD populations due to inconsistent discriminative patterns in speech and the heterogeneity of the disorder. Recent advances have established that there is an early brain dysfunction in autism which intensive intervention can alter. Given this scenario, it is possible that children with ASD have a delayed developmental trajectory and milestones followed by typical children might manifest at later time points.

Objectives:

The objective of this study was to find a consistent pattern in vocalisations of children with Autism Spectrum Disorders. Based on literature, which demonstrates the manifestation of 'atypical' prosody or pitch patterns in ASD speech, our hypothesis places a delayed developmental trajectory as cause for deviant pitch patterns in ASD speech.

Methods:

Spontaneous speech recordings of 15 high-functioning, verbal children with ASD (AUT) and 10 age-matched typical controls (TD) in the age group 4-10 years was obtained. Similar spontaneous recordings, of 8 mothers interacting with their 6-18 month-old neurotypical infants, were made. Following this, intonation patterns of children with ASD were compared with age-matched controls to determine differences in mean pitch, pitch range, pitch excursion and the nature of intonation contours, and compared with simliar patterns obtained from child-directed interactions

Results:

Our findings show that pitch patterns of children with ASD with verbal ability are different from age-matched typically developing children. Pitch patterns of the AUT group are characterized by exaggerated intonation contours, elevated pitch, higher pitch range and pitch excursion as compared to TD. It has also been shown that such exaggerated pitch patterns are also distinguishing features of motherese as demonstrated by analysis of child-directed vocalizations of mothers in the MOT group.

Conclusions:

Typically developing children respond to the prominent intonation contours of motherese prior to adult-like speech development and grow out of it by 2-3 years. These pitch patterns characterized by exaggerated contours are exhibited by AUT group at a later age of 4-10 years, suggesting that these features might follow a delayed developmental trajectory. Our preliminary findings suggest a basis for continued use of motherese-like speech in enhancing verbal communication in subpopulations of ASD individuals. Future research will aim at exploring these possibilities in greater detail.

105.017 17 The Relationship Between Gesture Use and Adaptive Functioning in Autism. K. Stamper*, R. Bernier and J. Gerdts, *University of Washington*

Background: Researchers have taken several different behavioral approaches to examine the deficits of imitation and gesture in children with autism. Results vary among studies but indicate impairments in gesture production during naturalistic interactions as well as during various tasks, including the performance of gestures to verbal commands, the imitation of manual and oral gestures, and the imitation of tool use. Some suggest that such deficits in gesture constitute a core feature of ASD symptomology and have a functional relationship to other areas of development such as language, social skills, and motor abilities.

Objectives: The purpose of the current study is to examine the relationship between gestures of children with ASD and areas of adaptive functioning using both parent report and direct observation.

Methods: The sample consists of 155 children diagnosed with ASD (*M* CA = 9 years, 3 months; *SD* = 3.70, range 4 years, 0 months-17 years, 10 months; 134 M, 21F) who are participating in ongoing genetics studies. Parent reports of gesture use and adaptive functioning (from the ADI-R, and Vineland Adaptive Behavior Scales (VABS)) and observational measures of gesture use (ADOS-WPS) were collected. The sample was divided into three gesture groups (significant, moderate, and no impairment in gesture use) based on a composite of current gesture use derived by ADI-R and ADOS-WPS item scores. Differences were investigated between gestural groups on areas of adaptive functioning, specifically social, communicative, and daily living skills. Additionally, gestural groups were split into two age groups (Group #1: ages 4 years, 0 months to 8 years, 11 months; Group #2: ages 9 years, 0 months to 17 years, 11 months) based on Capone & McGregor (2004).

Results:Using MANOVA a significant effect of gestural group was found for scores on the VABS personal (p = .006), domestic (p = .039), and community (p = .023) subdomains, as well as the daily living skills standard scores, (p < .002), with children with greater gesture use deficits showing greater adaptive deficits. A significant effect of age group was found for the following VABS subdomain scores: receptive (p = .012), expressive (p = .002), written (p = .015), fine motor (p < .001), gross motor (p < .001), interpersonal relationships (p = .018), and domestic (p = .009); and for the following standard scores: motor (p < .001), communication (p = .003), and composite (p = .032). For all effects of age group, the older age group showed fewer VABS deficits regardless of gestural ability, except for the written language subdomain for which there was a significant interaction effect between gesture and age (p = .028).

Conclusions: The preliminary findings in the current sample of children with ASD suggest that deficits in gesture use have meaningful effects on areas of adaptive functioning, specifically in the area of daily living skills. These results provide partial support for the theory that gesture deficits in autism may be part of more global impairments related to ASD but also indicate that age also has a strong effect on adaptive skills in ASD.

105.018 18 Utility of the Screening Tool for Autism in Two-Year Olds (STAT) as a Continuous Measure of Nonverbal Social-Communicative Behavior. E. H. Catania*[1], A. S. Nahmias[1], J. H. Foss-Feig[1], A. S. Carter[2], D. S. Messinger[3] and W. L. Stone[4], (1)*Vanderbilt University*, (2)*University of Massachusetts Boston*, (3)*University of Miami*, (4)*Vanderbilt Kennedy Center*

Background: The STAT is an autism screening tool designed for children between 24 and 36 months old based on direct measurement of play, imitation and communication behavior (Stone et al., 2000; 2004). Its screening properties have been described for children as young as 14 months (Stone et al., 2008). Because the STAT was designed to minimize language demands while measuring social-communicative behaviors that are disrupted in autism, the Total STAT score may be useful as a measure of nonverbal social-communication development in young children at risk for autism.

Objectives: To explore the validity of the STAT as a measure nonverbal social-communicative skill in toddlers with early autism symptoms by examining its relation to social-communicative items from parent report and other observational measures.

Methods: Participants included 48 toddlers (mean CA = 21.5 months, range = 15.5–25 months) from the initial assessment of a multi-site clinical randomized trial of the Hanen More than Words Intervention who met a predetermined cutoff score on the STAT and had a clinical presentation consistent with ASD. Pearson correlations between the Total STAT score (which ranges from 0-4, with higher scores indicating greater autism symptomatology) and related measures of social-communicative behaviors were examined. Observational measures

were the Early Social Communication Scale (ESCS) initiating joint attention (IJA), responding to joint attention (RJA) and initiating behavioral requests (IBR) scores and the Developmental Play Assessment (DPA) score for number of toys used during a 7-minute period. Parental report measures were the Parent Interview for Autism-Clinical Version (PIA-CV) Imitation and Nonverbal Communication scores and the Infant-Toddler Social and Emotional Assessment (ITSEA) Imitation/Play and Social Relatedness scores.

Results: The mean Total STAT score for this sample was 3.0 (*sd* = 0.54). Total STAT scores correlated significantly with RJA (r = -.35, p = .016) and IBR (r = -.39, p = .006) scores from the ESCS; but not with IJA score (r = .03, p = .909). Total STAT scores also correlated with the number of toys used in the DPA (r = -.31, p = .032). In addition, the Total STAT score correlated with the Imitation and Imitation/Play subscales of the PIA-CV (r = -.39, p = .006) and the ITSEA (r = -.35, p = .015), but not with the Nonverbal Communication (r = -.05, p = .723) or Social Relatedness (r = .09, p = .525) scales.

Conclusions: Correlations between the Total STAT score and several observational and parent report measures of communication, play, and imitation provide initial evidence for the use of the STAT as a continuous measure of nonverbal social-communicative behaviors in this unique sample of very young children with autism symptomatology. Replication with other samples and examination of its sensitivity to change will represent important next steps in exploring its utility as a continuous measure.

105.019 19 Auditory Preferences in Infants at Risk for ASD. R. Paul*, K. Chawarska, E. Schoen and A. Klin, *Yale University School of Medicine*

Background:

The role played by genetic factors in the incidence of ASD has led to studies of infants siblings of children with ASD. Observations of poor responsiveness to language in older children with ASD suggest the possibility that abnormal attention to language may be one root of the communication deficits in this population. Research in infant speech perception has demonstrated that preferences for listening to speech-like sounds change late in the first year from those that apply to any language toward those tuned to the sound patterns of the ambient language. We (Paul et al., 2007) have shown previously that there are significant differences in preferences for speech-like input between toddlers identified with ASD and TD peers.

Objectives:

This study reports on differences in auditory preferences in the first year of life in siblings of children with ASD.

Methods:

Participants. High Risk (HR) participants had a full sibling with a validated diagnosis of ASD. Low Risk (LR) infants had no sibling who had received a diagnosis of autism. Infants were seen multiple times during their first year. At 18 and 24 months, clinical identification of the presence/absence of autistic symptoms by experienced clinicians was also assessed. The present report examines data from the 9 month visit, and uses diagnostic data from the 18 and 24 month visits to assign children to three groups:

LR: children with low risk for autism, with no affected sibling;

HR/0: children at risk for ASD who showed no symptoms of ASD at 18 to 24 months;

HR/+: children with ASD who demonstrated some symptoms of ASD at the 18 -24 mo. (NB: not all HR/+ children met full criteria for ASD, some showed signs of a broader ASD phenotype).

Auditory Preference Procedure

A video monitor flashes a picture, calling the subject's attention. When the child orients to the display, an auditory stimulus is played. The stimulus continues until the child turns away for at least two seconds, or until the entire trial is completed (15 seconds).

Stimuli

Child-directed (CD) speech vs. Adult-directed (AD) speech: Nursery rhymes were read twice each; once with "motherese" intonation and once with adult-directed intonation. Time spent orienting to the (CD) vs. (AD) samples was compared across diagnostic groups.

Lexical stress: Words with the English-dominant strong/weak stress pattern (MO ther) or the non-dominant weak/strong pattern (gui TAR) were read by an female speaker. Time orienting to the strong/weak vs. weak-strong samples were compared.

Results:

There were no differences among the groups in terms CD or AD speech; all children preferred CD. There were significant differences in preference for lexical stress patterns. The LR and HR/0 groups performed similarly; the HR/+ group preferences differed.

Conclusions:

Children at risk for ASD show preferences for CD speech as typical peers do. However, HR children who show symptoms of ASD in their second year are less able to "tune in" to the details of English word structure during the first year of life, when templates for language acquisition are being established.

105.020 20 Enhancing Spontaneous Speech Production in a Previously Nonverbal Adult with Autism. E. P. Loughlin*, E. J. Pickett, J. Thorne and B. Gordon, *Johns Hopkins Medical Institutions*

Background: Individuals with autism who fail to develop speech normally rarely develop speech after age 5 (Pickett et al., 2009). However, we have succeeded in training one individual to produce oral speech, starting at 14 years of age (O'Grady et al., IMFAR 2004, 2005). AI (not his real initials) initially used individual consonants and vowels, with prompting, for communicative purposes. At age 16, AI began using, with prompting, 1-3 word utterances with carrier phrases. By age 21.1, although his speech capabilities had continued to improve, his intelligibility and initiation of communication were still limited. All observed spontaneous utterances consisted of requests for reinforcing items. Here we report on focused efforts to improve AI's spontaneous initiation and fluency with oral speech, beginning at approximately age 21.3.

Objectives: To determine if it was possible, to (1) increase expressive mean length of utterance, (2) increase intelligibility of expressive verbal communication, and (3) increase spontaneous use of expressive verbal vocabulary, in a previously non-verbal, low-functioning individual with autism, by a concerted, concurrent use of several approaches.

Methods: The speech and language curriculum was organized to teach expressive use and receptive knowledge of target words simultaneously. Targets were systematically chosen with consideration given to motor ability, language development, and reinforcing value. The five-step teaching procedure included (1) errorless exposure, (2) errorless prompting, (3) expansion of utterance to a two-word phrase, (4) use in novel context with delayed prompting, and (5) unprompted use in novel context. These teaching procedures were based upon such principles as errorless learning, generalization (Carter & Hotchkis 2002), feedback (Maas et. al. 2008, Hula et. al. 2008), and effects of over learning (Rohrer & Taylor 2005). Intelligibility was addressed via the PROMPT method (Chumpelik (Hayden) 1984; Hayden, 2006), addition of manual signs, and the Goldman Fristoe Test of Articulation–2 (Goldman & Fristoe, 2000). Data collection relied upon review of audio- and video-taped sessions (the bulk of the data), results recorded in instructors' contemporaneous notebooks, and family report.

Results: At age 21.3, 28 target words were introduced to AI's curriculum. Of these targets, 16 were believed to be novel or not previously programmed. The remaining 12 were carried over from the previous speech curriculum. By age 21.10, eleven words met criteria for improved usage: AI demonstrated the ability to use these words to verbally and manually express targets in two-word phrases, in novel situations, without prompting. Of the 28 target words, 19 have

been reported in spontaneous speech at least once.

Conclusions: Often, functional communication targets are chosen without consideration of the student's motor ability or current language ability. In this case, the same words were targeted simultaneously for intelligibility, functional communication, and receptive language. Generalization was programmed from the beginning, by words being taught in their naturally occurring environment and their use resulting in contextual reinforcement. It is hypothesized that this coordinated effort allowed for the maximum exposure and practice required to acquire the spontaneous use of spoken communication.

105.021 21 Increased Pitch Variability in Young Autistic Children. Y. S. Bonneh*[1], Y. Levanon[2] and O. Dean-Pardo[3], (1)*University of Haifa*, (2)*Netanya Academic College*, (3)*Child Development Center*

Background: Children with autism spectrum disorder (ASD) who can speak often show abnormal voice quality and speech prosody, but the exact nature of these abnormalities and the underlying mechanisms are currently unknown, and there is no available quantification method that has been used to assess the incidence and significance of these abnormalities.

Objectives: To develop a quantification method for the abnormal speech in ASD and conduct a preliminary assessment of the method on a large sample.

Methods: we recorded 82 children (41 autistic, 41 controls) ages 4 to 6 years (mean 5) while naming a sequence of daily life pictures pointed by the experimenter for 60 sec in a quite room in their preschools. We computed pitch across time and normalized pitch histogram peaks as a measure for pitch variability.

Results: Contrary to the common impression of monotonic speech in autism, the ASD children had significantly larger pitch variability across time. A measure of this variability yielded more than 80% success in classifying ASD in the sample.

Conclusions: Speech abnormalities in ASD are reflected in increased pitch variability during speech. Controlling pitch is likely to involve auditory feedback, and the current findings could imply abnormal interaction between speech reception and production in autism. It could also reflect elevated neural noise in the mechanisms that control speech, providing support to a neural-noise theory of autism, and possibly an early measure of such noise. The current results are a first step towards the development of speech-spectrum based tools for early diagnosis.

105.022 22 Instant Messaging as An Alternate Form of Communication for Adolescents with Asperger's Syndrome or High Functioning Autism. S. Carr* and B. Myers, *Virginia Commonwealth University*

Background:

Adolescents with AS or HFA lack interpersonal skills such as understanding personal space, reading facial expressions and body language, and staying on topic in a conversation. They can often feel like loners or outsiders. Peers often ridicule or reject them; at best, peers ignore them. People who have an AS or HFA diagnosis have a deficit in social understanding of what is being said, non-verbal social cues, and fluency which makes face-to-face conversations overwhelming. That said, with Instant Messaging, communicative partners do not need to worry about interpreting facial expressions, body language, or tone of voice. None of the individuals in an Instant Messaging chat can see the faces of others, and so the inequality in "face-reading" that usually exists is eliminated. By eliminating this stressor, youth may be better able to concentrate on the content of what is being said (or typed) to their peer.

Instant Messaging allows for a quick review of what was typed before sending. This allows for reflection about what to say and time to change the message before the communicative partner reads it. Unlike face-to-face conversation, this may reduce the number of inappropriate comments that are exchanged by youth with AS/HFA, thus reducing the potential negative response of the peer. The virtually real-time exchange of Instant Messaging can help an adolescent

with AS/HFA learn to appropriately initiate, maintain, and end conversations while reading and interpreting the concrete cues that computer communication permits.

Objectives:

This study was designed to address the social skill deficits of older children and adolescents with AS/HFA by offering an alternative communication tool, Instant Messaging (IM) by examining how youth with AS/HFA learned to use Instant Messaging and their willingness and ease of communicating with others through Instant Messaging.

Methods:

14 adolescents between 10 and 15 years of age with a diagnosis of AS or ASD were included in this IRB approved study. Parents and adolescents signed consent and assent respectively. Pre-test measures were taken for inclusion and baseline measures. Participants completed a 6 week Instant Messaging training to teach internet safety, setting up an email and IM account, appropriate IM'ing topics, how to initiate and end a conversation appropriately. All chats were monitored by the project investigator.

Results:

Participants reported enjoyment of instant messaging over face-to-face chats, and increased confidence exchanging chats with others. Over half (n = 8) of the participants continued IM'ing others in the study as well as peers from school and family at the 10 month online check.

Conclusions:

Providing adolescents who have a difficult time socializing with peers an easier way to develop competence in social skills before adding the additional challenge of being face-to-face with a peer may help youth feel included and less victimized, thus reducing the risk of depression, problem behavior, and unsafe activities. While Instant Messaging is not a substitute for face-to-face encounters, it can be a safe and effective way to practice the necessary skills needed to be an active and suitable participant in a conversation.

105.023 23 Interactive Visuo-Motor Therapy as a Supplementary Social Communication Treatment Model for Children with Autistic Spectrum Disorders. P. Leigh*, *Edinboro University*

Background:

A large number of brain imaging studies have been performed that have shown that the observation of actions done by others, as well as implementation of action by oneself, activates in typical humans a complex network of mirror neurons. Differences in the mirror neuron system of children with Autistic Spectrum Disorders have been identified and less activation occurs during action observation for these children than for those with typical development. This reflects deficiencies in the functioning of the observation / execution system within the mirror neuron system which may play a critical role in understanding and imitating the actions of others, the primary area of deficit for children with ASD. Evidence exists to suggest that performing action observation may facilitate motor activity and induce cortical plasticity.

Objectives:

Interactive visuo-motor therapy using the MeMoves® video has been discovered to facilitate neural functioning and increase social communicative functioning in a case study with ASD. MeMoves® is a commercially available video that was designed to increase focus and attention for all people. The video consists of children performing bilateral and cross-lateral movements that follow geometric shapes. The objectives of the current study were to identify if MeMoves® is an efficacious supplementary therapy model to improve mirror neuron functioning and ultimately imitative and social functioning for one five year-old case study child with ASD. Many families with children with ASD are looking for a fun way to interact with their child that is also therapeutically beneficial. MeMoves® has the potential to fill this need. The premise is imitation learning through watching & performing movements following children's models. A subsequent study of clinical trials with a larger number of children

with ASD will be implemented in the near future.

Methods:

An initial Electroencephalogram (EEG) of the five-year old child with ASD was performed to determine mirror neuron system function prior to engaging in MeMoves®. The child demonstrated the atypical pattern of functioning that has been discovered in children with ASD during the pre-test period. The child and his family engaged in the MeMoves® video protocol 5 days a week for 5 minutes a day for 12 weeks in duration. The family reported having fun and doing the video movements together. A post-test EEG was performed following the therapy protocol to determine if increased mirror neuron functioning was evident. Additionally, behavioral outcomes were measured at week 1, week 6, and week 12 to assess the child's ability to establish and maintain eye contact and imitate the clinician's movements during speech-language therapy sessions.

Results:

Results indicated improved mirror neuron functioning and an increase in behavioral outcomes following the 12 week MeMoves® interactive visuo-motor therapy protocol.

Conclusions:

This case study indicates that interactive visuo-motor therapy using the MeMoves® video may be an efficacious supplementary therapy protocol that is fun and engaging for children and their families to do at home together.

105.024 24 Joint Attention and Language Development in Young Children with Autism. S. Tek*, G. Jaffery, D. A. Fein and L. Naigles, *University of Connecticut*

Background: Joint attention (JA) occurs when two individuals focus on the same object or event (Baldwin, 1995). There are two major kinds of joint attention: response to joint attention (RJA), which refers to the process by which children follow the attentional focus of their social partners, and initiation of joint attention (IJA), which refers to the children's ability to direct their social partners' attention on an object or event (Corkum & Moore, 1995). Impairment in joint attention is an early sign of autism, and may be a major reason for the delayed language development seen in individuals with autism. Objectives: To investigate the JA of young children with autism across a 2-year time span. We report data from the first two visits (4 months apart). Methods: We included 10 typically developing toddlers (TD: mean age = 20.45 months), and 12 children with autism (ASD: mean age = 32.32 months), who were matched on expressive vocabulary at Visit 1. Children engaged in a 30-minute play session with their parents. Sessions at Visit 1 were coded for (a) duration and number of RJA episodes, (b) duration and number of IJA episodes, (c) duration and number of episodes in which the parent attends the same object as the child, but the child only passively participates (Passive Attention), (d) pointing and eye contact during a JA episode. At Visit 2, children's language during the play session was coded for (a) total number of words (types and tokens), (b) mean length of utterance (MLU), (c) wh-words and questions (types and tokens), (d) verbs (types and tokens). Children were also administered the MacArthur Communicative Development Inventory (CDI), Vineland Adaptive Behavior Scales, and Mullen Scales of Early Learning (Visit 1). Results: Compared to TD children, the ASD group engaged in significantly shorter episodes in which they had responded to JA (ASD M = 0.9 minutes per episode; TD M = 1.2 minutes per episode, $p < .05$), and fewer episodes of JA which they initiated (ASD M = .16; TD M = 1.0, $p < .05$). Moreover, children with ASD engaged in more episodes of Passive Attention with their parents (ASD M = 10.33; TD M = 1.5). For children with ASD, the duration and number of RJA episodes positively correlated with their scores on the CDI (Visit 1), Vineland (all subscales), Mullen (all subscales), as well as their total number of utterances and verb type (both types and tokens), and MLU. Their duration of IJA episodes correlated positively with their wh-words and questions (ps < .01). Regression analyses demonstrated that, for the ASD group, higher Mullen Expressive Language scores and longer RJA episodes at Visit 1 predicted both types and tokens of total

words, and verb tokens at Visit 2. Conclusions: This study showed that toddlers with ASD engage in less joint attention with their mothers and initiate fewer JA episodes compared to TD children. We conclude that both RJA and IJA seem to be related to later vocabulary development in children with ASD.

105.025 25 Maternal and Child Gesture Use and Language Outcomes in Infants at-Risk for Autism. M. Thompson* and H. Tager-Flusberg, *Boston University*

Background: Gestures play an important role in early language development - they are among the first forms of communication to emerge and also predict later language performance in typically developing infants (Rowe, Ozcaliskan, & Goldin-Meadow; 2008). Infant siblings of children with autism are at increased risk for both autism and language impairments, and delays in gesture production have been identified as early as 12 months of age in infants who go on to receive a diagnosis, and at 18 months of age in high-risk infants that do not (Mitchell, et al., 2006). For children with autism, concurrent gesture use is the most consistent predictor of both expressive and receptive language abilities (Luyster, Kadlec, Carter, & Tager-Flusberg, 2008), and therefore it is important to understand the factors that predict gesture use in high-risk infants. Recent work has identified maternal gesture as one such predictor in typically developing infants, but it is unclear what role maternal gesture might play in the gesture use and language development of high-risk infants (Rowe et al., 2008). Objectives: The present study sought to examine the role of maternal and child gesture use in predicting subsequent language ability. Additionally, factors related to maternal gesture use such as broader autism phenotype characteristics and maternal depression measures will be explored. Methods: 35 laboratory free play sessions between mothers and their 12-month old infants (21 high risk autism – HRA, 14 low risk controls - LRC) were transcribed and coded for gesture use. Based on a coding scheme developed by Goldin-Meadow and colleagues, gestures belonging to the following categories were coded: deictic, representational, conventional, beat, and sign. A `gesture index' score was computed for each parent by totaling the number of distinct gestures used within the session and then corrected for differences in session time. Children's raw scores on the Receptive Language subscale of the Mullen Scales of Early Learning (MSEL) administered at 18 months were used as the language outcome measure. Raw total scores from the CESD were used as a measure of maternal depression. The Broader Autism Phenotype Questionnaire (BAP-Q; Hurley, Losh, Parlier, Reznick, & Piven; 2007) was also collected. Results: 4 of the 21 HRA infants received a preliminary diagnosis of autism at 18 months. To ensure that these infants were not driving any effects, they were removed from the analysis, leaving a final group of 31 infants (17 HRA, 14 LRC). Although there were no significant differences between the groups on maternal gesture index or receptive language scores at 18 months, maternal gesture and child language scores correlated only for LRC, but not HRA dyads (LRC: r = .45, HRA: r = .07). Additionally, maternal depression was negatively correlated for HRA, but not LRC mothers (LRC: r = -.15, HRA: R = -.45). Conclusions: These results suggest that maternal gesture, and factors relating to it, may play different roles in the gesture use and language development of high and low risk infants. Results from child gesture and BAP measures will also be discussed.

105.026 26 Stability and Variation in the Social Communication and Shared Attention Behaviours of Preschoolers with Autism Across Two Naturalistic Observation Assessments. L. Brown*[1], K. Hudry[2], S. Clifford[3], K. Leadbitter[4], T. Charman[5] and .. PACT Consortium[4], (1)*Wessex Neurological Centre*, (2)*Department of Psychology and Human Development, Institute of Education*, (3)*King's College - University of London*, (4)*University of Manchester*, (5)*Institute of Education, University of London*

Background: Deficits in social-communication skills, including reduced initiations and responses to others and limited shared attention, are core features of autism spectrum disorders (ASD). While naturalistic observation measures exist to evaluate such behaviours in every-day settings, little research has yet examined the stability of social-communication abilities of children with ASD across different every-day contexts.

Objectives: The current study explores the social-communication and shared attention skills of a group of preschoolers with autism assessed using two naturalistic observation measures; a clinic-based parent-child play interaction, and a school-based interaction with teacher and peers.

Methods: Participants were 41 preschoolers with Autistic Disorder involved in the Preschool Autism Communication Trial (PACT). Assessment of parent-child interaction was conducted at the clinic as part of PACT and children were subsequently seen at school/nursery, in small-group interaction with a teacher and peers. Rates of child initiations of communication and responses to others' bids were compared across the two assessments, as were durations of their engagement in shared attention with others.

Results: Preliminary analysis suggests significant association of child initiating behaviours across the parent- and school-based interactions. By contrast, association of child response behaviours across contexts appears weaker. More detailed analysis of sub-functions of communication act and duration of engagement in shared attention are underway.

Conclusions: Consistencies and differences in behaviours across the parent- and school-based interaction settings will speak to the generalisability of social-communication skills in children with autism. Contextual factors varying across different naturalistic settings may be highlighted as facilitative or hindering of the communication and interaction skills of these preschoolers.

Keywords: Autism, Preschool, Social Communication, Shared Attention, Naturalistic Observation

105.027 27 Validation of the Autism Spectrum Screening Scale (ASSQ), Mandarin Chinese Version. Y. Guo[1], Y. Tang[2], C. E. Rice*[3], L. C. Lee[4], Y. F. Wang[1] and J. Cubells[2], (1)*Institute of Mental Health, Peking University Health Science Center*, (2)*Emory University*, (3)*National Center on Birth Defects and Developmental Disabilities*, (4)*Johns Hopkins Bloomberg School of Public Health*

Background: International studies of Autism Spectrum Disorders (ASDs) require development of linguistically and culturally appropriate screening and diagnostic instruments. The Autism Spectrum Screening Scale (ASSQ) is a 27-item checklist originally developed in Sweden and published in English for assessments of Asperger syndrome and other high-functioning ASDs. The utility in Chinese-speaking populations has yet to be established.

Objectives: As a first step in establishing the validity of a Mandarin Chinese translation of the ASSQ, this study screened children in several psychiatric diagnostic groups, as well as unaffected children using the Chinese ASSQ.

Methods: The ASSQ was initially translated by two native-speaking experts (Y-LT, Y-QG) and pilot data were collected. We then recruited children diagnosed with ASD, attention deficit/hyperactivity disorder (ADHD), childhood-onset schizophrenia (SCZ) (DSM-IV diagnoses made independently by two senior psychiatrists) from the Institute of Mental Health, Peking University, and children attending a public school in Beijing. Their parents were asked to complete the ASSQ. As part of the pilot phase, the instrument was further refined through back-translation making minor changes that two native-speaking experts (Y-LT and L-CL) and two English-speaking experts (CR, JFC) felt would make the translation more culturally appropriate while maintaining the clinical meaning of the items. Procedures were approved by the Ethics Committee of the Sixth Hospital, Peking University Health Science Center.

Results: Data from the parents of 94 children with ASD (mean age: 81+/142 months), 45 with ADHD (110+/-27 months), 26 with SCZ (166+/-36 months), and 20 unaffected control (104+/-13 months) were collected. The total scores of ASSQ in children with ASD, ADHD, SCZ, and unaffected controls were 25.4+/-9.0, 10.1+/-6.4, 12.1+/9.3, and 4.3+/-5.0 respectively. Total ASSQ scores of children with ASD were significantly higher than in any other group (all $p<0.0001$). Receiver-Operating Characteristic (ROC) analysis showed the area under curve was 0.982, with a cutoff score of 11 having the

maximum sensitivity (0.98) and specificity (0.90).

Conclusions: Our pilot data of the Chinese translation of the ASSQ successfully differentiated clinically diagnosed ASD from unaffected controls. A total score of 11 as the cut-off score has the highest sensitivity and specificity (ASD vs unaffected controls). While children with other clinical psychiatric diagnoses had higher scores than the affected controls, children with ASD had significantly higher scores compared to any group. Our results suggest the Chinese ASSQ may be a useful component of a strategy for screening for ASD in situations where time consuming expert evaluation is not practical. Work is under way to replicate and extend the results reported here.

***CDC* disclaimer:** *The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention.*

105.028 28 A Generalisability Study to Estimate Optimal Design When Using the Classroom Observation Schedule to Measure Intentional Communication (COSMIC). G. Pasco*[1], R. K. Gordon[2], P. Howlin[3] and T. Charman[4], (1)*University of Cambridge*, (2)*Institute of Psychiatry*, (3)*Institute of Psychiatry, King's College London*, (4)*Institute of Education, University of London*

Background:

Researchers investigating the social communication behaviour of nonverbal children with autism often use observational measures in order to reflect children's communicative skills in familiar everyday settings with their regular communication partners. Decisions relating to the number of sessions in which children should be observed are often made in relation to resource issues rather than via a systematic procedure. Generalisability theory provides an objective means of estimating the optimal study design, in terms of both the number of sessions observed and the number of raters required, in order to provide a stable measure of a variable of interest.

Objectives:

We conducted a Generalisability study to estimate the optimal study design for key variables from the Classroom Observation Schedule to Measure Intentional Communication (COSMIC). We investigated the stability of these variables in relation to changes in context and in relation to observations made at different time points within one context.

Methods:

Eight children with autism (5 boys, 3 girls, mean age 75 months) attending an autism-specific school were videoed in snack, free play and work-based sessions for 10 minutes each on one day. Each child was also videoed in a second snack session within the next few days. Each video was independently rated by two researchers according to the COSMIC protocol. The frequency, variance, distribution and skewness of the COSMIC variables *initiation*, *correct response*, *speech* and *request for object* were examined. Only *correct response* had sufficient statistical properties to merit further examination. The variance components relating to participants, participants x sessions, participants x sessions x raters and participants x raters were calculated via ANOVA and entered into a Generalisability calculator spreadsheet. Optimal study designs (where the value of $g \geq 0.70$) were derived from this spreadsheet.

Results:

The mean nonverbal mental age was 23.4 (SD = 9.3). The mean frequency of each of the key variables was less than 2 per 10-minute session with the exception of *correct response*, for which the frequency was 5.4. Inter-rater reliability for correct response was very high (ICC = 0.97). The optimal study design relating to changes within snack sessions across time was 1 rater x 8 sessions and for changes in context was 3 raters x 16 sessions.

Conclusions:

Generalisability studies provide a means of determining optimal designs relating to the number of sessions and raters required in order to provide a stable estimate of a variable of interest. This study demonstrates

that it may be necessary to observe children in more sessions than may typically be the case in studies involving observational measures. For example, within one context, the results suggest that each participant should be observed in 8 10-minute sessions. If the study aims to investigate children's behaviour across a range of sessions, then as many as 16 10-minute sessions coded independently by 3 raters would be required. Furthermore, the relatively infrequent nature of the social communication of low-functioning children with autism means that certain variables may not be amenable to this method of calculating optimal study designs.

105.029 29 Automatic Identification of Children at-Risk for ASD Using Audio Recording. D. Xu*[1], J. A. Richards[1], J. Gilkerson[1], S. F. Warren[2] and D. K. Oller[3], (1)*LENA Foundation*, (2)*University of Kansas*, (3)*The University of Memphis*

Background: Children with Autism Spectrum Disorder (ASD) exhibit functional impairments in social interaction and communication as well as restricted and repetitive behavior. In addition, researchers have reported abnormalities in the vocal production of children with ASD. However, there has been no fully-automatic quantitative modeling of specific vocal abnormalities. Recent advancements in hardware and software technology provide the opportunity to collect large quantities of audio data and apply advanced statistics to investigate the vocal behavior of children with ASD.

Objectives: This research reports an analysis of automatically-generated phone-level vocalization composition of children from three groups (TD: typically developing; LD: language-delayed but not with ASD; AD: children diagnosed with ASD). Pattern recognition and machine-learning approaches were applied to vocalization data to build a fully automatic model for identifying children at risk for ASD.

Methods: A lightweight recorder is worn by a child to record his/her vocalizations and environmental sound over 16 hours. Child vocalizations in the recording are automatically identified using speech signal processing and recognition software. They are decomposed by applying adult-phone-model and child-vocalization-clusters to recognize phone-like units. The frequency of each unit is calculated, resulting in 63 features based on child-clusters and 50 features based on the adult-phone-model. Frequency features are analyzed using Linear Discriminant Analysis (LDA) and other machine-learning and statistical methods. Posterior probabilities for recording vocalizations being produced by a child with ASD are estimated based on the statistics after LDA or other transforms. For a child with multiple recordings, the probability is simply the geometric average of the probabilities of all recordings. The ASD at-risk identification is done by comparing the probability to a threshold.

Results: Two datasets were examined. Set-1 includes 76 TD children (712 recordings), 30 LD children (290 recordings) and 34 AD children (225 recordings). An independent Set-2 includes data from 30 TD children (90 recordings), 12 LD children (36 recordings) and 45 AD children (132 recordings). All AD children were formally diagnosed with ASD. Three detection tasks were tested: 1) AD versus TD; 2) AD versus LD and 3) AD versus TD+LD. Performance was evaluated via "leave-one-out-cross-validation" which is commonly used in pattern recognition and machine-learning research. For the LDA method using leave-one-CHILD-out-cross-validation, the equal-error-rates (EER) for each task are reported below in the exact order as above. For the recordings in Set-1, the EERs are 11.5%, 15.5% and 12.6% respectively. By including Set-2, the EERs become 11.7%, 16.3% and 12.6% correspondingly. For children in Set-1 (with multiple recordings), the EERs are 9.2%, 10.0%, 9.4% respectively. By including Set-2, the EERs become 8.9%, 12.7% and 10.8% correspondingly. Analyses utilizing other modeling methods yielded similar results.

Conclusions: Results for independent data sets and using different methods consistently show that child vocalization composition contains rich information for identification of children at-risk for ASD. We discuss the possibility of improving the performance by incorporating the modeling of other child

vocal behaviors through audio recording, and the potential of these results and methodology for early ASD screening.

105.030 30 Communicative Repair Skills in Boys with Autism and Fragile X Syndrome. R. L. Cardwell*[1], G. E. Martin[2] and M. Losh[2], (1)*UNC Chapel Hill*, (2)*University of North Carolina at Chapel Hill*

Background: The ability to repair breakdowns in communication is highly important for children with language deficits, as communicative breakdowns are likely to occur due to phonological, grammatical, or pragmatic difficulties. There is some evidence that individuals with autism have difficulty repairing breakdowns in communication (Geller, 1998; Volden, 2004). Fragile X syndrome (FXS) is the most common known genetic cause of autism. Individuals with FXS also show difficulties in conversational discourse, which may be attributable to comorbid autism (Roberts et al., 2007), although repair skills have not been previously investigated in this population, and so comparisons between children with autism and FXS on this key aspect of pragmatic language are lacking.

Objectives: This study examined communicative repair skills of boys with autism and boys with FXS in order to identify potentially overlapping profiles in this aspect of pragmatic language.

Methods: A structured task tapping communicative repair ability was administered to boys with autism only (n=11), FXS with autism (FXS-A; n=12), and FXS only (FXS-O; n=15), as well as a group of younger typically developing controls (n=11). Boys were asked to describe a set of cartoon pictures. For predetermined pictures, the examiner initiated a stacked sequence of neutral requests for clarification (i.e., Huh?, What?, I didn't understand) using procedures described by Brinton et al. (1986). Boys' responses were coded for repair strategy used – no response, repetition, revision (e.g., changing word order), addition (of new information), and inappropriate (e.g., off-topic responses).

Results: Statistical analyses controlled for nonverbal mental age and expressive vocabulary skills. Surprisingly, boys with FXS-A repaired the communicative breakdown by adding new information significantly more often than did boys with autism only (51% vs. 43%). Results also revealed many similarities across groups. For all groups, addition and repetition were the most common repair strategies used, with the other strategies occurring less often. Further, all groups varied repair strategies as the breakdown persisted. Finally, boys in all groups were more likely to respond inappropriately or not respond at all to repeated requests for clarification compared with the first request.

Conclusions: The similarity across groups in repair ability suggests that this aspect of pragmatic language may represent a relative strength for boys with autism and FXS. Findings also suggest that communication partners should limit neutral requests for clarification to one or two, since repeated requests may be met with inappropriate or no responses. We continue to examine communicative repair skills in our samples, and will be presenting data on additional children in each group.

105.031 31 Embarking On the Journey through Pediatric Transplantation with An Autistic Child. M. A. Peralta* and A. M. L. Lefebvre, *The Hosptial for Sick Children*

Background: Children and adolescents with Autism and Autism Spectrum Disorder have a "triad of impairments (Hartley, Sikora & McCoy, 2008, p. 819)," including deficits in communication, in social reciprocity, or behaviours that are repetitive with restrictive interests (Hartley, Sikora & McCoy, 2008). Sometimes these children display maladaptive behaviours, such as obsessions and/or anxiety that can interfere with interventions like medical procedures. Children with chronic medical illness, particularly organ failure, who require organ transplant, have their own emotional challenges. These children tend to worry more, are more socially isolated, have increased school absenteeism and maladjustment. Non-adherence to treatment is a huge challenge for this population and their caregivers (Berney-Martinet, Key, Bell, Lepine, Clermont & Fombonne, 2008). It has

been demonstrated that children with low self-esteem, poor social skills, challenging behaviours and cognitive defficits are particularly at risk for non-adherence. Children who have Autism Spectrum Disorders and happen to require a transplant face double challenges that interfere with medical intervention and adherence to treatment. The transplant process involves multiple invasive procedures that cause cumulative stress with little opportunity for recovery in between procedures. Furthermore, it is difficult to communicate with these children and explain why such multiple invasive procedures are necessary. Anxiety, communication deficits and cognitive impairments contribute to maladaptive behaviour, such as withdrawal, anger, and aggression; busy transplant professionals with limited experience with ASD symptoms have no idea how to handle these children/adolescents.
Objectives: To answer the following questions:
1) How can a child with ASD be involved in the transplant process?
2) How does a transplant team prepare a child with ASD for transplant? (a case example will be discussed)
Methods: Our interdisciplinary team, led by medical psychiatry, embarked on a project to create guidelines to support patients undergoing transplants. The outcome of this process was the creation of an individualized tool-kit that has guided the Nephrology team in providing supportive carefor a patient with symptoms of ASD who required a kidney transplant.
Results: This patient's kidney transplant was successful. The child's symptoms actually improved post-transplant, rather than his experiencing further regression and the interdisciplinary team now feels much more comfortable dealing with patients with ASD.

Conclusions: From this case an individualized toolkit was created and piloted successfully. A generic toolkit has been created for patients with ASD spectrum disorders. A guideline and toolkit are being developed for use with other transplant populations presenting with any challenging behaviours.

105.032 32 Factors Influencing Knowledge about Childhood Autism Among Final Year Medical, Nursing and Psychology Students in Enugu, Nigeria. M. N. Igwe*[1], M. O. Bakare[2], G. M. Onyeama[1] and K. O. Okonkwo[1], (1)*Department of Psychological Medicine, University of Nigeria Teaching Hospital Enugu, Nigeria*, (2)*Federal Neuro-Psychiatric Hospital, New Haven, Enugu, Enugu State, Nigeria*

Background: Knowledge and awareness about childhood autism is low among health care workers and the general populace in Nigeria and other Sub-Saharan African countries. Poor knowledge and awareness about childhood autism, especially among final year medical, nursing and psychology students who would form tomorrow's child health professionals can compromise early recognition and interventions that are known to improve prognosis in children with childhood autism. Educational factors that could be influencing knowledge about childhood autism among these students are unknown.

Objectives: This study assessed knowledge about childhood autism among these final year students and determined the associated factors.

Methods: A total of 300 consented final year students were interviewed with socio-demographic and knowledge about childhood autism among health workers (KCAHW) questionnaires. One hundred final year students were randomly selected from each of the departments of medicine and surgery, nursing sciences and psychology respectively of University of Nigeria, Nsukka, Nigeria. The Knowledge about childhood autism among health workers (KCAHW) questionnaire is a nineteen item self-administered questionnaire that is divided into four domains. Results: Total mean score for the three groups on KCAHW questionnaire was 10.67 ± 3.73 out of a possible total score of 19. Mean score for the three groups showed statistical significant difference for domain 1 (impairment in area of social interaction, $p = 0.000$), domain 3 (area of repetitive and compulsive pattern of behaviour, $p = 0.029$), domain 4 (type of disorder, possible co-morbid conditions and usual time of onset of childhood autism, $p = 0.000$) and total score, with medical students more likely to recognise symptoms and signs of autism compared to nursing and psychology students. Mean score in domain 2 did not

show statistical significant difference among the three groups (p = 0.769). The total score on KCAHW is positively correlated with number of weeks of posting in psychiatry (r = 0.316, p = 0.000) and number of weeks of posting in paediatrics (r = 0.336, p = 0.000). Total score on KCAHW is also positively correlated with credit hours of lectures in psychiatry/abnormal psychology (r = 0.298, p = 0.000) and credit hours of lectures in paediatrics (r = 0.336, p = 0.000). Field of study is the only socio- demographic variable that showed a statistical significant difference on total score of KCAHW questionnaire (p = 0.000).

Conclusions: Modifications in academic programmes for medical, nursing and psychology students in terms of increased duration of clinical postings and lectures in psychiatry and paediatrics is advocated for improved recognition of childhood autism by these future child health care professionals.

105.033 33 Maternal Language Directed to CHILDREN with AUTISM Spectrum Disorders, DOWN Syndrome and Typical DEVELOPMENT. S. De Falco*[1], G. Esposito[1], M. Zaninelli[1], M. H. Bornstein[2] and P. Venuti[1], (1)*University of Trento*, (2)*National Institute of Child Health and Human Development, National Institutes of Health, Department of Health and Human Services*

Background: Parental speech directed to their children is crucial for their development in many ways. During parent-child interaction, language is among the most relevant means the parents use to convey both affect and information. As a result, child directed speech as been thoroughly investigated in typical development, and associations between parent speech and child language, social, and emotional development emerge consistently in the literature (Bornstein & Lamb, 1992; Garton, 1992; Hampson & Nelson,1993; Thiessen, Hill, & Saffran, 2005). However, the characteristics of parental speech to children with intellectual disabilities is far less well documented (but see Longobardi, Caselli & Colombini, 1998; Spiker, Boyce & Boyce, 2002).

Objectives: The aim of the present study was to compare the functional characteristics of maternal language directed to children with Autism Spectrum Disorder, Down syndrome and typical development of the same developmental age.

Methods: Participants were 60 mothers and their children with ASD (n =20), Down syndrome (n =20) or typical development (n =20). Children's mean developmental age was 24.77 months (*SD* = 14.45) and did not significantly differ across groups. The diagnosis of ASD was confirmed based on the Autism Diagnostic Observation Schedule (ADOS - Lord, Rutter, DiLavore, &. Risi, 1998). The Bayley Scales of Infant and Toddler Development (2nd ed., Bayley, 1993) was used to determine child developmental age. The mothers' child directed speech was studied through 10-min observation of joint play interactions. Word-for-word transcripts were made of maternal language using the CHAT system (MacWhinney, 2000). Maternal speech was categorized in terms of the primary function of each utterance, using a coding scheme validated in previous studies of maternal speech that highlighted its appropriateness across cultures (Venuti er al, 1997; Rossi et al., 1998; Bornstein et al., 1992)

Results: Both mothers of children with ASD and Down syndrome used more directives and less questions compared to mothers of typically developing children. Moreover, these mothers named their children more often than mothers of typically developing children. Also, mothers of children with ASD referred more often to themselves than the mothers in the other groups. Finally, mothers of children with Down syndrome used more affective-salient language compared to mothers with ASD and typical development.

Conclusions: Verbal interactions between parents and children with ASD and Down syndrome, show some non-optimal features that might profitably be targeted for early intervention with foci not only on specific child skills but also on parent-child language interaction; such programs may help the parents recognize effective ways of speaking with their children which in turn might facilitate their language acquisition (Venuti, 2007).

105.034 34 Request for Social Interaction in Prelinguistic Milieu Teaching for Young Children with Autism. H. Kinugasa* and S. Sonoyama, *University of Tsukuba*

Background: Prelinguistic Milieu Teaching (PMT) is an intervention that teaches early intentional communication acts composed of gestures, coordinated eye gaze, vocalizations, to increase a child's rate and complexity of intentional communication prior to learning language. This intervention focuses on shifting function from initiating behavior request (IBR) to initiating joint attention (IJA). Few studies have showed change in IBR for social interaction from instrumental use of others into sharing the intentionality.

Objectives: To assess joint attention skills through building social routine to elicit children's request for social interaction in PMT.

Methods: Three children with autism (age 4-5) with 5 or less functional words received PMT once a week at university clinic session. Participants were assessed using the Early Social Communication Scale (ESCS) and the Japanese MacArthur Communicative Development Inventory (JCDIs) at pre- and post-intervention. In PMT, a participant requested other's behavior in a social routine which could not be achieved by one. When the target behavior based on ESCS at pre-intervention increased its rate in PMT, it was gradually modified into more complex behavior.

Results: Preliminary results suggest that frequency and complexity of behavior request increased across PMT, as well as joint attention skills in ESCS increased.

Conclusions: The social routine in PMT made children with autism easier to predict what would happen next after their IBR as well as to show expectation toward other's behavior.

105.035 35 The Experiences of Latina Mothers During the Diagnosis of ASD in Their Children. S. K. Dickson* and E. Giarelli, *University of Pennsylvania*

Background: Previous research has shown that Latino children are diagnosed on average two years later than Caucasian children. Factors influencing delayed diagnosis include limited access to services, cultural expectations, and parents' perceptions of disability. The mothers' perspective on autism, in particular, affects the process. Data from this study could inform ways to improve awareness to the Latino community and modify resources.

Objectives: The primary objective is to describe the experiences of Latina mothers during the diagnosis of her child with an ASD. The specific aims of this study are to: 1) describe the challenges that Latina mothers face as they access diagnostic and treatment services; and 2) identify cultural influences on the process of seeking a diagnosis, type of social support, and access to treatment.

Methods: This qualitative study used thematic analysis. Data were collected by semi-structured telephone interviews with Latina mothers. The interviews focused on the mother's story of her child's diagnosis and her account of accessing care. The specific outcome variables include factors affecting the decision to seek a diagnosis, knowledge of autism before and after diagnosis, support networks, and barriers to accessing care.

Results: Thirteen Latina mothers between the ages of 30 and 41 (mean age 36.3 yrs) were interviewed. Their children ranged in age from 5 to 10 (mean age 6.9 yrs) (4 girls and 9 boys). Thematic analysis generated three thematic categories: 1) mother's knowledge of autism 2) the role of communication with family, the community, doctors and school and 3) gender expectations. For most mothers (n=13, 85%) the diagnosis of ASD for their child was their first significant encounter with autism and awareness of autism was limited in their community, particularly among their parent's generation and extended families in Latin America. All mothers used the internet as a primary source of information about ASD. Following the diagnosis of ASD, all mothers expressed that communication between herself and her family and/or community had broken down. Mothers reported feelings of isolation and depression and more difficulties

communicating with doctors and teachers. Finally, the gender expectations of having a son presented as a significant factor in coping with the diagnosis in (n=9, 56%) participants with sons.

Conclusions: Preliminary analysis shows that Latino culture has an influence on the experiences of Latina mothers during the diagnosis of their child with autism. Limited understanding of autism among extended families weakened the support networks on which Latina mothers rely and impaired supportive communication. Finally, gender expectations for an affected son appear to influence both the diagnosis of autism and the subsequent adjustment to the diagnosis. Analysis is ongoing.

105.036 36 The Use of a Digital Language Processor to Examine the Effectiveness of a Parent-Training Aimed at Improving the Language Learning Environments of Children with Autism. S. Patterson* and V. Smith, *University of Alberta*

Background: There is evidence that parent-training programs are effective in improving the communication and language skills of young children with language delay (Law, Garrett, & Nye, 2004). However, we know very little about the language learning environments of young children with autism spectrum disorder (ASD) and whether parent-training programs are effective in enhancing language development for these children. The purpose of this pilot study was to examine the viability of utilizing a digital language processor (DLP; Infoture, 2006) to explore the effect of parent-training on the interactions between parents and their toddlers with ASD. In order to obtain child communicative data in the child's natural environment and lessen the confounding factors presented by artificial laboratory situations, the DLP allows for data capture in unstructured environments (Gilkerson & Richards, 2009). However, this technology has not been used to assess the effect of parent communication training.

Objectives: Specific questions addressed in this pilot study include: (1) what is the base frequency and amount of communicative interaction between toddlers with autism and their parent(s)? (2) to what degree does a parent education program influence the nature and frequency of communicative interactions?

Methods: Seven families and their children (age 29-39 months) were recruited from a local agency providing the More Than Words (MTW) program (The Hanen Centre, 2007), a parent-training program in early language development. Parent-child interaction data were collected over a four month period including measures prior to, during, and immediately after participation in the parent-training program as well as at two month follow up. The DLP was utilized to obtain estimates of the following: (a) number of adult words, (b) number of child vocalizations, and (c) number of conversational turns.

Results: Children entered the study with developmental ages ranging from 6m to 32m and on average gained 9m in developmental age. Frequency of adult communication did not appear to be related to the child's level of expressive language. Families demonstrated a range of communicative frequencies from approximately 5400 to nearly 21000 adult words spoken and from approximately 180-680 conversational turns across a 12 hour day. Overall, families with parents of higher levels of education (i.e., advanced degrees) engaged in higher daily talk frequencies. Patterns of family talk across the child's day differed between families but were found to remain relatively constant within families across time points. The majority of families demonstrated increased communicative frequencies immediately post engagement in parent training. Few families demonstrated maintenance of these gains at two-month follow up.

Conclusions: Results revealed a wide variability in both base frequencies of communicative interaction and response to the parent-training program. The results of this study will add to our understanding of the use of DLP technology to capture the effects of early language parent-training programs. This study is currently being extended to explore whether providing families with feedback regarding the amount and pattern of their daily communicative

interactions using the data collected from the DLP, will increase parents' use of language facilitation strategies provided in the MTW program.

105 Imitation

105.037 37 The Influence of Goals On Movement Kinematics and Eye Movements During Imitation in Autism. K. S. Wild*, E. Poliakoff and E. Gowen, *University of Manchester*

Background: It has been reported that individuals with autism have reduced imitation abilities, specifically when the action to be imitated does not have a goal (Hamilton 2008). Imitation is a process which is important in learning how to communicate, and understand others, and therefore may have implications for understanding autism. It has been proposed that reduced imitation abilities in autism may be a result of impaired sensory motor integration (Gowen and Miall 2005), which may have a greater effect on the direct visuomotor mapping of novel, non-goal actions, than on actions directed towards a goal, which may rely more heavily on stored representations.

Objectives: To investigate the influence of visual goals on movement kinematics and eye movements, during imitation in autism.

Methods: Sixteen adults (mean age 30.63 ± 7.9 yrs, 5 females) diagnosed with Autism or Asperger Syndrome, along with sixteen age, sex and IQ matched controls took part in an imitation experiment. Participants were required to observe, and then imitate, movie clips of hand movements, which were either directed towards goals, or towards nothing (no-goals). Goal and non-goal movements were displayed in separate blocks, each made up of movements which varied in speed (slow/fast), size (normal/short) and trajectory (flat/elevated). Hand movements were recorded using a magnetic Polhemus motion sensor, which was attached to the index finger of the dominant hand, recorded at 120 Hz. Eye movements were recorded using an Eyelink II head-free eye tracker, and were recorded at 250 Hz. The degree to which participants modulated their own movement parameters with changes in the observed movement was investigated.

Results: Movement duration was not adjusted when goals were present; both groups performed movements of similar duration during slow and fast trials. When goals were absent, however, the control group exhibited longer movement durations in slow trials compared to fast trials, but the autism group did not differ. The same pattern was found for the average peak velocity of the movement. In measures of movement amplitude, the autism group performed better than the control group, showing a larger difference in movement size between short and normal trials. Eye movement data showed that the autism group spent a significantly longer time looking at target areas, and significantly less time between targets, in both goal and no goal trials.

Conclusions: The results show that people with autism are able to successfully imitate aspects of goal-less actions, namely the start and end-points of movement, which are perhaps attributed goal status in order to be imitated. In contrast to the control group, kinematics inherent in the movement, such as duration and velocity, were not successfully modulated in the autism group during goal-less imitation. Eye data indicates that the autism group spent more time looking at goal areas, even in the non-goal condition. This implies that people with autism do not switch to the direct visuomotor pathway for the imitation of goal-less action, supporting the idea that the route may be impaired as a result of deficient integration of visual information with the motor system.

105.038 38 Differences in Imitative Synchronicity in Children with High Functioning Autism (HFA) and Children without Autism Spectrum Disorders (ASD). P. Rao*, A. Faherty and R. Landa, *Kennedy Krieger Institute*

Background: An important component of social engagement involves a synchronicity of ‘body language’ between communicative partners. One measure of a child’s ability to synchronize body language with others is the ability to imitate the quality of others’ actions (imitative synchronicity). Children with ASD have been found to have difficulties with tasks that require Imitative synchronicity (IS). The literature suggests that some of these difficulties may be related to low

nonverbal IQ and social communicative impairments.

Objectives: The purpose of this study was to examine differences in IS in children with and without ASD, and to investigate the relationship between IS and social communication functioning.

Methods: Participants were 111 children, aged 4 to 8 years, participating in a longitudinal study of child development beginning in infancy. Children with ASD (n=44; mean age=5.5 years; mean NVIQ=98) and without ASD (n=67; mean age=5.2 years; mean NVIQ=109) were included. The non-ASD group had significantly higher NVIQ than the ASD group ($p<0.001$). Children with ASD whose NVIQ was below 70 were excluded from the analysis.
IS was assessed using an adaptation of Hobson and Lee's (1999) paradigm. Examiners demonstrated the novel use of four sets of objects in randomly varying order across subjects. Following a 10-minute interval, children were instructed to "use" the objects. Sessions were videotaped and later coded blind to group membership. To measure IS, a 'matching score' was generated for each task on a five point scale, with higher scores reflecting a greater quality in degree of matching the examiner's movements. The IS dependent variable was calculated by summing the scores for all four tasks. Other dependent variables included the Stanford-Binet V nonverbal IQ score (NVIQ) and the Social +Communication algorithm score from the Autism Diagnostic Observation Schedule.
Results: The ASD group was significantly less likely than the non-ASD group to match the quality of the examiner's actions [$t(2,109)=-2.05$, $p<0.05$]. Within group correlational analyses using NVIQ and social communication scores determined that NVIQ was not correlated with IS in either group. However, IS was significantly negatively correlated with social communication scores (lower scores indicate less impairment) for the non-ASD group only [$r(67) = -0.26$, $p < 0.05$]. Given this finding, we hypothesized that fine motor difficulties may interfere with IS in the ASD group. Using the Mullen Fine Motor standard score obtained from the subjects' 36-month assessment, we found that fine motor functioning at 36 months of age predicted future IS performance in the ASD group only [$F (1,43) = 4.4$; $p < 0.05$].

Conclusions: Consistent with previous research, children with HFA demonstrated IS impairments as compared with children without ASD. Contrary to other studies, nonverbal IQ was not related to IS in either group of children and social communicative functioning was related to IS in the non-ASD group only. For the ASD group, fine motor difficulties at 36 months of age predicted IS impairment at a later age. Thus, this study suggests that motor skill impairments may adversely affect IS in children with HFA.

105.039 39 The Impact of Familiarity On Imitation of Hand Gestures and Face Expressions in Autism Spectrum Disorders. B. Aaronson* and R. Bernier, *University of Washington*

Background: Imitation is a primary deficit associated with autism spectrum disorder (ASD). As reviewed by Williams et al. (2004), this deficit has been demonstrated in a variety of imitation contexts, including meaningful and non-meaningful gestures, sequential imitation, actions on objects, as well as spontaneous and differed imitation.
Objectives: The first aim is to investigate the impact of familiarity on imitative ability, by assessing participant imitation of a parent or guardian versus a stranger. The second aim is to investigate the consistency of imitation impairment across hand gestures and face expressions.
Methods: Imitative ability was assessed in a sample of children (mean= 6.4, SD=1.2) with an autism spectrum disorder (N=18) and typical development (N=22) participating in an ongoing study of imitation. Imitation of hand gestures and face expressions, modified from the Mature Imitation Task (Rogers et al., 2006), were pre-recorded and displayed on a video screen. The task included the presentation of 8 face expressions and 8 hand gestures, half of which were executed by the participant's mother or guardian, with the remaining gestures executed by an individual unfamiliar to the participant. Imitative acts were then

scored offline by a coder blind to subject status.
Results: Preliminary analysis reveals differences between the typical and ASD groups, with the ASD group performing significantly poorer than typical group on all imitation measures ($p<.000$). Differences in type of imitative act (hand or face) were found, with ASD individuals scoring significantly poorer on hand imitation than facial imitation ($p<.05$), while no significant differences were found between imitative acts in typical individuals. In this preliminary analysis familiarity of model did not impact imitation ability across groups, although group differences approached significance ($p=.07$).
Conclusions: Our results are consistent with previous findings demonstrating a deficit in imitation ability among individuals with ASD. Our findings further indicate an inconsistency across type of imitative act (hand or face) within the ASD group, showing a greater deficit in hand gesture imitation. Ostensibly, this finding is counterintuitive considering well-documented deficits of face processing in ASD. However, typical children may better utilize the opportunity for visual self-correction available during hand imitation than do children with autism. Future analyses will assess time engaged in self-corrective behavior during the imitative act.

105.040 40 Prevalence of Early Imitation Problems and Its Risk Factor for Autism. M. Vanvuchelen*[1], H. Roeyers[2] and W. De Weerdt[3], (1)*Katholieke Universiteit Leuven - PHL University College - Vrije Universiteit Brussel, Belgium*, (2)*Ghent University*, (3)*Katholieke Universiteit Leuven*

Background:

There is a growing body of research suggesting that young children with ASD have imitation difficulties. However, the prevalence of early imitation problems and its risk factor for ASD at preschool age is unknown.

Objectives:

To establish imitation retardation in preschoolers suspected of ASD using a cohort type diagnostic accuracy study design.

Methods:

86 children (aged 1.9-4.5 years) suspected of autism and consecutively referred to University Autism Clinics in Flanders (Belgium) participated in this study.

A multidisciplinary clinical consensus classification revealed 68 children with ASD and 18 children with Non-Spectrum Developmental Disorders (NS-DD). The two groups did not differ significantly in chronological and nonverbal mental age.

Differences between imitation, language, motor age-equivalents and nonverbal mental age were used to predict the diagnosis of autism.

Bodily (gestures and facial expressions) and procedural (actions with objects) imitation levels were determined with the Preschool Imitation and Praxis Scale (PIPS; Vanvuchelen, 2009).

The PIPS consists of 30 actions with different effects (salient environmental and internal), representational levels (meaningful and non-meaningful, goal directed and non-goal directed), temporal complexities (single and sequential) and visual monitoring possibilities (transparent and opaque).

Bodily and procedural imitation age-equivalent scores were derived from PIPS scores of 654 typically developing children between 1 and 4.9 years of age.

Receptive and expressive language levels were examined with the Dutch version of the MacArthur-Bates Communicative Development Inventories (N-CDI; Zink & Lejaeghere, 2002) and the Reynell Developmental Language Scales (RTOS; Schaerlaekens, Zink, & Van Ommeslaeghe, 2003).

Gross and fine motor levels were determined with the Peabody Developmental Motor Scales-2 (PDMS-2; Folio & Fewell, 2000).

The nonverbal mental level was examined with the Dutch version of the Bayley Scales of Infant Development (BSID-II-NL; Van der Meulen, Ruiter, Lutje Spelberg, & Smrkovsk_, 2000) and the Revised version of the Snijders-Oomen Nonverbal Intelligence Test

for Children (SON-R 2.5-7; Tellegen, Winkel, Wijnberg-Williams, & Laros, 1998).

Results:

There is evidence for bodily and procedural imitation retardation in relation to nonverbal mental age in 72%, respectively 69% of the preschoolers with ASD.

Two factors were found to be significantly associated with ASD using simple logistic regression analyses: procedural imitation [OR 1.07 (95% CI: 1.01-1.13)] and receptive language retardation [OR 1.08 (95% CI: 0.99-1.16)].

Using the optimal cut-off for the procedural imitation retardation score based on the Receiver Operating Characteristic (ROC) curve yields a sensitivity of 82% (95% CI: 71%; 90%) and specificity of 50% (95% CI: 26%; 74%).

In a multivariate model, only procedural imitation retardation remained a significant predictor of ASD [OR 1.21 (95% CI: 1.05-1.40)].

Conclusions:

Findings suggest that retardation in procedural imitation that goes beyond the nonverbal mental retardation may predict the diagnosis of autism.

Results are new to the literature and therefore require replications in other settings.

105.041 41 Intact Imitation of Emotional Facial Actions in Autism Spectrum Conditions. C. Press*[1], D. Richardson[1] and G. Bird[2], (1)*University College London*, (2)*Birkbeck College, University of London*

Background:

Some have proposed that the core impairment in individuals with ASC is to a system which maps sensory and motor representations of action (the 'broken mirror hypothesis'). Impairments in this system may result in those with ASC being unable to infer intentions and mental states of others, if observed actions cannot be translated into the motor codes used to perform those actions. However, evidence for this hypothesis is mixed, with some studies finding sensory-motor mapping impairments in ASC and others finding intact mapping.

The studies which have and have not demonstrated impaired sensory-motor mapping tend to differ in two respects. First, the studies which have found impairments have used simple action observation tasks, where actions are observed and incidental motor activations are recorded. In contrast, the studies which have found no impairments have implemented motor tasks dependent on observed actions, and measured the degree to which observing action primes execution of matching action. Second, the studies finding impairments have tended to use facial actions, while the studies which have found no impairments have used manual actions.

Objectives:

The present study investigated whether it is the task or the effector that determines whether sensory-motor mapping impairments are observed in ASC, to gain a better understanding of whether those with ASC have any impairment to sensory-motor mapping systems. Adult participants with ASC, and age-, gender-, and IQ-matched control participants, were required to perform a facial motor task dependent on observed facial actions. If impairments were found, this would suggest that the effector determines whether impairments are observed, and if impairments were not found, the task is more likely to be responsible for these differences.

Methods:

Participants watched stimuli of the upper or lower half of the face. The face first appeared in a neutral posture, and after a period the eyebrows would raise or lower (upper half) or the mouth would open or close (lower half). Participants were required to execute a pre-specified response (e.g. raise their eyebrows) whenever the face moved. This generated trials where the response was compatible with the observed movement (eyebrows lifting) and trials where

the response was incompatible (eyebrows lowering). The reaction time (RT) on compatible trials was subtracted from the RT on incompatible trials to obtain a measure of the degree to which the observed action primed its execution ('automatic imitation'), and therefore, the strength of the sensory-motor mapping.

Results:

Those with ASC demonstrated 'automatic imitation' of both eyebrow and mouth actions, comparable with effects seen in the control group.

Conclusions:

Intact imitation of facial actions in the present study indicates that previous findings of sensory-motor mapping impairments in ASC may be driven by the task used. Specifically, requiring participants simply to observe actions while measuring motor activations may have generated apparent impairments to this system if those with ASC were not actually observing the actions. These findings suggest that those with ASC do not have 'broken mirrors' mapping sensory and motor representations of action, and that their core impairments lie elsewhere.

105.042 42 Social Responses of Children with Autism to Attention and Imitation. C. McCormick*[1], G. S. Young[2], A. Herrera[3], T. Oden[2] and S. J. Rogers[2], (1)*M.I.N.D. Institute, University of California Davis*, (2)*M.I.N.D. Institute, University of California at Davis*, (3)*University of Minnesota*

Background: Children with autism are characterized by a lack of socially responsive and initiative behaviors, including a deficit in eye contact. Some studies have documented that children with autism respond with increased social behaviors, such as gesturing and proximity, when an adult imitates their actions as opposed to other forms of interactive play. However there is some research indicating that children with autism do not respond as well to other forms of attention and at the extreme have adverse reactions to eye contact.

Objectives: The aim of this study was to investigate the responses of children with autism when an adult attends to the child during play compared to being ignored or imitated. We hypothesized that children with autism would be similarly unresponsive to being ignored and receiving attention, in comparison to being imitated which would increase their social behaviors.

Methods: Participants included 20 children with ASD (18 male, 2 female) with an average chronological age of 41 months and 13 children with typical development (8 male, 5 female), with an average chronological age of 24 months. The groups were matched on non verbal mental age. All children sat across a table from the experimenter and were given a set of toys to play with. The protocol consisted of three conditions for interaction between the child and experimenter: 1. the experimenter ignored the child's activities, 2. the experimenter showed interest in child's play with eye-contact and non-directive comments, 3. the experimenter imitated the play and vocalizations of the child. Each condition was one minute long and was administered in the above set order. All conditions were coded for frequency of social bids of the child including giving, showing, pointing and looks to the experimenter's face.

Results: Social bids were collapsed within each condition. A group by condition repeated measures ANOVA was evaluated using a Greenhouse-Geiser correction due to a lack of sphericity. The ANOVA yielded a significant group effect ($F_{(1,31)}$= 10.422, $p<.01$), with the typical group exhibiting significantly more social bids overall (M=16.1, SD=8.9) than the group with ASD (M=7.5, SD=6.3). A significant main effect of condition ($F_{(1, 31)}$= 14.284, $p<.001$) was also found. Examination of helmert contrasts for condition revealed that the ignore condition was significantly different than the combined attention and imitation conditions $t_{(1,31)}$=35.188, $p<.001$, but there was no difference between the attention and imitation conditions ($t_{(1,31)}$=.55, p=.46). The interaction effect between group and condition was not significant ($F_{(2,62)}$=.82, p=.42).

Conclusions: Our results contradict the hypothesis that children with autism would not respond similarly to interest and imitation from the examiner. Our findings revealed that although children with autism engaged in fewer social behaviors overall than mental age matched peers with typical development, the children with autism, as well as those with typical development, responded as strongly to social attention as they did to being imitated. This implies that young children with autism, like those with typical development, find simple noncontingent social attention, involving gaze and language, rewarding, and that they discriminate attention from non-attention.

105.043 43 Spontaneous Imitation and Social Synchrony in 24-Month-Old Toddlers with Autism Spectrum Disorders. T. V. Barker* and R. Landa, *Kennedy Krieger Institute*

Background: Research has consistently demonstrated that preschool and school-aged children with autism spectrum disorders (ASD) show marked deficits in their ability to imitate. The importance of imitation in early development is evident in its relationship with language, play, and social functioning. Given the important role that imitation plays in social functioning for older children with ASD, very early spontaneous imitation ability may play a pivotal role in a child's ability to engage with others in a synchronized way. This study is the first to examine correlates of spontaneous imitation in 24-month-old toddlers with ASD.
Objectives: 1. Do 24-month-old toddlers with ASD spontaneously imitate during semi-structured play with an unfamiliar adult? 2. If so, what is the relationship between the quality of imitation and overall social synchrony with others, as well as concurrent fine motor skills and nonverbal cognition?
Methods: Seventeen toddlers (mean age=24.4 months) participated in a prospective, longitudinal study of infant siblings of children with autism. Participants in this imitation study received ASD diagnosis at 36 months of age based on gold standard diagnostic criteria (ADOS, ADI, & expert clinical judgment). The measures for spontaneous imitation were extracted from videotaped footage of an adapted version of the Communication and Symbolic Behavior Scales Developmental Profile (CSBS DP; Wetherby and Prizant, 2002). At specified times during the CSBS DP, the examiner modeled simple play actions with objects, then placed the object within the child's reach without providing verbal instructions. The child's actions on the object were scored based on how closely the action matched the model. The measures of fine motor and nonverbal cognitive ability were obtained from the Fine Motor (FM) and Visual Reception (VR) scales, respectively, of the Mullen Scales of Early Learning (Mullen, 1995). Social synchrony was measured by clinician ratings on the ADOS Social Reciprocity algorithm at the 24-month assessment.
Results: Results revealed that 94% of the toddlers demonstrated imitative behavior, spontaneously imitating on average 37% of the models that they observed (Range= 0-86%). To explore the social influences of spontaneous imitation, a zero-order correlation was conducted between the frequency of spontaneous imitation and the total score on ADOS Social Reciprocity algorithm. After controlling for VR, there was a significant negative relationship ($r(14)=-.43$, $p>.05$) between the variables, where higher Social Reciprocity scores (more deviance from the norm) was negatively related to spontaneous imitation. To examine whether FM and VR could account for qualitative differences in imitation ability, children were divided into two groups based on the proportion of models imitated ("High Imitators" ≥ 40%, "Low Imitators"<40%). A Mann-Whitney U test revealed no differences in FM or VR *t*-scores between High Imitators and Low Imitators.
Conclusions: There is great variability in the frequency of spontaneous imitation in toddlers with ASD, and this variability appears to be unrelated to fine motor ability and nonverbal cognitive ability during the early phases of development. In addition, the frequency of spontaneous imitation was related to clinician's ratings of social reciprocity, which we interpret as self-other synchronization.

105.044 44 Imitation Abilities in Children with Autism Spectrum Disorders Correlate with Autism Severity but Not with Motor Skills. I. Tzaig[1], E. Ben Itzchak*[2] and D. A. Zachor[3], (1)*Bar*

Ilan University, (2)*Ariel University Center of Samaria*, (3)*Tel Aviv University / Assaf Harofeh Medical Center*

Background:

Imitation plays a significant role in the early social development of infants and toddlers. Impaired performance in a range of imitation tasks has been described in children with autism spectrum disorders (ASD). Several possible mechanisms underlying imitation deficits in ASD have been proposed. Of these, the extent of social-reciprocal interaction and responsiveness deficits, cognitive level and motor development problems appear to affect imitation development the most.

Objectives:

1.To examine whether imitation abilities in ASD correlate with autism severity and gross and fine motor skills. 2. To examine imitation abilities in children with ASD by comparing their performances in two imitation types i.e. body movements and 'action on objects, using meaningful and non-meaningful tasks. 3. To evaluate whether performance in these four imitation situations is related to the severity of autism symptoms or to motor abilities.

Methods: Twenty-five children aged 32-51 months (M=40.0, SD=5.7) were diagnosed with autism (23) and ASD (2) using the Autism Diagnosis Interview-Revised and the Autism Diagnosis Observation Schedule (ADOS). Autism severity was evaluated using The ADOS new algorithm and the socio-communication total scores and repetitive and restrictive behaviors (RRB) total scores. Cognitive abilities were assessed using the Mullen scales; gross and fine motor skills were examined by the Peabody Developmental Motor Scales; and imitation abilities were assessed using items from the Motor Imitation Tasks (MITs).

Results: Controlling for cognitive level, the new ADOS algorithm that measures overall severity of autism symptoms correlated significantly only with meaningful imitation situations. Looking at the specific autism domains, imitation abilities in all four situations correlated significantly only with socio-communication deficits and not with RRB scores. Gross and fine motor abilities were generally below average in the examined group and did not correlate with imitation abilities or with autism severity. Comparison of the four imitation situations revealed that performances of meaningful actions were better than non-meaningful actions ($p<.001$), and imitation of 'action on objects' was better than imitation of body movements (almost reaching significance). When the entire group was divided into two autism severity subgroups, low and high ADOS groups (based on the new ADOS algorithm median scores), a significant autism severity effect ($p<.05$) was found. The group with less severe impairments had better imitation scores than the group with more severe autism symptoms. No autism severity x imitation situation interaction was found, meaning that the low ADOS group performed better than the high ADOS group in all the imitation situations. Investigating the differences in imitation abilities of low and high gross and fine motor skills groups (scores above or below the median on the Peabody Motor scales), revealed no gross or fine motor ability effects on imitation skills.

Conclusions:

Imitation is a complex developmental skill that requires intact motor, cognitive and social abilities. The present results suggest that out of several possible mechanisms that could underlie imitation deficits in ASD, the social reciprocal impairments are mostly associated with imitation performance.

105 Language

105.045 45 The Efficacy of the Speech and Language Therapy for Autism Spectrum Disorders. A. C. Tamanaha*, J. Perissinoto and B. M. Chiari, *Federal University of São Paulo*

Background: Conditions that make up the Autism Spectrum disorders are characterized by severe chronic impediments to social interaction, communication and interests. Although there are numerous clinical manifestations of these disorders, we judge it important to highlight the difficulties in both verbal and non-verbal communication, as these have a significant impact on the social

and cultural inclusion of individuals affected by these clinical conditions.In recent decades, language and speech intervention has been emphasized as a method for social adaptations of communicative behavior, enabling better inclusion of autistic children in their social environment.

Objectives: The aim of the present study was to evaluate the efficacy of the speech and language therapy for Autism and Asperger Syndrome.

Methods: This was a **c**linical trial pilot, approved by the Research Ethics Committee of the Federal University of São Paulo, under process n° 1570/08. All parents/guardians of the children signed terms of informed consent. The sample was composed of 11 children diagnosed with Autism (6) and Asperger Syndrome (5) attended in the Language and Speech Laboratory – Autistic Spectrum Disorders at Federal University of São Paulo. These children were randomly divided into two groups: Six were receiving both direct and indirect intervention (Therapy Group-TG), and five were receiving exclusively indirect intervention (Orientation Group-OG). We used the following parts of ASIEP-2 (Krug et al, 1993): Autism Behavior Checklist (ABC), Interaction Assessment (IA) and Sample of Vocal Behavior (SVB) on three occasions: at the beginning, six months later and 12 months later. Results: We observed there was greater evolution of Therapy Group –TG in the Autism Behavior Checklist, Interaction Assessment and Sample of Vocal Behavior. The mothers and the Speech and Language Therapist perceived behavioral changes. The influence of the multidisciplinary diagnosis, age and measures of the adaptive functioning was analysed. The performance of children with Asperger Syndrome was considered more positive. There was greater evolution in the children with age 73 month or more, and in the children with normal, mild and moderate adaptive functioning,
Conclusions: The tendency of better performance of the children attended in direct and indirect intervention showed that this association was fundamental.

105.046 46 Autistic Traits and Lexical Effects On Speech Perception in Children. M. Ota*[1], C. Dickie[1], C. Hien[2] and M. E. Stewart[2], (1)*University of Edinburgh*, (2)*Heriot-Watt University*

Background: Recent research on linguistic aspects of Autism Spectrum Disorder (ASD) shows that individuals with ASD tend not to employ top-down processing to resolve ambiguities in linguistic structures such as homographs, homophones and sentences with multiple interpretations. Stewart and Ota (2008) examined the use of lexical information to resolve phonetic ambiguity, and showed that typically developed adults with high scores on the Autism-Spectrum Quotient (AQ; Baron-Cohen et al., 2001) were less likely than low AQ scorers to interpret acoustically ambiguous auditory stimuli to be part of a real word (e.g., *kiss*) than a non-word (e.g., *giss*). In other words, autistic tendencies in neurotypical adults are related to an attenuated lexical effect on speech perception. There was no evidence that this effect was due to increased acoustic sensitivity or poor lexical access of individuals with high AQ scores.

Objectives: Our main objective of the study was to explore such a connection between autistic traits and lexical effects on speech perception among neurotypical children. Given that signs of ASD manifest themselves during childhood, it was hypothesized that the same relationship should be found in young individuals.

Methods: Participants were 4-6 year old typically developing children. None of them had been diagnosed with ASD. Their parents completed the Social Responsiveness Scale (SRS; Constantino et al., 2003), as a measure of the children's autistic traits. The main experimental task was a phoneme identification task with three pairs of /k/-/g/ non- to real word 7-step acoustic continua: *kiss-giss, kift-gift*; *keep-geep, keese-geese*; *kept-gept, kess-guess*. Stimuli were created by digitally cross-splicing endpoint items (e.g., *kiss* and *giss*) to interpolate the intermediate items. In addition, as measures of their acoustic sensitivity and lexical access ability, participants were given an auditory discrimination task on the same voice onset time continuum as well as a auditory lexical

decision task involving non- vs. real word pairs on voicing contrasts (e.g., *cake*, *gake*).

Results: Preliminary data collected from 12 participants show a significant negative correlation between the SRS and the mean identification shift between the two VOT continua (r = -.75, p < 0.01). There was also a significant positive correlation between the SRS and the reaction time in the lexical decision task (r = .617, p < 0.05).

Conclusions: Like adults, children who have more behavioral traits typically associated with ASD tend not to be influenced by lexical information in their phonemic identification. There are also indications that this effect may be caused by slower lexical access, although it remains to be seen whether this correlation will be upheld when more data are added.

105.047 47 Adolescents with ASD and TD Show Equivalent Patterns of Gesture Use During Lexical Retrieval. A. B. de Marchena* and I. M. Eigsti, *University of Connecticut*

Background: Researchers have studied co-speech gestures to gain insight into cognitive and communicative processes including problem solving, language acquisition, and speech production. Gesture plays an important facilitating role in these processes for typically-developing individuals. In contrast, gesture is thought to be reduced across the lifespan in individuals with autism spectrum disorder (ASD), though this assumption has received limited empirical attention. It remains unknown whether gesture can be used to study these important processes in ASD, and if so, how specifically gesture *is* used in this population. If individuals with ASD gesture similarly to individuals with typical development (TD), then we may be able to apply paradigms employed in the typical literature to use gesture to explore cognitive and communicative functions in ASD.

Objectives: Gesture is thought to play an important role in lexical retrieval. Using two confrontation naming tasks that have been shown to elicit gesture in TD, we examine the role of gesture in lexical retrieval by adolescents with ASD. If individuals with ASD gesture during lexical retrieval in the same way as individuals with TD do, then this suggests that gesture may be an important tool for studying speech production in ASD.

Methods: Participants were 15 high-functioning adolescents with ASD and 14 TD adolescents matched for age, gender, IQ, and receptive vocabulary (all p's > .18). Participants completed two lexical retrieval tasks. In Task 1, the Boston Naming Test, participants were shown line drawings of natural kinds and artifacts (e.g., octopus, abacus) and were asked to produce their names. In Task 2, administered only to participants who made fewer than five errors on Task 1 (n = 18), participants were given definitions of obscure words and asked to name the word that was being defined. Videos were coded for accuracy, gesture frequency, and gesture type.

Results: Accuracy on both tasks was equivalent for the ASD and TD groups. Across tasks, adolescents in both groups were equally likely to gesture (Task 1, p = .61; Task 2, p = .47). In addition to similar rates of gesture, the two groups also produced the same types of gestures; although some gesture types were used with greater frequency than others (main effect of gesture type: Task 1, p = .01; Task 2, p = .003), this pattern was followed by both groups equivalently (group X type interaction: Task 1, p = .54; Task 2, p = .81).

Conclusions: When asked to retrieve lexical items based on target pictures or word definitions, adolescents with high-functioning autism gestured as often, and produced the same gesture types, as TD adolescents. Although the group-level comparisons in this study represent null results, this finding is uniquely informative, given that gesture deficits have been so widely assumed by both clinicians and researchers. These results suggest that adolescents with ASD use gesture in the same way as TD adolescents when retrieving words from the lexicon, and that gesture may in fact prove useful in the study of speech production in ASD.

105.048 48 Using the Preschool Language Scale-IV (PLS-IV) to Characterize Language in Young Children with ASD. J. Volden*[1], I. M. Smith[2], P. Szatmari[3], S. E. Bryson[4], E. Fombonne[5], P. Mirenda[6], W. Roberts[7], T. Vaillancourt[8], C.

Waddell[9], L. Zwaigenbaum[1], S. Georgiades[3] and A. P. Thompson[3], (1)*University of Alberta*, (2)*Dalhousie University & IWK Health Centre*, (3)*McMaster University*, (4)*Dalhousie University/IWK Health Centre*, (5)*McGill University*, (6)*University of British Columbia*, (7)*University of Toronto*, (8)*University of Ottawa*, (9)*Simon Fraser University*

Background: Early vocabulary has sometimes been used as a proxy for language competence for children with ASD. Charman et al. (2003) and Luyster et al. (2007) found that receptive and expressive vocabulary in ASD were delayed relative to chronological (CA) and nonverbal mental age (NVMA) norms, and that participants were relatively more skilled at expressive than receptive vocabulary.

Objectives: To determine if a broader measure of early language skill (the Preschool Language Scale - Version 4; PLS-4) would reveal the same relationships as previously found for vocabulary. Research questions were: (1) Are PLS-4 Auditory Comprehension (AC), and Expressive Communication (EC) (a) standard scores lower than CA norms and (b) age-equivalent scores equal to or lower than those expected for NVMA and (2) What is the relationship between AC and EC on the PLS-4?

Methods: Participants were 296 newly-diagnosed children with ASD, aged 2-4 years, in a multi-site longitudinal study. Data are taken from the first assessment point. A battery of tests was administered, including the PLS-4 and the Merrill-Palmer-Revised Scales of Development (M-P-R). NVMA was taken from the age-equivalent score of the M-P-R Cognitive subscale. Participants were divided into age bands; one set based on CA and another based on NVMA. Average AC and EC standard scores in each CA band were compared to the normative average of 100. AC and EC age-equivalent scores were compared with participants' mean NVMA, organized by NVMA band, using a series of paired sample t-tests, with alpha level corrected for multiple t-tests. The discrepancy between EC SS and AC SS at each NVMA band was also calculated and results inspected.

Results: Mean standard scores for AC and EC were at least 1 SD and in most cases 2 SD below the normative means. Average AC age-equivalent scores were significantly below average NVMA in the following NVMA bands: 12-17 (NVMA $\underline{M}$=15.24; AC $\underline{M}$=11.63; t(50)=5.92, p<.001), 18-23 (NVMA $\underline{M}$=21.10, AC $\underline{M}$=15.56; t(81)=11.001, p<.001) and 48-78 months (NVMA $\underline{M}$=57.55, AC $\underline{M}$=50.65, t(19)=3.78, p=.001). Mean EC age-equivalent score exceeded NVMA in the <12 month band (NVMA $\underline{M}$=9.05, EC $\underline{M}$=14.05, t(19)=5.724, p<.001), but was significantly lower than NVMA in the 18-23 month (NVMA $\underline{M}$=21.10, EC $\underline{M}$=9.09, t(81)=4.629, p<.001) and the 48-78 month (NVMA $\underline{M}$=57.55, EC $\underline{M}$=49.45, t(19)=4.378, p<.001) NVMA band. EC SS was in advance of AC at the younger NVMA levels (mean discrepancies of 5.11, 7.51, 9.12 and 5.24 at NVMA bands of <12, 12-17, 13-23 and 24-29 months). At older NVMA levels, AC was higher than EC (mean discrepancies of -1.65, -3.7, -.95 at NVMA bands of 30-35, 36-47 and 48-78 months).

Conclusions: As expected, AC and EC standard scores were significantly lower than CA norms and generally equal to or lower than scores expected for NVMA. Contrary to expectations, EC did not consistently exceed AC. For children with NVMAs of 30 months or more, AC was greater than EC.

105.049 49 Predictors of Pragmatic Language Use in Toddlers with Autism Spectrum Disorders. L. R. Edelson* and H. Tager-Flusberg, *Boston University*

Background:

While the grammatical ability of individuals with autism spectrum disorders is quite heterogeneous, pragmatic impairment is universal across the spectrum. Most studies of predictors of linguistic development in autism focus on the structural and lexical features of language as assessed on standardized assessments (e.g., Charman, 2003; Dawson et al., 2004); however, little is known about predictors of pragmatic language use. To assess this, it is necessary to examine natural language samples.

Objectives:

The objective of this study is to explore the predictors of pragmatic language use in toddlers with autism spectrum disorders.

Methods:

Language samples for this study were taken from a subset (N=60) of toddlers who participated in a larger longitudinal study. The children were initially seen when they were approximately two-years-old (range: 20-33 mo) and again one year later. Fifty-two of the children in our sample returned for the third year of the study. During the visit, a number of standardized assessments were administered, including the ADOS, Mullen Scales of Early Learning, and the Early Social Communication Scales. Several episodes of the ADOS and a brief mother-child play session and mother-child snack were used for the language samples, which were transcribed and coded for pragmatic language use.

Results:

Each child utterance was coded according to its pragmatic function (e.g., requesting, expanding on a previous utterance, asking a question, etc.). The relationship between these various linguistic functions at ages 3-4 and predictors such as joint attention and other forms of behavior regulation will be discussed.

Conclusions:

The findings show promising evidence that measures of prelinguistic communicative skills such as joint attention in young toddlers might be a reliable predictor of future language gains, not only in relation to structural/lexical linguistic development, but also with respect to the pragmatic functions of language use.

105.050 50 Automatic Detection of Idiosyncratic Word Use in Autism Spectrum Disorders. E. T. Prud'hommeaux*, J. van Santen, L. M. Black and B. Roark, *Oregon Health & Science University*

Background: Stereotyped and idiosyncratic use of words and phrases is one of the coded behaviors used in the ADOS algorithm for autism diagnosis. Characteristic of this behavior is the use of neologisms and of "inappropriately formal" or pedantic words. Existing methods for assessing these language features during ADOS administration typically rely on overall impressions and observations of apparent trends in a child's speech. Natural language processing (NLP) techniques can be used to quantify these features and automate their detection.

Objectives: The goals of this study are to apply principles of NLP in order to 1) identify neologisms and patterns of overly formal word use; 2) compare the relative prevalence of these features in spontaneous language samples of children with Autism Spectrum Disorders (ASD) and Typical Development (TD); and 3) determine whether these features can be used to distinguish the two groups.

Methods: The ADOS was administered to children ages 4 to 8 with TD and with ASD. (Module 3 was administered to the majority of subjects; module 2 was used only for those subjects whose expressive language age equivalency was less than 4.0.) The two groups were roughly matched in terms of various measures of utterance complexity and acceptability as measured by standard NLP methods. The entire ADOS for each child was recorded and digitized for analysis. The subject utterances from the following ADOS activities were transcribed from these audio recordings: Make-Believe Play, Joint Interactive Play, Description of a Picture, Telling a Story From a Book, and Conversation and Reporting.

Relative frequencies of occurrence of single words and word-sequences were generated from two corpora: 1) the Wall Street Journal training corpus of the Penn Treebank, and 2) the Child Language Data Exchange System (CHILDES) database of child speech. For each child, we determined the relative frequencies of each word in the two respective corpora. Words whose relative frequency is zero (i.e., those that do not occur in a given corpus, known as out-of-vocabulary words, or OOVs) are likely to be neologisms.

Results: The average relative frequencies of the words, based on either corpus, were not significantly different in the two groups.

However, neologism use, as measured by OOV rate, was significantly higher in the ASD group than in the TD group, using both the Wall Street Journal corpus and the CHILDES corpus. Very low-frequency words from the Wall Street Journal corpus were also used significantly more often in ASD speech. This trend was not observed using the CHILDES corpus, which suggests that ASD speech is characterized not only by neologisms but also by the use of very infrequent formal words.

Conclusions: Neologistic and formal word use, which are both characteristic of ASD speech, can be identified automatically using natural language processing techniques. Incorporating automated analysis of speech could enhance the coding of these behaviors and reveal word distribution properties that might go unrecognized during examination.

105.051 51 Predicting Early Language Gains in Young Children On the Autism Spectrum. S. Ellis-Weismer*[1], M. A. Gernsbacher[1], C. Karasinski[1], E. R. Eernisse[1], C. Erickson[1], H. Sindberg[1], C. E. Ray-Subramanian[2], N. Huai[2] and S. Stronach[1], (1)*University of Wisconsin-Madison*, (2)*Waisman Center, University of Wisconsin-Madison*

Background: There is a scarcity of information regarding predictors of language outcomes in young children on the autism spectrum. Some research has examined predictors of language and communication within investigations of the predictive validity of early autism diagnostic assessments more generally (Charman et al., 2005), whereas other studies have focused specifically on predicting language outcomes (Charman et al., 2003; Paul et al., 2008). Prior investigations have comprised small samples and have yielded conflicting findings. Additional research is needed to provide a clearer characterization of early predictors of language development in young children on the autism spectrum.
Objectives: The goal of this investigation was to examine predictors of early language *gains* from 2 _ to 3 _ years of age in a large and well-specified group of young children on the autism spectrum.
Methods: A total of 102 children on the autism spectrum who are enrolled in an ongoing longitudinal investigation of language development participated in this study. Autism spectrum diagnoses were determined using comprehensive evaluations including the ADI-R and ADOS/ADOS-T. Participants had a mean chronological age of 31 months (25-36 mo) at Visit 1 (V1). Language and communication abilities at V1 were measured using the Communicative Development Inventory: Words & Gestures (CDI), Vineland Receptive and Expressive Communication scales, and Preschool Language Scale (PLS-4). Cognitive abilities were assessed by the Bayley Scales of Infant and Toddler Development – III, and joint attention was evaluated using the Early Social Communication Scales. SES was indexed by years of maternal education. Visit 2 occurred approximately one year after the initial evaluation, at a mean age of 44 months (37-53 mo). Language outcomes at Visit 2 (V2) were measured using the Auditory Comprehension and Expressive Communication Scales of the PLS-4.
Results: Pearson correlation coefficients indicated that V1 and V2 performance on the PLS-4 was significantly correlated, both for Auditory Comprehension ($r=.71$, $p=.000$, $n=89$) and Expressive Communication ($r=.77$, $p=.000$, $n=91$). Regression models ($n=78$ by excluding cases that did not have all measures at both visits) were constructed to conduct a residualized gain analysis such that V2 outcome was modeled both as a function of the same variable at V1 as well as other variables suspected to relate to growth in performance on the PLS-4. Gains in PLS-4 Auditory Comprehension scores were significantly predicted by Response to Joint Attention ($p=.013$); CDI words understood approached but did not reach statistical significance ($p=.066$). Gains in PLS-4 Expressive Communication scores were significantly predicted by SES ($p=.003$), Response to Joint Attention ($p=.014$), and Bayley cognition ($p=.026$). Variables that were non-significant were calibrated ADOS scores, Initiating Joint Attention, Vineland and CDI comprehension and production.
Conclusions: Language abilities at 2 _ years were strongly predictive of language skills at 3 _ years. Several non-linguistic measures predicted gains in early language (as measured by the PLS-4). Cognitive skills predicted gains in language production but not comprehension. Higher SES was

associated with more gains in productive language. Response to joint attention was the only significant predictor of gains in both language comprehension and production.

105.052 52 Advancing the Measurement of Receptive Language in Nonverbal Individuals with Autism. L. V. Van Droof*, K. Ledoux, E. J. Pickett, E. Buz, N. M. Billings and B. Gordon, *Johns Hopkins Medical Institutions*

Background: Many individuals affected by autism fail to develop useful speech, and many of these individuals never learn to express themselves in any functional way. An important question about such individuals is whether this lack of expressive ability is accompanied, or perhaps even caused, by deficits in receptive language knowledge. However, because of the general problems that such individuals have with responding, this question has been difficult to address. Nonetheless, there is considerable (albeit usually anecdotal) evidence from families and therapists that such individuals may actually have greater receptive capabilities than is evidenced by traditional measures. We have used eye movements, pupillary dilation, and the N400 component of event-related potentials (ERPs) as measures of receptive vocabulary knowledge in three populations (normal adults, normally developing children, and high-functioning individuals with autism) in which self-report and behavioral accuracy served as measures of comparison (Ledoux et al, 2009).

Objectives: To test whether eye movements, pupillary dilation, and the N400 component of ERPs could provide evidence of single-word comprehension in nonverbal individuals with autism.

Methods: Participants included three low-verbal or nonverbal males between 15 and 21 years of age who met criteria for ASD based on the Autism Diagnostic Interview Revised (ADI-R) and the Autism Diagnostic Observation Schedule (ADOS). Caregivers completed the MacArthur-Bates Communicative Development Inventory and other checklists. These sources were used to determine stimuli that were expected to be known receptively by the participants; unknown stimuli were drawn from a pool of items developed for other subject populations (Ledoux et al., 2009). Training programs were implemented on an individual basis to acclimate the participants to our experimental tasks and equipment. There were two tasks: forced choice recognition and congruity. During the *forced choice recognition* task (throughout which we simultaneously collected eye movement and pupillary dilation data), four pictures (either all known or all unknown) were presented simultaneously on a computer screen, along with an auditory token that named one of the objects/concepts pictured. ERPs were recorded during the *congruity task*, in which single pictures were presented on the computer screen, accompanied by the auditory presentation of a word that either matched (congruous condition) or did not match (incongruous condition) the name of the pictured item. The congruous and incongruous conditions were equally matched in number of known and unknown words. Participants were not required to make behavioral responses for either task.

Results: As predicted, differences were observed for all three measures between the known and unknown word conditions. Specifically, eye movements were faster to named pictures for known words, and fixations at the end of each trial were on the named picture more frequently for known words than unknown words. Pupillary dilation from baseline was greater in the unknown condition. An N400 congruency effect was observed for known words, but not for unknown words.

Conclusions: Eye movements, pupillary dilation, and the N400 component of ERPs differentiated known from unknown words, suggesting that these may be valid measures of single-word comprehension in otherwise "nonverbal," non-responding, low-functioning individuals with autism.

105.053 53 Comparison of Children with Autism Spectrum Disorders and Developmental Language Disorders On Measures of Language Impairment. L. M. Black*, J. van Santen, M. K. August, B. Langhorst and R. Sanger-Hahn, *Oregon Health & Science University*

Background:

Children with autism spectrum disorders (ASD), whose core symptoms include impairments in communication, social interaction, and repetitive, stereotyped behaviors, are typically distinguished from

children with developmental language disorders (DLD). DLD itself cannot be diagnosed in a child with ASD (DSM-IV-TR). Yet, there are areas of overlap between these two disorders that pose challenges for differential diagnosis. One area of overlap has been in language impairment, which can influence a child's communicative competence and social-emotional behaviors.

There have been varying reports over the years in the types of language issues, degree of severity, and percentage of children with ASD who show language impairments. High functioning verbal children with autism have been reported to have no specific deficits in phonology, syntax, or lexical knowledge; deficits mainly in pragmatics; and, then again, in as many as 50% of such an ASD group, significant difficulties in structural language and a pattern of impairments that resembles DLD (Kjelgaard and Tager-Flusberg, 2001).

Objectives:

Objective is to document incidence of language impairment in a well-characterized group of high functioning verbal children with ASD and to compare their language issues with those of an equally well-characterized group of children with DLD.

Methods:

Children, ages 4-8, were given a comprehensive battery of language and neurocognitive measures. Language measures included the CELF-Preschool 2/CELF-4, Nonword Repetition, PPVT-III, NEPSY Narrative, Verbal Fluency. Spontaneous language analyses were also obtained.

Classification into the ASD group (N=29) utilized the Social Communication Questionnaire (SCQ); the revised algorithm of the ADOS; and DSM-IV-TR-based clinical diagnosis of ASD made via independent ratings and consensus agreement by a team of licensed psychologists and speech language pathologists. Classification into the DLD group (N=19), following an equally rigorous process, utilized Tomblin's Epi-SLI criteria (Tomblin et al., 1997) or a CELF index score at -1 s.d. plus a spontaneous language measure at -1 s.d.; and DSM-IV-TR-based consensus clinical diagnosis. ADOS scores were not used to make or rule out a diagnosis of DLD; clinical diagnosis did rule out ASD in every child with DLD.

The DLD and ASD groups were well matched on nonverbal IQ (104 and 109, respectively) and age (6; 3 and 6; 5), $p>0.50$ in both cases.

Results: In the ASD group, 50% met the EpiSLI criteria, 65% the CELF + Spontaneous Language criteria, and 69% either criteria. In the DLD group, these percentages were 77%, 94%, and 100%. Across the 3 Epi-SLI sub-domains (vocabulary, grammar, and narrative) and 2 modalities (receptive and expressive), the shapes (but not the elevations) of the profiles of the two groups were similar (e.g., more issues in expressive language than receptive; more issues in grammar and narrative than in vocabulary).

Conclusions:

These findings support research that demarcates the high percentage of high-functioning, verbal children with ASD who have language impairments. It also contributes to our understanding of the overlap between ASD and DLD in patterns of language impairment. It beckons for further disclosure areas of essential difference between these two disorders, especially in the area of language and communication.

105.054 54 Parents Use of Language That Follows the Attention of Toddlers with ASD. J. L. S. Bartley*, L. B. Swineford and A. M. Wetherby, *Florida State University*

Background: Research has shown that preschoolers with autism spectrum disorders (ASD) whose parents use more language that follows their child's focus of attention have better long-term language outcomes. With reliable diagnoses of ASD now possible before the age of three, it is important to examine parent language in the toddler years.

Objectives: The objectives of this study were: 1) to compare parents use of utterances that

follow their child's focus of attention during a parent-child play sample gathered in the second year of life in toddlers with ASD and with typical development (TD); and 2) to examine the relationship between parent utterances and child outcomes at age 2.

Methods: Seventy-three parent-child dyads were recruited from the ongoing longitudinal prospective study of the FIRST WORDS® Project for this study. Dyads participated in both the *Communication and Symbolic Behavior Scales* (CSBS; Wetherby & Prizant, 2002) *Behavior Sample* and an interactive play sample (*M*=16.46 months; *SD* = 3.47). The dyads included 32 children with ASD and 41 children with TD matched on mental age. Additionally, all children were assessed using the *Mullen Scales of Early Learning* (MSEL) around 2 years of age (*M*=26.26 months; *SD* = 5.57).

Play samples were coded for parent synchrony using the Observer® Video-Pro Software. Parent utterances were coded as either synchronous (referring to the child's focus of attention) or asynchronous (not referring to the child's focus of attention), and further coded as demanding (requiring the child to do something s/he was not already doing) or undemanding (not requiring the child to do something s/he was not already doing).

Results: Analyses of 73 parent-child dyads indicate that parents in both groups used predominantly synchronous language in similar proportions. However, parents of children with ASD used less undemanding and more demanding language than parents of children with TD. More specifically, when parents of children with ASD used synchronous language, they used more demanding and less undemanding utterances. Additionally, parents of children with ASD used more asynchronous-demanding language. For children in the ASD group, parent use of asynchronous-undemanding language was related to the child's nonverbal developmental quotient on the MSEL at age two. No significant correlations were observed between synchronous or asynchronous language and verbal developmental quotient.

Conclusions: Similar to the findings of Siller and Sigman (2002), our findings indicated that parents of toddlers with ASD talked about their child's focus of attention as often as parents of toddlers with TD matched on mental age. Additionally, consistent with parents of preschool children, parents of toddlers with ASD used more demanding language than parents of children with TD (Watson, 1998). In our sample, synchronous caregiver language, both demanding and undemanding, did not predict child language outcomes. Previous findings demonstrating that synchronous caregiver language predicted child language outcomes together with our findings suggest that synchronous language may be necessary, but not sufficient for positive child language outcomes.

105.055 55 Perceptual Dialect Classification by Adults with High-Functioning Autism. K. L. Rohrbeck*, C. G. Clopper and L. Wagner, *Ohio State University*

Background: The speech signal contains information about linguistic meaning, and about indexical properties of the speaker, such as regional background (Klatt, 1989). Neurotypical (NT) adults can use indexical information in the speech signal to accurately categorize unfamiliar talkers based on dialect (Clopper & Pisoni, 2004). Categorization requires an intact perceptual system, which adults with high-functioning autism (HFA) appear to have: people with autism spectrum disorders (ASD) have normal abilities in the domains of phonological discrimination (Constantino et al., 2007), prosodic tune recognition (Jarvinen-Pasley et al., 2008) and unfamiliar talker identification (Boucher et al., 2000). By contrast, adults with HFA have problems with social aspects of language (e.g., Baron-Cohen et al., 2000) which may impair their ability to identify talkers by dialect. Indeed, one previous study (Baron-Cohen & Staunton, 1994) found that, in marked contrast to NT teens, ASD teens modeled their own dialect use on the dialect of their mother as opposed to that of their peers.

Objectives: Dialect variation sits at the intersection of linguistic and social information, and this study examined how people with HFA use those two sources of

information to make dialect classification judgments about unfamiliar talkers. Can adults with HFA categorize talkers based on dialect, and if so, are their categories comparable to those produced by NT adults?

Methods: An auditory free classification procedure (Clopper & Pisoni, 2007) was used to assess the perceptual similarity structure of dialect variation in American English. Fourteen adults with HFA and 27 NT adults listened to 20 male talkers from four different dialect regions and were asked to group the talkers based on where they believed the talkers were from. All participants also completed the Autism Quotient (Baron-Cohen et al., 2004).

Results: As expected, the adults with HFA had significantly higher average Autism Quotients than the NT adults. In the dialect classification task, both the NT and HFA adults grouped the talkers into an average of 6-7 dialects. However, the NT adults were significantly more accurate than the adults with HFA in grouping talkers from the same dialect together. Further, a clustering analysis revealed that both the NT and HFA participants sorted speakers from the New England and Southern dialects into distinct groups, and both perceived a high degree of similarity between talkers from the Midland and Northern dialects. However, the HFA adults produced noisier dialect groupings, and the perceptual similarity between the more marked New England and Southern dialects and the less marked Midland and Northern dialects was higher for the HFA adults than the NT adults.

Conclusions: These findings suggest that adults with HFA can perceive relevant dialect differences in the speech signal, and can use this variation to categorize talkers by dialect. However, the differences between the HFA and NT groups suggest that the HFA adults' perceptual dialect categories are less robust than the NT adults' categories. Ongoing work is examining the extent to which HFA performance differences in perception are related to differences in social categorization of dialects.

105.056 56 Influence of Theory of Mind On the Written Compositions of Adults with High-Functioning Autism Spectrum Disorders. H. M. Brown* and P. D. Klein, *The University of Western Ontario*

Background: Successful participation in most educational, work and social settings necessitates solid writing competence. Research suggests this is an area of particular weakness in people with high-functioning autism spectrum disorders (HFASD), and is out of keeping with their average to above average intelligence. However, previous research lacks systematic description of their writing difficulties and the extent to which such problems are evident across the HFASD population. Further, no previous research has attempted to identify the cognitive factors that underlie written expression problems in HFASD.
Objectives: The current study sought to: (1) compare the expository and narrative writing of adults with HFASD and their peers without disabilities, and (2) to compare the HFASD group to controls on theory of mind (ToM) skill and to correlate ToM skill with various textual measures.
Methods: Sixteen adults with HFASD and sixteen neurotypical (NT) adults were recruited to participate in this study. Participants completed the Social Attribution Task, a ToM task (Klin, 2000) and wrote expository and narrative texts. Four composites, Length, Mechanics, Text Quality and Textual evidence of Theory of Mind (Textual ToM), were assessed across both genres.
Results: (1) Adults with HFASD wrote narrative texts that demonstrated a limited understanding of the inner worlds of the characters (Textual ToM) and that were shorter than the texts of the NT group. In contrast, the frequency of ToM elements in expository texts of individuals with HFASD were similar to those of their NT peers, and both groups' essays were of similar length. (2) Across both genres, there were no significant differences between groups in their competency with the mechanics of their texts. (3) The HFASD group were less able than the NT group to create high quality narratives and expositories; that is, texts which were well structured, locally and globally coherent, and had appropriate background information. (4) Performance on the Social Attribution Task was significantly weaker in the group with

HFASD relative to the NT group. (5) Social Attribution Task performance was significantly correlated with the Length and the Text Quality Composites across both genres, and with the Narrative Textual ToM and the Expository Mechanics Composites. Conclusions: This study was the first to systematically describe strengths and weaknesses in the writing of adults with HFASD and examine the influence of ToM on their writing abilities. Descriptively, individuals with HFASD tended to have greater difficulties writing in the narrative genre than in the expository genre, and they had problems creating high quality texts across both genres. It is noteworthy, however, that there was great variability in the scores of those with HFASD, with some individuals with HFASD scoring as well as or better than the mean of the NT group on several writing variables. Finally, results suggested that the ToM skills of adults with HFASD may impact their success at writing. Detailed description of the strengths and weakness in the writing of individuals with HFASD has instructional implications and it increases our understanding of this population and the nature of autism itself.

105.057 57 Statistical Word Learning in Children with ASD. J. Mayo* and I. M. Eigsti, *University of Connecticut*

Background: Using statistical cues (i.e., transitional probabilities between syllables) to determine word boundaries is critical for learning language; extracting words from a continuous speech stream, in order to learn their meanings, hinges upon this ability. Children with Specific Language Impairment (SLI), a language disorder, are impaired in using transitional probabilities to determine word boundaries (Evans et al., 2009). Individuals with Autism Spectrum Disorders (ASD) have impaired communication, including delays in acquisition, but the underlying mechanism is poorly understood. It is unknown if weakness in tracking transitional probabilities contributes to these impairments. Based on common language difficulties, some have proposed an overlap between language deficits in SLI and those in ASD. Exploring whether children with ASD have a similar weakness in statistical word learning will clarify the relationship between these disorders.

Objectives: We examined whether children with ASD demonstrate similar deficits in using transitional probabilities to extract words from a continuous speech stream as those reported in children with SLI. Similar weaknesses would support a connection between these disorders. In contrast, successful performance would suggest that language delays in ASD reflect different underlying processes.

Methods: To clarify the role that transitional probabilities play in word learning, 17 children with ASD and 24 children with typical development (TD) ages 7-17 were recruited. Participants listened to a 21-minute speech stream containing 12 syllables. Six combinations of syllables formed trisyllabic "words" with high internal transitional probabilities (32-100%); transitional probabilities of syllables not forming "words" were lower (10-20%). As they listened, children engaged in a drawing task that directed their attention away from explicit processing of the speech stream. Immediately following presentation of the speech stream, children completed a 36-trial, two-alternative forced-choice test, indicating which trisyllabic "word" sounded more like the speech sounds that they heard while drawing.

Results: Participants had IQ>80 (ASD=103.88(11.46); TD=105.38(11.46) and receptive and expressive vocabulary>80 (expressive vocabulary: ASD=105.44(15.24), TD=110.96(16.33); receptive vocabulary(ASD=109.88(13.95), TD=115.92(10.76)). Groups were matched on age, verbal IQ, and expressive and receptive language. On the syllables task, the ASD and TD groups performed significantly above chance, and, importantly, did not differ from each other. Children in both groups were better able to detect "words" with the highest internal transitional probabilities (>75%) than words with lower transitional probabilities (<42%).

Conclusions: In contrast to children with SLI, participants with ASD were as sensitive as their IQ- and language-matched peers to the transitional probabilities that distinguished "words" from "non-words" in an artificial miniature language. This finding could

indicate that (1) children with SLI and ASD do *not* share a common underlying mechanism for language impairment; or, (2) the strong language skills in the ASD group precluded the detection of any deficits. The participants in this study had strong language skills that do not reflect the large variability of language skills among people with ASD. The relationship between SLI and ASD may be further clarified in subsequent studies exploring the ability of children with ASD and weaker language skills to use statistical cues to learn words.

105.058 58 Stability of Language Improvements One Year After the End of ABA Intervention in ASD Children. L. Ferretti*[1], G. Doneddu[2], G. Saba[3], S. Marras[3], P. M. Peruzzi[1] and R. Fadda[4], (1)*A.O. Brotzu*, (2)*Azienda Ospedaliera Brotzu*, (3)*A.O.B. (Azienda Ospedaliera Brotzu)*, (4)*University of Sheffield*

Background:

Children with Autism Spectrum Disorders (ASDs) show significative improvements thanks to intensive and early ABA intervention (Howlin, 1998). Usually, the great deal of knowledge about the stability of the effect of prolonged ABA intervention consider the diagnostic reclassification and the academic achievements of children in regular education classrooms (Reichow,2009). No studies, for the best of our knowledge, monitored the stability of IQ scores and adaptive abilities after the end of ABA intervention. In particular, no study examined receptive and expressive language skills after the end of ABA intervention.

Objectives:

This study was designed to evaluate if the gain on Adaptive Skills and on IQ, obtained thanks to 4 yrs of ABA intervention, remain stable 1 yr after the end of ABA intervention and the start of an Eclectic intervention (play group, psicomotricity, music therapy).

Methods:

35 participants with ASDs (26 M; 9 F; aver.chron.age=6;3 yrs; DS:2;6; aver.IQ=66; DS=25), divided at the beginning of the study in three groups of intervention: ABA-int (10 hrs of Discrete Trial Teaching [DTT] a week, 5 hrs of speech therapy a week); ABA-non int (5 hrs of DTT a week, 2 hrs of speech therapy a week); Eclectic intervention(an average of 4 hours a week). At the end of the 4th year, both ABA-int and ABA non-int intervention groups finished the ABA treatment and switched to Eclectic intervention. The participants were tested for the duration of this study (5 yrs) with the Vineland Adaptive Behavior Scale (VABS) and with the Leiter-R once a year.

Results:

The IQ scores remained stable at the end of the ABA intervention (F=7,413; df= 4; p <0,05) in the ABA-int goup (IQ scores: t1= 56; t2=92; t3=90; t4=87; t5=80) and in the ABA-non int group (IQ scores: t1= 49; t2=69; t3=55; t4=67; t5= 61) but not in the Eclectic group (IQ scores: t1= 76; t2=73; t3=70; t4=71; t5= 69). The VABS scores increased significantly in all the groups from t1 to t5 (F= 76,57; df=4; p<0,05). Only ABA-int and ABA non-int group improved in VABS Receptive Language (F=33,77; df=4; p<0,05) and in VABS Expressive Language (F=2,6; df=8; p<0.12).

Conclusions:

The results highlight the stability of IQ scores in ABA groups after one year of interruption of ABA treatment. Moreover the data showed a significant improvement of Receptive and Expressive language in the ABA groups. This study shows evidences that ASD children maintain the gain obtained from ABA intervention when switching to an Eclectic intervention.

105.059 59 Indicators of Linguistic Processing Constraints in the Narratives of Individuals with High-Functioning Autism. K. M. Belardi* and D. L. Williams, *Duquesne University*

Background: Few standardized measures are available to assess the language skills of adolescents and adults with HFA. Furthermore, current measures fail to capture the "idiosyncratic" and "stereotyped" speech productions that are characteristic of HFA. The overuse of formulaic language is one of the behaviors that is suggestive of autism on the ADOS, however, methods to measure the use

of this type of language have not been formalized. Wray (2000) proposed that the overuse of formulaic language or prefabricated patterns may be evidence of linguistic processing constraints. The measurement of formulaic language would be important with respect to information processing models of autism. Systems for the measurement of formulaic language have been developed and used with adults with brain injuries (Van Lancker Sidtis & Postman, 2006) and second language learners (Wray, 2000), populations that are reported to overuse formulaic language. These analyses may be useful for characterizing the language of individuals with HFA.

Objectives: To analyze spoken language samples of individuals with HFA as compared to age- and IQ- matched controls to determine if differences occur in measures of formulaic expressions (FE) under two different language formulation conditions.

Methods: Language samples for analysis were taken from 15- to 35-year old males with HFA (n=20) and neurotypicals matched for age and IQ all with verbal IQs greater than 85. Autism diagnosis was established for the affected group with the ADOS and ADI-R, and confirmed by expert clinical impression. Narrative language samples for both groups were collected from the ADOS "Telling a Story from a Book" and "Create a Story" tasks. Language samples were transcribed using Hunt's (1970) utterance boundary coding procedure. Transcript reliability was established (.99) with another graduate student. The Systematic Analysis of Language Transcripts (SALT) software (Miller & Chapman, 2000) was used for standard language analyses (e.g., type token ratio and mean length of utterance). Analysis of the transcripts for evidence of FE is ongoing using a classification system developed by Van Lancker Sidtis and Postman (2006).

Results: Initial analyses suggest a wide range of verbal fluency among the individuals with HFA. Four participants with HFA had clinically significant rates of speech disruptions (11.49, 11.51, 13.24, and 18.09). Classification and measurement of FE is ongoing for both groups. Further analyses will be reported and comparisons will be made to the performance of age- and IQ-matched controls. The relation between the rate of occurrence of FE between the two tasks that differ in linguistic formulation demands (one with a given story with picture support and the other requiring creation of a novel story with generic props) will also be discussed.

Conclusions: High-functioning adolescents and adults with autism are reported to produce "stereotyped" and "idiosyncratic" utterances at higher rates than neurotypical individuals with similar language abilities. However, objective methods of measuring this type of language use are not generally available. Measurements of FE during spontaneous speech productions may be useful for characterizing the language production of individuals with HFA and may provide evidence related to the use of linguistic processing resources.

105.060 60 Receptive and Expressive Language in Autism. A. M. Girardot*[1], S. De Martino[2], C. Chatel[2], D. Da Fonseca[2], V. Rey[2] and F. Poinso[2], (1)*Hopital sainte marguerite*, (2)*Hopital Sainte Marguerite*

Background: The language development in autistic children is largely described as impaired in literature (DSM IV), but few relationships are established between different domains of language development. In typical child, pointing appears before naming. In autistic children, the naming and the pointing are heterogeneous.

Objectives: The purpose of our study is to observe the linguistic particularities in autism. Does the language acquisition respect the, even late, typical development? Furthermore, are there correlations between the capacities in picture naming or word identification and others domains as: cognitive level, structural language, pointing and echolalia in children with autism?

Methods: 27 autistic verbal children participated in this study. Patients were recruited from the « Autism Resource Center » of Psychiatric Unit of Ste Marguerite Hospital in Marseille (France). A first group is constituted by autistic children with mental delay and a second group by autistic children

without cognitive delay. Every child is tested on a word identification task and on a picture naming task (from the WPPSI III).
For every child, we observe the structural level of language, the pointing skills (no pointing, imperative pointing, or declarative pointing) and the presence of echolalia.

Results: Preliminary results reveal that all the autistic children have better performances in the picture naming task than in word identification task. We find a correlation between language structural level and echolalia in autistic children with mental delay. However none of these two factors has any correlation with picture naming.
In high-level autistic children, there is a correlation between VIQ and picture naming, between PIQ and word identification, between structural level and picture naming, and between pointing and structural level.

Conclusions: The autistic children name more easily than they identify the words. The scores in word identification are not correlated with level of pointing. We can not thus explain the low performances on the word identification task by the low skills in pointing. We also suggest that the difficulties result of the use of pointing in communicative situation.
In children without deficit, the results in word identification task are correlated with the perceptive reasoning skills. The identification task seems implicate perceptive reasoning processes while naming task implies verbal reasoning.

105.061 61 Maternal Noun Phrase Complexity and Child Language in Autism. A. T. Meyer*, L. R. Edelson and H. Tager-Flusberg, *Boston University*

Background:

Maternal speech has been found to predict child language acquisition in typically-developing children (e.g. Tamis-LeMonda, Bornstein, & Baumwell, 2001). Parents of typically-developing children have been shown to adjust their speech to their child's linguistic ability (Phillips, 1973). Little is known about whether the same effect holds true in children with autism spectrum disorders.

Objectives: The objective of this study is to examine the relationship between the complexity of mothers' noun phrases and language in children with autism.

Methods:

Natural language samples were taken from a group of children with autism spectrum disorders (n=60) at age 3 (range 31-50 months) that were part of a larger longitudinal study. Standardized assessments such as the Mullen Scales of Early Learning and the ADOS were administered. A natural language sample was transcribed from a mother-child play session. The nouns used by the mother during play were coded based on their complexity (e.g. use of determiners, possessives, plurals) and omissions of essential determiners.

Results: Mothers' complexity of noun phrases is related to their children's current linguistic abilities. The effect of maternal noun phrase complexity on language development in children with autism will also be explored longitudinally.

Conclusions:

Mothers of children with autism are sensitive to their children's language abilities and adjust their speech accordingly. Future studies will explore other aspects of maternal speech.

105.062 62 Prosody in School-Age Children with ASD. E. Schoen*[1], R. Paul[1], L. Berkovits[2] and F. R. Volkmar[3], (1)*Yale University School of Medicine*, (2)*Yale Child Study Center*, (3)*Yale School of Medicine*

Background: Prosodic deficits in individuals with autism spectrum disorders (ASD) have been consistently reported in the literature (Kanner, 1943; Paul, 1987; Shriberg et al., 2001). However, the majority of these studies report solely on prosodic production. Little information is known regarding the understanding of prosody in individuals with ASD.
Objectives: The purpose of this study is to compare the production and perception of prosodic information in children with high-functioning autism (HFA) and children with

typical development (TD).
Methods: Participants, ages 9-17, underwent extensive cognitive, behavioral, and language testing to establish research diagnoses of autism. Each participant completed the Prosody Protocol (PP). The PP, adapted from Peppé and McCann (2003), consisted of 8 computer-based tasks examining grammatical, pragmatic and affective prosody. Four of the tasks examined the participant's production of the aforementioned prosodic domains while the other four tasks examined the participant's understanding of each prosodic domain.
Results: Preliminary results indicate decreased accuracy in understanding and producing prosodic information in children with HFA compared to the TD group. Children with HFA have greater difficulty in understanding and using grammatical and pragmatic prosody as compared to their age-matched peers. No differences in affective prosody were found.
Conclusions: Although children with HFA demonstrate age-appropriate language relative to syntax and grammar, they continue to show difficulties with both their production and perception of prosodic information. Although affect is usually thought to be impacted in this population, the current results suggest that it is the linguistic aspects of prosody that are more difficult for these high-functioning individuals, at least in the structured tasks presented here. Their inability to use and understand the linguistic import of prosody may negatively impact social, academic and vocational success. Having a better understanding of specific prosodic difficulties could help interventionists design a more effective treatment program.

105.063 63 Differences in Receptive and Expressive Language Abilities in Children with ASD. M. K. McCalla*, E. H. Sheridan, M. W. Gower and E. M. Griffith, *University of Alabama at Birmingham*

Background: Autism spectrum disorders (ASD) are a set of complex developmental disabilities characterized by both receptive and expressive language deficits. It is important to understand the heterogeneous nature of these deficits because they are often among the first symptoms observed and play a critical role in the assessment and differential diagnosis of ASD. Additionally, the degree of language impairment is a key component in predicting a child's prognosis. Some evidence suggests that when compared with children with other language disorders, children with ASD show more severe receptive language deficits. Further understanding of the different types of language impairments demonstrated, their trajectories, and the measures used to assess them should advance the diagnosis and treatment of children with ASD.

Objectives: The purpose of this study is to investigate the relationship between receptive and expressive language deficits and ASD symptomatology across multiple measures. The study compared children who were diagnosed with an ASD and children with other clinical impairments (i.e. language delays and developmental delays).

Methods: The current sample consists of 28 children (age 2 to 7, *mean* = 53.39 months, *SD* = 13.48) who received a comprehensive ASD evaluation using both the ADI-R and the ADOS. Additionally, each child's language abilities were assessed using the Preschool Language Scale (PLS-3 or PLS-4). Seventeen of these children were diagnosed with an ASD (15 male, 2 female). The clinical comparison group was comprised of 11 children (6 male, 5 female) who were not diagnosed with ASD. Data collection is ongoing and it is anticipated that there will be at least 25 participants in both groups. None of the participants in this study had hearing impairments or co-morbid psychiatric diagnoses.

Results: Preliminary results indicate that there were significant group differences in receptive language abilities dependent upon whether or not a child had an ASD. Specifically, children with ASD had significantly lower receptive language scores on the Preschool Language Scale than children in the clinical comparison group, ($t = 1.82$, $p < .05$). In contrast, there were no significant differences between the two groups for expressive language scores, ($t = 0.25$, $p > .05$). Additional analyses were conducted to determine if there were differences in receptive and expressive abilities for each

group. The children with ASD scored significantly higher on expressive language compared with receptive language, (t = -3.99, p < .001), whereas the clinical comparison group showed no difference between expressive and receptive skills, (t = -0.49, p > .05).

Conclusions: These preliminary data support the idea that investigating both receptive and expressive language skills is critical in order to thoroughly understand the communication abilities of children with ASD. Additionally, examining receptive deficits may be more informative than exploring expressive deficits when differentiating between children with ASD and those with other types of developmental delays. This is particularly important because receptive language deficits are more difficult to assess. Therefore, it is critical that clinicians utilize measures that reliably elicit all components of language.

105.064 64 Consistency Among Language Assessment Scores in School-Aged High-Functioning Children with Autism Spectrum Disorders. J. Lomibao*[1], N. Coggins[1], M. Galdston[1], R. Travolta[1], M. Szkolka[1], R. Luyster[2], A. Duda[1] and S. L. Santangelo[1], (1)*Massachusetts General Hospital*, (2)*Children's Hospital Boston/Harvard Medical School*

Background: Prior reports have documented considerable variability in language abilities among verbal children with ASD (Kjelgaard and Tager-Flusberg, 2001). A variety of measures are used to assess language abilities in school-age children including direct face-to-face assessments with the child, and questionnaires that are completed by the child's primary caregiver. At least one previous study found consistent agreement among different measures of early language in toddlers (Luyster et. al., 2008). However, consistency among various measures of language abilities in school-age children has not previously been studied.

Objectives: This study investigated the relationships among scores on standardized language assessments obtained from school-aged children with ASD by both direct observation and parent reports. These assessments were obtained from children with fluent speech who were able to complete the direct-observation measures.

Methods: Twenty-nine participants (age range 5 – 12 years; IQ M=102.31; SD=21.71) were given a battery of language assessments. Direct observation measures included the Clinical Evaluation of Language Fundamentals (CELF-IV), which measures different aspects of language development, and the Peabody Picture Vocabulary Test (PPVT-IV), which tests receptive vocabulary. Parent-report questionnaires included the Vineland Adaptive Behavior Scales (VABS-II), which assesses an individual's adaptive skills, and the Children's Communication Checklist (CCC-2), which measures children's communication skills in the areas of pragmatics, syntax, morphology, semantics and speech.

Results: Analysis of the CELF-IV core language scores revealed no significant difference between expressive (EL) and receptive (RL) language standard scores. Significant correlations emerged between core standard scores on the CELF-IV and standard scores on the PPVT-IV (r=0.888**). CELF-IV and PPVT-IV standard scores were also significantly correlated with the VABS-II Language Composite Score (CELF & VABS r=0.682**; PPVT & VABS r=0.616**). However, the CCC-2 General Communication Composite score was found to correlate with only the VABS Language Composite Score (r=0.506**). [**p<0.01]

Conclusions: This is the first report of consistency among language measures in school-age children with ASD, including measures of receptive and expressive language derived from both direct assessment and parent-report measures. Results suggest that the parent-report and direct observation assessments used in this study are consistent and reliable measures of language in school-age children with ASD.

105.065 65 Exploring the Use of the Language Environment Analysis (LENA) System in Preschool Classrooms of Children with Autism Spectrum Disorders. J. Dykstra*[1], M. Sabatos-DeVito[1], D. Irvin[2], B. Boyd[1], K. Hume[3] and S. Odom[4], (1)*University of North Carolina at Chapel Hill*, (2)*UNC-Chapel Hill*, (3)*Frank Porter Graham Child Development Institute, University of North Carolina, Chapel Hill*, (4)*University of North Carolina*

Background: Language deficits are a core behavioral feature of autism spectrum disorders (ASD). Traditionally, language progress is measured with standardized tests. However, researchers debate the validity of using standardized language assessments on young children with ASD because most measures are normed on samples of typically developing children (Charman, 2004; Koegel, Koegel, & Smith, 1997). Researchers are promoting the use of varied methods of language assessment for children with ASD, including data collection in natural contexts (Luyster et al., 2008; Tager-Flusberg et al., 2009). The Language Environment Analysis (LENA) system is a language recording device that collects and analyzes child and adult language in the natural environment.

Objectives: To explore the utility of using LENA with children with ASD in preschools by: a) examining LENA data, which includes child vocalizations, adult word counts, and child-adult conversational turns; and b) assessing relationships between these variables and standardized assessments of language, cognition, and autism severity.

Methods: Twenty-one children with ASD, ages 3 to 5, enrolled in self-contained classrooms from a Southeastern school district participated in this study. Fifteen of the 21 children were in five classrooms which followed the TEACCH approach; 6 were in two "business as usual" (BAU) classrooms, which used an eclectic approach. All children met ASD diagnostic criteria and had an educational or clinical diagnosis of ASD or DD. Children wore the LENA device one day for an average of 2 hours, 40 minutes. LENA data were converted to rates (frequency/minute), since language samples varied in length. LENA data and baseline measures of language (PLS-4), cognition (Mullen), and autism severity (CARS) will be reported.

Results: Descriptive language data for 21 children include rates of child vocalizations (CV) (M=3.2, SD=1.6) and child-adult conversational turns (CT) (M=1.0, SD=.5). Adult word counts (AWC) averaged 28.8 words per minute (SD=11.9). Language age-equivalents on the PLS-4 were significantly correlated with LENA variables: CV (r=.45), AWC (r=.44), and CT (r=.52). Mullen Visual Receptive scores were significantly correlated with AWC (r=.45). No significant correlations were found between LENA measures and CARS scores. Data will be analyzed for 17 additional children.

Conclusions: This study has produced three compelling findings. First, LENA language data indicate low rates of child vocalizations and conversational turns for children with ASD at the beginning of the school year. Second, the three LENA variables were correlated with a standardized measure of language development (PLS-4), demonstrating that standardized and naturalistic language data collection methods captured similar information. Finally, there was a correlation between children's cognitive abilities and adult word counts, which provides support for the transactional nature of teacher-child interactions (Yoder & McDuffie, 2006). Overall, LENA appears to be a feasible tool for research and clinical use in the classroom. Some of the inherent challenges of using LENA in classroom settings also will be shared.

105.066 66 Achievements and Correlations Among Emergent Literacy Skills in Children with Autism Spectrum Disorders.

E. Lanter*[1], L. Watson[2], D. Freeman[1], D. Millar[1], A. Lorenzi[1] and A. Morgan[1], (1)*Radford University*, (2)*University of North Carolina at Chapel Hill*

Background:

Emergent literacy skills lay the foundation for children's later development of the conventional literacy skills unequivocally required for their educational and vocational success. Unlike children developing typically, surprisingly little research has explored emergent literacy development for children with autism spectrum disorders (ASD). Longitudinal research reveals that for children developing typically, the following emergent literacy skills are predictive of later literacy success: oral language ability (e.g., vocabulary, grammar, story comprehension), print concepts knowledge (i.e., environmental print recognition, knowledge of print forms, conventions, and functions), alphabet knowledge (i.e., letter name and letter sound), emergent writing (e.g., name

writing), and phonological awareness knowledge (National Early Literacy Panel, 2007; Scarborough, 1998). These skills are presumably affected by children's interest in literacy and the behaviors of their parents, such as reading to their children (National Research Council, 1998).

Objectives:

This study sought to describe, for young children with ASD: (a) What emergent literacy skills and understandings they possess in terms of their oral language ability, print concepts knowledge, alphabet knowledge, emergent writing, and phonological awareness knowledge, (b) What associations may exist among these skills, and (c) How these children's interest in literacy and parents may promote development in these areas.

Methods:

Forty-one child participants with ASD between the ages of 4 years, 0 months and 7 years, 11 months were assessed. Assessments of oral language, print concepts, and emergent writing were administered to the children. Parents of thirty-five of these children took part in a structured interview using the *Home Emergent Literacy Profile for Children with Autism Spectrum Disorders* (Lanter, 2008) which further explored these emergent literacy skills, as well as the children's phonological awareness, interest in literacy, and behaviors of the parents believed to promote emergent literacy development.

Results:

Approximately 75% of the children in this study had oral language impairments. Their oral language skills, as well as other emergent literacy skills, were moderately to highly correlated with one another (*r*s between .34-.76). Some children performed better than would be expected on some skills given their oral language ability. Variable performance was observed both within and across emergent literacy skills. Discrete print concepts skills (e.g., environmental print recognition, print conventions such as book orientation) and discrete alphabetic knowledge skills (i.e., letter identification), were relatively stronger than more holistic print concepts skills (e.g., print functions such as pretend reading and understanding the purpose of reading and writing) and holistic oral langauge skills (e.g., story comprehension). A strong interest in literacy was reported for most of the children, as well as active parental teaching of literacy skills.

Conclusions:

The relative difficulty with understanding the social communicative purpose of written communication for the children in this study parallels what we know about conventional literacy and oral language development in children with ASD. That is, pragmatic language abilities are more universally adversely affected than structural language abilities (Tager-Flusberg, 2004). The implications for educators are to consider the emergent literacy development of children with ASD within a broader linguistic framework, and employ instructional methods that teach the components of literacy in meaningful activities.

105.067 67 Do Early Language Milestones Predict Later Language Abilities and Adaptive Skills in Children with High Functioning Autism Spectrum Disorders?. K. K. Powell*[1], G. L. Wallace[2], C. Anselmo[1], D. O. Black[2], A. M. Bollich[1], R. Roberson[2] and L. Kenworthy[1], (1)*Children's National Medical Center*, (2)*National Institute of Mental Health, National Institutes of Health*

Background:

While language ability is an important predictor of outcome in children with autism, the role of language among high functioning children with autism spectrum disorders (HF-ASD) is more controversial. Language milestones and current language functioning are key elements of the diagnostic distinction between Asperger Syndrome and high functioning autism. However, disagreement currently exists in the field regarding whether early language milestone attainment and structural language are predictive of later communication and language abilities in high functioning autism. This confusion may in part be due to the definitions used in previous studies examining the impact of language delays. Some studies have relied

on the DSM-IV definitions, which are not representative of typical language development. Twenty-four, not 36, months is the accepted milestone for phrase speech and is recommended as a developmental language benchmark by an NIH ASD working group. Milestones are easily obtained and knowledge of their implications for later language abilities would be useful in both clinical and research settings.

Objectives:

In this investigation, we examine whether attainment of typical early language milestones in children with HF-ASD predicts better outcome, as measured by core language abilities and adaptive communication skills, at school age.

Methods:

Subjects were a clinically referred sample of 77 children (mean age: 9.1 ± 2.8 years; 88.3% male; verbal, nonverbal or full scale IQ≥70) diagnosed with an ASD (autism n=35, Asperger Syndrome n=24; PDD-NOS n=18) based on DSM-IV criteria, the Autism Diagnostic Interview (ADI) and Autism Diagnostic Observation Schedule. The sample was divided into two groups: on-time versus delayed-onset of phrase speech. Milestone data was collected retrospectively through the ADI interview. The Vineland Adaptive Behavior Scale (VABS) was used to measure functional communication and socialization. Because of its previously demonstrated predictive power, a sentence repetition task was used to estimate current core language abilities.

Results:

The on-time language milestone group achieved higher scores on three measures of cognitive ability including verbal ability, nonverbal ability, and full scale IQ (all *p*s<.05). After controlling for nonverbal ability, the delayed language milestone group showed greater impairment in structural language and functional communication, but not functional social skills.

Conclusions:

We find that milestones are useful for capturing language performance at school age even in high functioning, verbal children on the autism spectrum. When a detailed assessment of language is not possible, data on early milestones may be useful for treatment planning in clinical settings and language phenotyping in the laboratory. Language milestones might offer an easy, early-available method for parsing the heterogeneity in ASD that confounds many inquiries into its biology. Milestone information can also be used by pediatricians and other practitioners when they are predicting trajectories and as an impetus for early intensive language intervention even for children with HF-ASD.

105.068 68 Ostensive Cueing Enhances Retention of Fast Mapped Words in Typically Developing 24-Month-Olds but Not Those at High-Risk for Autism Spectrum Disorders (ASDs). R. Bedford*[1], T. Gliga[2], K. Frame[3], K. Hudry[1], T. Charman[3], M. H. Johnson[2] and .. The BASIS Team*[4], (1)*Department of Psychology and Human Development, Institute of Education*, (2)*Birkbeck, University of London*, (3)*Institute of Education, University of London*, (4)*BASIS*

Background:

Individuals on the autistic spectrum are characterised by social-communication impairments and, in some cases, language deficits. In typical development, children use various strategies to disambiguate the referent of a new word. Impairments in these mechanisms may offer a potential explanation for the subsequent language problems often seen in autism. Preissler and Carey (2005) demonstrated that under conditions of referential ambiguity children with autism are able to use their knowledge of familiar labels to constrain hypotheses about the meaning of novel words (mutual exclusivity; ME). On the contrary, autistic children benefit less from social cues when learning words (Preissler and Carey, 2005; Parish-Morris, Hennon, Hirsh-Pasek, Golinkoff and Tager-Flusberg, 2007).

Objectives:

In order to explore development of this word learning strategy in the broader autism phenotype (BAP), our study examines ME in a group of 24-month-olds at high risk for

autism (due to having an older sibling with autism) and low-risk controls. We also aimed to extend these findings to include a memory component and explore performance in novel word retention to see whether memory performance is affected by ostensivelly correcting or reinforcing children's initial choices.

Methods:

Participants were 24-month-old children, 40 at high risk for ASD and 40 low-risk controls, recruited through the British Autism Study of Infant Siblings (BASIS).
On each of the eight trials, the child was presented with three objects, two familiar and one novel, and asked for either a familiar object (four trials) or a novel object (four trials). On all familiar object trials and two of the novel trials the experimenter responded 'thank you' irrespective of the child's choice of object. On the remaining two novel trials the experimenter either corrected (if the child made an incorrect or no object selection) or reinforced (if the correct object was selected) the word-object mapping, by labelling it ostensivelly. Following a five minute delay, four memory trials were presented.

Results:

There were no group differences between high-risk and control children in the ME mapping task with both groups performing significantly above chance in both the familiar and novel objects trials. In the memory trials, the performance of both groups for the non-reinforced trials was at chance level. However, performance of the control group was improved significantly when initial choices were corrected or reinforced using ostensive cueing. In contrast, high-risk children did not benefit from the ostensive labelling.

Conclusions:

Both typically developing 24-month-olds and those at high risk for autism are able to use the principle of mutual exclusivity. However, for the children in the high-risk group, unlike the control children, the retention of word-object mapping is not helped by ostensive naming. This suggests that the observed difficulties may reflect social characteristics, rather than word learning ability per se.

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[a]University of Cambridge, [b]Institute of Psychiatry, [c]Institute of Education, [d]Birkbeck, University of London

105.069 69 Empathic Response Predicts Language Development in Infants at Risk for Autism and Low-Risk Comparison Infants. T. Hutman*[1], A. D. DeLaurentis[1], A. Rozga[2], M. Sigman[1] and M. Dapretto[1], (1)*University of California, Los Angeles*, (2)*Georgia State University*

Background: 12-month-olds subsequently diagnosed with autism pay less attention and demonstrate less affective response to another person's distress relative to typically developing infants and the infant siblings of children with autism who do not meet criteria for autism at 36 months (Barnwell et al., 2009). Infants' distress responses have been related to the development of empathic concern (Zahn-Waxler, Radke-Yarrow, Wagner, & Chapman, 1992). Thus, they are theoretically linked with early social cognition (Rochat & Striano, 1999) and, thereby, with language development (Woodward, 2001).
Objectives: This study sought to identify links between empathic response at 12 months and language skills at 36 months in children whose language skills are in the normal range. The study also sought to determine whether the relationship between empathic response and language development differed between groups of infants at high- and low-risk of developing autism.
Methods: Participants were 53 high-risk siblings of children with autism and 38 low-risk infants with no family history of autism. None of these children met criteria for ASD at 36 months, as determined by the ADOS and clinicians' judgment. Twelve-month-olds' reactions to an examiner's display of distress were coded for attention and affective response, using four-point Likert scales. Median splits were used to form high/low attention and affective-response groups. Mean differences were evaluated for expressive and receptive language scores (Mullen Scales of Early Learning, 1995) at 36

months.
Results: High- and low-risk groups' language scores did not differ at 12 or 36 months. Infants who paid more attention to distress at 12 months had higher expressive and receptive language scores at 36 months relative to the low-attention group. Infants who demonstrated any affective response to distress had higher receptive language scores at 36 months than children who did not respond affectively (all p values < 0.05). These results held when we controlled for 12-month verbal and non-verbal mental age and for household income. Effect sizes were modest (_2 range 0.06 to 0.09). Group membership (high-risk vs. low-risk) did not moderate the relationship between empathic response and language scores at 36 months.
Conclusions: Twelve-month-olds who pay more attention and demonstrate any affective response to another person's distress have better language skills at 36 months than those who are less responsive to other people's distress. These findings suggest that the ability to detect and interpret changes in affective expression contributes to infants' developing understanding of others' internal states and intentions and, thereby, to language acquisition. Empathic responsiveness should be studied experimentally for impact on language skills and should be targeted in early intervention programs designed to improve language outcomes.

105.070 70 Repeated Prospective Assessments of Communication Abilities in Infants at High Risk for Autism Spectrum Disorders. M. V. Parladé*, J. Johnson and J. M. Iverson, *University of Pittsburgh*

Background: Infant siblings of children with ASD are at heightened biological risk for ASD and other developmental delays (High Risk; HR; e.g., Zwaigenbaum et al., 2007). Receptive and expressive language impairments, well documented in children with ASD (e.g., Tager-Flusberg et al., 2005), may be early indicators of risk (e.g., Zwaigenbaum et al., 2005). Recent estimates suggest that as many as 15-30% of HR infants are likely to exhibit patterns of delay in early communicative and language development (e.g., Gamliel et al., 2007). However, because most studies sample communicative behavior relatively infrequently (e.g., at 14 and 24 months) or at a single time point, the extent to which these delays are persistent versus more transient is unclear.

Objectives: The current study investigated communicative behaviors in HR infants and infants with no family history of ASD (Low Risk; LR) at regular and frequent intervals from 8 to 24 months.

Methods: Fifty-two HR infants (23 males) and 33 LR infants (16 males) were observed at home monthly from 8 to 14 months with follow-up at 18 and 24 months. Caregivers completed the MacArthur-Bates Communicative Development Inventory (CDI; Fenson et al., 2007) at every observation. The CDI was scored according to manualized procedures (norms are based on age and gender), and two variables were analyzed: Words Produced and Words Understood. The percentages of HR versus LR infants who received scores at or below the 10th percentile on each measure (considered to be an indicator of risk for communicative delay; e.g., Heilmann et al., 2005) were examined, as was the number of times infants' scores fell below cut-off.

Results: Seventy-one percent of HR infants, as compared to 40% of LR infants, scored at or below the 10th percentile on Words Produced at some point during the assessment period. Relative to LR infants, a significantly greater percentage of HR infants scored at or below cut-off at 13, 14, and 24 months, Fisher's exact tests, *p*s < .1. Further, all LR infants falling at or below the 10th percentile on Words Produced did so only once or twice; however, seven HR infants (30%) received at-risk scores three or more times. The pattern was similar for Words Understood. Seventy-five percent of HR infants versus 48% of LR infants scored at or below cut-off at least once. Compared to LR infants, the percentage of HR infants scoring below cut-off was significantly higher at 10, 11, and 14 months, Fisher's exact tests, *p*s < .1. Additionally, while most LR infants scored at or below the 10th percentile fewer than 5 times and only one LR infant reached cut-off at all seven observations, 30% of HR infants received at-risk scores six or seven times.

Conclusions: Although delays in communication development were apparent among some LR infants, there appears to be an HR subgroup that is susceptible to increased disruption in communication. Children exhibiting this profile over time may have a greater probability of showing long-term developmental problems. These findings underscore the utility of assessing HR infants' development serially over time.

105.071 71 Do Children with High-Functioning Autism Appropriately Mark Contrastive Stress in Speech to a Partner?. A. Nadig* and H. Shaw, *McGill University*

Background: Expressive prosody is often atypical in people high-functioning autism (McCann et al., 2007; Paul et al., 2005; Shriberg et al., 2001). It has been suggested that pragmatic prosody, which has a communicative rather than grammatical function, may be particularly impaired in autism due to its contextual nature. One instance of pragmatic prosody is contrastive stress, used to emphasize new or distinguishing information. The prominence of contrastive stress is created through an increase in syllable pitch, amplitude, and length relative to the surrounding sentence. Previous studies using perceptual ratings to evaluate contrastive stress marking report misplacement of stress by individuals with autism (Baltaxe, 1984; Fine et al., 1991).

Objectives: This study employed acoustic analyses of speech from an interactive communication task to examine the marking of contrastive stress in a naturalistic setting. The use of increased pitch, amplitude, and length were measured, as were the location of this marking and the location of the longest pause in the instruction.

Methods: Participants were 8- to 14-year-olds with HFA or typical development (TYP), matched on language level, age and gender. Fifteen HFA and 11 TYP children gave listeners instructions to select objects from a display. Instructions were of the form "Pick up the big cup" (where a small cup was also present in the display). Audio recordings were analyzed using PRAAT software (Boersma & Weenink, 2008) which allowed for automated calculations of pitch, amplitude, and length of instructions. The syllable containing the primary vowel in the adjective (e.g. li in "little"), which we expected to be marked for contrastive stress, was compared to the average pitch, amplitude, and length of the carrier phrase. An increase in these features suggests the use of contrastive stress. The syllables to the left and right of the target syllable were also analyzed to examine whether placement of stress differed between groups. Finally, the location of the longest pause in the utterance (before the determiner, adjective, or noun) was analyzed.

Results: Both groups demonstrated the use of contrastive stress by marking the adjective with increased pitch, amplitude, and length. However, typically-developing children used changes in amplitude to mark contrastive stress more reliably than children with HFA. Position analyses showed that both groups place marking on the expected syllable, rather than the syllable before or after. Pause location did not differ reliably between groups and generally came before the determiner. Finally, children with HFA who had higher levels of Performance IQ demonstrated greater use of contrastive stress marking.

Conclusions: When adjectives were included in an instruction, as called for by the referential context, both groups marked contrastive stress in similar manner. However some participants with HFA did not produce distinguishing adjectives when necessary, and others produced adjectives with contrastive stress marking when this was irrelevant from their partner's perspective.

105.072 72 Maternal Input Correlates with Wh-Question Comprehension in Young Children with Autism. A. Goodwin*, J. Piotroski, G. Jaffery, D. A. Fein and L. Naigles, *University of Connecticut*

Background: Wh-questions play a central role in many social interactions. However, these forms are often absent from the speech of young children with autism (ASD), and are challenging for them to understand (Naigles et al., 2008). Recent studies have reported that variation in maternal linguistic input correlates significantly with variation in subsequent speech production (word use, MLU) of children with ASD (Swensen et al.,

2007); the current research investigates whether such correlations might be found with children's language comprehension in general, and with their grasp of Wh-questions, in particular. The current research is part of a longitudinal language study in which children with ASD are visited every four months across a 3-year time span. This report includes maternal input from visits 1 and 2, and comprehension data from visits 3 and 4.

Objectives: We investigated the comprehension of subject- and object-Wh-questions in 3-year-old children with autism. We then correlated their comprehension scores with maternal input measures from earlier visits.

Methods: At visit 1, the children had a mean age of 33 months, had begun intensive ABA therapy, and produced 27% of the words on the MacArthur CDI checklist. At Visit 3, they averaged 45 months and produced 45% of the words on the CDI. Mothers and children participated in 30-minute semi-structured play sessions at each visit. Maternal Wh-questions during the sessions were coded for various linguistic features. At visits 3-4, children watched a Wh-question video in an Intermodal Preferential Looking paradigm. This video showed 'hitting' events (e.g., an apple hitting a flower), followed by test trials in which the apple and flower were shown on separate screens. Three types of Wh-questions were tested: Object questions ("What did the apple hit?"), Subject questions ("What hit the flower?") and Where questions ("Where is the apple?"). Children's eye movements were recorded and coded off-line to assess comprehension.

Results: Approximately 11% of maternal utterances at these visits were Wh-questions; 60% of these included the copula as the main verb (e.g., "What's this? Where is the cookie?"). Many significant correlations were found between maternal input at visits 1 and 2 and later comprehension by their children; we report only the ones that were still robust once maternal MLU and child vocabulary were partialled out. Maternal speech forms that correlated negatively with later child Wh-question comprehension included Wh-questions with the copula as the main verb, and Wh-questions that repeatedly used the same few verbs (e.g., want, see, have). Maternal forms of speech that correlated positively with later child Wh-question comprehension included questions with inverted auxiliaries (e.g., "What did she eat?" rather than "What I'm going to do?") and those with content-rich verbs (e.g., build, eat).

Conclusions: Wh-question acquisition in children with ASD appears to progress more slowly when their input consists more heavily of Wh-questions with the copular "be" than Wh-questions with a wide variety of content-rich verbs. Moreover, good examples of Wh-questions (e.g., with inverted auxiliaries) also seem beneficial. Thus, some kinds of input seem especially accessible to children with ASD for learning about Wh-questions.

105.073 73 Word Learning in Preschoolers with ASD: Is Word Learning Easier with a Computer Than with a Person?. H. Noble*[1], S. McCurry[1], L. G. Klinger[1], M. R. Klinger[1], J. Scofield[1] and A. W. Duncan[2], (1)*University of Alabama*, (2)*Cincinnati Children's Hospital Medical Center*

Background:

Children with typical development learn words by following the gaze of the person who is using a new word (i.e., by using joint attention). However, they are also able to learn new words when another person is not present (i.e., by watching television; Scofield & Behrend, 2007). Joint attention impairments are some of the earliest symptoms of autism spectrum disorder (ASD) and have been linked to future language delays (e.g., Mundy, Kasari, & Sigman, 1992; Sigman & Kasari, 1995). Because of impaired joint attention, children with ASD may need to rely on other learning strategies that do not require joint attention to learn new words (McDuffie, Yoder, & Stone, 2006).

Objectives:

The present study examined novel word learning in preschool-aged children with ASD. We compared word learning in a traditional joint attention paradigm with word learning in the absence of joint attention (i.e., words were presented via a computer instead of a

social partner). It was hypothesized that preschoolers with ASD would show more word learning in the nonsocial condition.

Methods:

Thus far, 12 preschoolers with typical development (TD) and 10 preschoolers with ASD have completed the study. In the social joint attention condition, the examiner placed a novel object between herself and the child and labeled the novel object 3 times (e.g., " Look a zog, a zog, it's a zog."). The novel object was then removed for 2-3 seconds and then presented a second time alongside another novel object. The examiner asked the child to locate the labeled object ("Can you point to the zog. Where is the zog?"). The nonsocial task was identical except that the object and label were presented via computer with no help from a person. For both social and nonsocial conditions, control trials were administered in which the examiner or computer presented the object and merely commented on it without providing a label (i.e. "Look, Look").

Results:

Across social and nonsocial tasks, children with ASD showed less language learning than children with TD, $F(1,17) = 5.93$, $p = .03$. Follow-up comparisons showed that children with ASD showed more language learning on the social than the nonsocial task, $t(8)=3.6$, $p = .01$). In the control trials, children with ASD were less likely to link a label (e.g., "koba") with the object that the examiner had previously commented on (e.g., "Look, Look"), $F(1,17) = 30.05$, $p < .001$.

Conclusions:

These results suggest that like children with TD, children with ASD do learn new words when interacting with a social partner. However, children with ASD were less likely to infer that a new word went with a novel object in the more ambiguous control condition. Contrary to expectations, children with ASD did not learn words better in the nonsocial computer condition than the social partner condition. Thus, language interventions that are nonsocial may not be as effective in children with ASD as has been previously hypothesized.

105.074 74 Using a Developmental Framework to Evaluate Expressive Language Abilities in Children with Autism Spectrum Disorders (ASD). C. Colombi*[1], K. Lopez[2] and C. Lord[1], (1)*University of Michigan*, (2)*University of Michigan Autism & Communication Disorders Center (UMACC)*

Background: The identification of common measures of expressive language is needed to evaluate the efficacy of interventions targeting language in children with Autism Spectrum Disorders (ASD). Tager-Flusberg et al. (2009) recently proposed the use of a developmental framework to describe children's expressive language abilities. Moreover, they proposed that researchers move away from using the traditional "functional speech" framework for evaluating language acquisition.

Objectives: The aim of this studyis to test the use of Tager-Flusberg et al.'s developmental framework of expressive languagein a group of children with ASD, children with developmental delays (DD), and typically developing children. 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 72 months of age. Expressive language development was measured with Tager-Flusberg et al.'s developmental framework by using data collected through the following standardized measures: MacArthur-Bates Communicative Development Inventory (Fenson et al., 1993), ADOS (Lord et al., 2000), ADI-R (Lord et al., 1994), and Vineland Adaptive Behavior Scales (2005). Expressive language trajectories of children with ASD will be compared with children with DD as well as typically developing children.

Results: Results of the data analysis described above will be presented.

Conclusions: Benefits of using a developmental framework to evaluate expressive language abilities of children with ASD will be presented. The implementation of this framework to measure changes in language acquisition studies will be discussed.

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105.075 75 Mother-Child Interaction, Symbolic Play, and Productive Speech in Preschool Children with Autism. E. Dromi*[1], L. Cooper[1] and D. A. Zachor[2], (1)*Tel Aviv University*, (2)*Tel Aviv University / Assaf Harofeh Medical Center*

Background: Irregularities in patterns of adult-child interaction, symbolic play, and productive speech comprise major clinical signs of autism in young children. These areas have been extensively studied in relation to cognitive growth as well as to social competence (e.g., Leslie, 1987). Most previous studies targeted groups of children with autism spectrum disorder (ASD) and utilized quantitative measures to compare them to children with typical development or with mental retardation (e.g., Lord, Risi, & Pickles, 2004; Rice, Warren, & Betz, 2005; Rutter & Schopler, 1987). The present study design derived from social interaction theories, which regard the mother-child unit as a system that supports the emergence of symbolic representation (Bruner, 1975; Vygotsky, 1978; Werner & Kaplan, 1963).

Objectives: Our goal was to examine the quality of mother-child interaction, symbolic play, and speech production in preschool children with autism in order to verify possible interrelations among these domains.

Methods: Ten mother-child dyads (9 boys and 1 girl) participated in the study. Ages ranged from 37 to 51 months (*M* = 45 mo). All children had previously been diagnosed with ASD using the ADOS (Lord, Rutter, DiLavore, & Risi, 1999) at age 12-30 months (*M* = 20.9 mo). Participants demonstrated DQs above 70 on the Mullen Scales of Early Learning (1984). All children attended the same ABA intensive intervention program for at least 12 months prior to data collection (Zachor et al., 2007). Ten minutes of mother-child interaction in semi-structured situations were video-recorded and analyzed using micro-developmental analytic methods. Joint engagement measures were computed for each pair. Ten minutes of solitary play with two sets of toys were also video-recorded and scored for symbolic play levels utilizing a revised code that was initially developed by Belsky and Most (1981) and modified by Ungerer and Sigman(1981) . The solitary play recordings were also used for evaluating each child's speech production levels.

Results: All children demonstrated difficulties in establishing eye contact for social purposes, physical touch, as well as social smiles. A strong correspondence was identified between the overall joint dyadic engagement scores and children's levels of symbolic play. In dyads that maintained longer durations of triadic interaction (i.e., child-mother-object), the children demonstrated higher levels of symbolic solitary play. Levels of symbolic play were also associated with levels of speech production.

Conclusions: Speech production, socioemotional interaction, and symbolic play interrelate in interesting ways in this population. Importantly, social-emotional engagement between mothers and their young children seems related to the levels of solitary symbolic play achieved by the children. Qualitative analysis of mother-child interaction in dyads where the child has autism reveals the importance of considering socioemotional dyadic goals for early intervention. The detailed qualitative analyses in the present cross-case investigation substantiated previous findings of comparative group designs.

105.076 76 Play Behaviors in Infants at High-Risk for Developing Autism. J. Gibson*[1], A. Sabatino[1], M. Sabatos-DeVito[1], J. T. Elison[1] and J. Piven[2], (1)*University of North Carolina at Chapel Hill*, (2)*University of North Carolina*

Background: Autism is a developmental disorder characterized by social impairments, communication deficits, and repetitive and restricted behavior. It is possible that early deficits in autism may be evident in the development of play behavior because play behavior has been shown to be a forum through which infants develop skills and strategies for goal-directed and social activities (Weisler & McCall, 1976; Belsky & Most, 1981). Differences in play behavior have already been identified between toddlers with and without autism (Naber et al., 2008); therefore, we sought to explore if

differences in play behavior are evident at 12 months of age in infants at high versus low risk for developing autism.

Objectives: As part of the Infant Brain Imaging Study (IBIS) ACE Network investigating early brain and behavior development at 6, 12, and 24 months in infant siblings of children with (high risk) and without (low risk) autism, our study aims to investigate the frequency and variety of object exploration behaviors and the level of or sophistication of play during a semi-structured play session at the 12 month visit.

Methods: As part of the IBIS Network 12-month behavioral battery, each infant is assessed with the Communication and Symbolic Behavior Scales (CSBS; Wetherby and Prizant, 2002). Independent, reliably trained coders evaluated recordings of the final portion of the CSBS behavioral scales using the IBIS-PlayGrid. The session involves a variety of play kitchen utensils (i.e. spoons, bowls, bottles, a frying pan, etc.) and a doll.The IBIS-PlayGrid captures the frequency with which actions occur, forms an inventory of the objects explored, and classifies actions into four levels of play: simple exploratory (i.e. mouthing, banging, shaking), relational (i.e. stacking), functional-relational (i.e. stirring), and pretend (i.e. pretending to feed Big Bird).

Our current sample includes 14 13-month-olds: n = 7 high-risk infants [mean age = 56.6 weeks (sd=2.2)];n = 7 low-risk infants [mean age = 60.2 weeks (sd=2.5)]. Coding is ongoing, and our sample size will have at least 75 high-risk and 40 low-risk infants for presentation at IMFAR in May of 2010.

Results: Student *t*-tests were conducted to evaluate group differences. Preliminary analyses indicate that high-risk infants perform significantly fewer functional-relational actions than low-risk peers (p=0.003). Additionally, statistical trends are present, indicating that high-risk infants play with fewer objects in a functional-relational manner (p=0.06) and a larger proportion of their actions are simple exploratory behaviors (p=0.06) as compared to low-risk peers.

Conclusions: Data collection is ongoing and the majority of children in our high-risk group will develop on a typical trajectory (approximately 1 out of 20 might develop autism). However, the large group differences in play behavior by 12 months demonstrates the potential value of the play behavior coding scheme as a tool for identifying and monitoring behavioral markers in the domain of play and object exploration. These results also provide evidence that differences in play behavior in the first year of life may be a distinguishing characteristic between children at high versus low risk for developing autism.

105.077 77 Validation of a Measure of Early Object Knowledge in Toddlers with Early Autism Symptomatology. A. H. Brown*[1], A. S. Nahmias[1], D. S. Messinger[2], A. S. Carter[3], W. L. Stone[4] and P. Yoder[1], (1)*Vanderbilt University*, (2)*University of Miami*, (3)*University of Massachusetts Boston*, (4)*Vanderbilt Kennedy Center*

Background:

Diversity of differentiated (functionally appropriate) object play is thought to index greater object knowledge in young children exhibiting signs of autism. It is often defined as the number of unique play actions observed during an assessment (Yoder, 2006), and has been shown to positively predict later language development in children with autism (Sigman & Ruskin, 1999; Yoder, 2006). However, little is known about assessing play behavior in very young, non-verbal children (less than 24 months) with autism symptoms.

Objectives:

This study examines the validity of an observational measure of object knowledge in toddlers exhibiting early symptoms of autism.

Methods:

Participants from the initial assessment of *A Multi-Site Clinical Randomized Trial of the Hanen More than Words Intervention* included 63 toddlers (mean CA = 21.2 months, range = 15.5 – 25.0 months). They met a predetermined cutoff on the STAT and had a clinical presentation consistent with ASD. A nomological network approach (Cronbach & Meehl, 1955) and a divergent validation approach were utilized to assess the construct

validity of a proposed measure. Diversity of play was defined as the number of differentiated play actions by the child during a 7-minute portion of the Developmental Play Assessment. The constructs predicted to be associated with diversity of play actions were (a) attention, (b) mastery motivation, (c) play and imitation, and (d) object-oriented turn-taking. The four variables used to represent these constructs were a) the Attention Subscale of the Infant/Toddler Social and Emotion Assessment (ITSEA), b) the Mastery Motivation Subscale of the ITSEA, c) the sum of the number of items failed on the Screening Tool for Autism in Two-Year-Olds (STAT) Play and Imitation domains, and d) the sum of the number of action turns and give turns by the child during an experimental measure of object turn-taking (Yoder & Stone, 2006). For the divergent validation approach, we examined these same correlates with frequency of initiating joint attention (IJA) in the Early Social Communication Scale (ESCS).

Results:

As predicted, the number of differentiated play actions was correlated with the ITSEA Mastery Motivation subscale, the number of items failed on the STAT Play and Imitation domains, and the sum of the action and give turns ($r = .31$, $-.48$, and $.46$ respectively). The number of differentiated play actions was not correlated with the ITSEA Attention subscale. To provide further evidence of validity, relationships between the 4 comparison variables and a positive, but theoretically unrelated variable, the IJA total score from the ESCS, were tested. IJA was not significantly correlated with attention, mastery motivation, play/imitation, or turn-taking.

Conclusions:

These results support the hypothesis that the number of differentiated play actions by a child may be a valid measure of object knowledge in toddlers showing early signs of autism. These findings are encouraging, given that there are currently no measures of early object knowledge validated for use with very young, non-verbal children. This study provides support for further examination and validation of the diversity of play measure with this unique population.

105.078 78 Associations Between Elevated Cortisol, Age and Social Engagement During Play in Children with Autism. C. Schupp*[1], D. Simon[1], N. Ryan[1], S. Mendoza[2] and B. Corbett[1], (1)*M.I.N.D. Institute, University of California at Davis*, (2)*University of California, Davis*

Background: Play is critical for the development of social, cognitive, and motor skills. Even though poor reciprocal social interaction is the hallmark deficit in autism, surprisingly few ecologically valid observational studies of play exist. Autism is heterogeneous and the social behavior that defines it is diverse. It may be the case that differences in social behavior may also reflect distinct underlying psychobiological profiles related to LHPA responsivity.

Objectives: The purpose of the investigation was to evaluate cortisol responsiveness in a naturalistic playground social setting. This ecologically valid design permits the careful investigation of social interaction in a play-based paradigm. In contrast to many studies of physiological responsivity, which inherently aim to solicit a stress response, the paradigm was designed to emulate a "real life" playground to determine whether such environments would be deemed physiologically stressful. The current study was designed to examine stress responsivity as measured by salivary cortisol comparing children with autism to neurotypical peers during a 20-min playground paradigm. 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 to more thoroughly capture the dynamic social exchanges.

Methods: The experiment involved sets of 3 children; a child with autism, a neurotypical child, and a neurotypical confederate. Participants included 45 prepubescent males between 8 to 12 years (21 with autism). Each twenty minute playground sequence included three children: a neurotypical child, a 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. Four salivary samples were obtained: (S1) a baseline sample taken after arrival (~15 min acclimation) just prior to the playground peer interaction, (S2) post-play, (S3) 20-min post play, and (S4) 40-min post play.

Results: Repeated measures analysis of the cortisol values revealed a significant model

(__(4)=22.76, P<0.0005) that included time of measurement, diagnosis, and age as main effects and an interaction between diagnosis and age. Thus, older children with autism exhibited enhanced cortisol responsivity compared to their average afternoon cortisol levels, baseline, and compared to younger peers. Stress responsivity was associated with group play and reduced nonverbal social skills.

Conclusions: The enhanced cortisol response was observed in children who voluntarily engaged in interaction; thus, it does not support the notion of a response to social threat; rather, it appears to reflect attendant metabolic preparedness and enhanced arousal from engaging socially. The peer interaction paradigm resulted in a significant stress response in children with autism. Furthermore, distinct patterns emerged within the autism group based on developmental (older), biological (cortisol responder) and behavioral patterns (engaged in group social interaction). The data suggest that many children with autism mount measurable stress responses in relatively benign social situations, which appear to be a function of age and level of social engagement.

105.079 79 Improving Play Skills and Decreasing Challenging Behavior by Reducing the Reinforcing Value of Stereotypy in Young Children with ASD. R. Lang*, *University of California, Santa Barbara*

Background: Children with ASD often experience substantial delays in the development of play behavior. Interventions to teach play skills are often complicated by challenging behavior and stereotypy. Previous research has demonstrated a potential relationship between stereotypy, challenging behavior and play in children with ASD. However, few research-based methods for addressing stereotypy and challenging during play interventions are available to practitioners. An abolishing operation is any stimuli or series of events that reduces the value of a particular reinforcer. If an individual has unrestricted access to a particular reinforcer for an extended period of time that stimuli may eventually lose its reinforcing value. Incorporation of the abolishing operation concept into play interventions may allow practitioners to effectively reduce the reinforcing value of stereotypy prior to beginning a play intervention. If the reinforcing value of stereotypy is reduced, then the child may engage in less stereotypy and less challenging behavior when stereotypy is interrupted.

Objectives: The purpose of this study was to reduce stereotypy and challenging behavior during a play intervention for five children with autism by adding an abolishing operation component to a common research-based procedure for teaching play skills.

Methods: The effects of two conditions were compared in an alternating treatment design. In one condition (abolishing operation condition) the child is allowed to engage in stereotypy freely prior to the implementation of an intervention targeting play skills.This free period lasted until the child engaged in a predetermined rejecting topography. Occurrence of the rejecting topography suggested the child was in a state of satiation in terms of the automatic reinforcement produced by the stereotypy. In the second condition the same play intervention was implemented without the prior free play period. The levels of functional play, symbolic play, stereotypy, and challenging behavior were compared across these two conditions.

Results: Data show decreased levels of stereotypy and challenging behavior and increased levels of functional play following the abolishing operation condition. Symbolic play did not occur following either condition.

Conclusions: When designing an intervention to teach functional play to a child with autism who engages in stereotypy, this data set suggests two points. First, modeling, prompting with contingent reinforcement, and naturalistic instruction are potential effective intervention components. Second, it may be beneficial to allow the child to engage in stereotypy freely for a period of time prior to intervention. Two implications concerning stereotypy arise from this data set. First, for four of the five participants, stereotypy decreased as functional play increased. This data set provides evidence of a negatively correlated relationship between stereotypy and play skills. The possible existence of such a relationship suggests that one method for effectively treating stereotypy may be to teach children to play. Second, it is possible that allowing a child to engage in stereotypy freely prior to providing instruction in play skills (as was done in the AOC condition) may decrease the level of stereotypy during subsequent play instruction. This, in turn, may make it easer to engage the child and prompt functional play during the intervention session

105.080 80 Play Trajectories in Infant Siblings of Children with Autism. L. Christensen*, M. Sigman and T. Hutman, *University of California, Los Angeles*

Background: Christensen, et al. (2009) examined the play behavior of infant siblings of children with autism who later met criteria for ASD (ASD siblings), infant siblings with other non-ASD delays (Other Delays siblings), infant siblings with no delays (No Delay siblings), and typically developing controls (TD controls) at 18 months of age. Findings indicated that the ASD siblings showed fewer novel functional play actions and more non-functional repeated actions than the TD controls. The Other Delays and No Delays siblings also demonstrated more non-functional repeated play actions than the TD control group.

Further examination of the sample at 24 months of age indicated that there continued to be group differences in functional play between the ASD siblings and TD controls, with the ASD siblings showing fewer novel functional play behaviors. The No Delays and Other Delays siblings did not differ from the TD controls and there were no other group differences in play.

Objectives: The current paper examined play behaviors at 36 months of age and the development of play from 18 to 36 months of age. In particular, this paper addressed whether or not the trajectory of development differs across these four groups of children.

Methods: This paper examined a sub-sample of the participants from the previous study who have data at 18, 24 and 36 months of age. This sample consists of 41 of the original 77 participants drawn from the study site at UCLA. The participants were divided among the aforementioned four groups with ASD siblings (n= 7), Other Delays siblings (n= 7), No Delays siblings (n= 19), and TD controls (n= 7). A four-minute free play assessment performed at 18, 24 and 36 months of age was coded for symbolic, functional and repeated (functional and non-functional repeated) play actions.

Results: Results indicate that all three sibling groups display significantly more non-functional repeated play than the TD controls ($p < .02$ for all). Multilevel modeling techniques were used to examine the trajectories of play over time with observations at 18, 24 and 36 months nested within individuals. Results indicate significant linear increases in object-directed functional play and decreases in self-directed and non-functional repetitive play. The effect of time did not differ across individuals. There was significant variability in the intercepts of each play variable examined, which is not explained by group membership.

Conclusions: The results speak to the importance of play as an early indicator of autism and highlight the robust role of non-functional repeated play behaviors in differentiating individuals at risk from individuals not at risk for ASD. The results also indicate that the trajectory of change in play from 18-36 months of age may not differ across children with and without risk for ASD. Instead, the starting point may be more important in predicting outcomes.

105.081 81 High-Atypicality Infant Siblings of Children with Autism: A Prospective Study of Mother-Infant Interaction. M. W. Wan*[1], J. Green[1], M. Elsabbagh[2], M. H. Johnson[2] and .. The BASIS Team*[3], (1)*The University of Manchester*, (2)*Birkbeck, University of London*, (3)*BASIS*

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 difficulties than typically developing siblings (TD-sibs). Prospective observational studies, including our own, further show that mother-infant interactions in A-sibs show specific subtle but consistent differences in early-middle infancy from TD-sibs, 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 between A-sib infants at 6-10 months and 12-15 months, with and without high phenotypic autism risk, and TD-sib controls.

Methods: Ninety 6-min mother-infant unstructured play interactions were videotaped within the British Autism Study for Infant Siblings (BASIS). The videotapes were rated, blind to dyad information, on a global rating scheme which involved 3 maternal, 3 infant and 2 dyadic dimensions. The rating scheme has been revised from previous presentations of our data, and was developed based on typical developmental, attachment, and autism literatures and previously validated scales.

Results: A preliminary analysis of N=55 at 6-10 months found that, as a group, the mothers of A-sib infants with high phenotypic atypicality were more likely to show lower sensitive responsiveness and low acceptance of infant behaviour. Here, we will present findings for the full sample across two time points in infancy.

Conclusions: Measures collected in this study reflect dyadic characteristics and hence neither maternal nor infant behavior could be described as causing the atypicality. The amelioration, stability or exacerbation of such interactional characteristics would have implications for early (prodromal) intervention.

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105.082 82 Symbolic Acts in Children with Autism Spectrum Disorder: a Case of Triune Representation. C. H. Chiang*[1] and H. F. Lu[2], (1)*National Chengchi University*, (2)*Gang Shan Armed Force Hospital*

kBackground: There is considerable empirical evidence for deficits in pretend play in children with ASD compared with children with developmental delay (DD) and typically development (TD). However, mostly in pretend play may not be symbolic from the child's point of view; it is the adults interpret as symbolic. In the study, we referred Tomasello, et al (1999) suggestion and used the 'triune representation' point of view to measure the child's play behaviors.
Objectives: The purpose of this study was to (1) examine the performance of symbolic acts in children with ASD from the perspective of 'triune representation' point of view; (2) explore the nature of symbolic acts in play context.
Methods: Based on the perspective of 'triune representation', a modified paradigm from Striano, et al (2001) was tested to 17 children with ASD (mean CA= 69 months, mean MA= 56 months), 17 MA-matched children with DD and 19 children with TD. Two experiments were arranged. In experiment 1, examiner (E) introduced the doll house divided into four rooms with appropriate prop sets and used the three pairs of actors, including replica (a toy man and toy woman), instrumental (a pencil and a scissors), and natural (a rock and a stick) to play. Study session consisted two phases: baseline and testing phases. In baseline phase, E introduced the doll house and encouraged the child to use each of the three actors set in turn. Each pair can play in the doll house for two minutes. In testing phase, E modeled with the Action or Language conditions first

and then encouraged the child to play each pairs of actors for 2 minutes. We measured child's symbolic acts spontaneously in the Action and Language conditions. In experiment 2, children were given the 'functional sets' (i.e., doll + bed and pegboard + hammer) first and then 'symbolic sets' (i.e., doll + block and pegboard + brush) to play in front of E. We counted the child's looking behaviors as he/she engage in the functional and symbolic acts with object.
Results: (1) in experimental 1, there was no significant difference of symbolic acts among the three groups in the baseline phase. After E's modeling, children with ASD displayed lower novel symbolic acts on replicate set and natural set, and imitated less symbolic acts on instrumental set comparing with the two controls. (2) in experimental 2, the three groups all looked to E immediately after performing a symbolic acts more often than when they performed functional set. The children with ASD displayed less looks to E than children with DD and TD after they displayed the symbolic acts.

Conclusions: Using the perspective of 'triune representation' to measure the spontaneous symbolic play acts, children with ASD showed impairments on both imitative and novel symbolic acts. Furthermore, even children with ASD have developed the basic symbolic play behaviors, they displayed less looks to the adult. The theory of intersubjectivity deficit (Rogers & Pennington, 1991) in ASD was provided to explain the phenomenon.

105 Sensory Systems

105.083 83 A Pilot Randomized Control Trial of a Parent-Delivered Massage Intervention for Pre-School Children with Autism: The Qigong Sensory Training (QST) Home Program. L. M. Silva, M. Schalock and K. R. Gabrielsen*, *Western Oregon University*

Background: A recent randomized controlled trial of a Chinese massage intervention for pre-school children with autism showed significant improvement of behavioral and social/language measures of autism in treated children, as well as improvement in sensory impairment and self-regulation at five months of treatment. The intervention involved dual delivery of a simple version of the massage to children by trained parents on a daily basis, as well as a skilled version by trained Early Intervention (EI) staff. The EI staff component of the intervention was ten hours - delivered in twenty treatments over five months - more than the usually allotment of service time for local programs in Oregon. Given the current situation of shrinking budgets for autism services, the research team was asked to develop a parent-delivered massage program that would require less staff time and no direct treatment from staff.

Objectives: To determine whether a parent-delivered Qigong massage program would be effective in improving behavioral and social/language measures of autism, reducing impairment of sensory and self-regulation, and reducing measures of parent stress relative to caring for the child.

Methods: 39 children were randomly assigned to treatment and wait-list control conditions. Parents delivering the massage treatment received a three-hour group training followed by seven, weekly, half-hour support sessions from trained EI staff. Parents gave the massage daily for a four month duration. Pre and post testing was done with the Autism Behavior Checklist, the Pervasive Developmental Disorder Behavioral Inventory, the Sense and Self-regulation checklist and the Parent Stress Index.

Results: Treated children had significant improvement in measures of autism ($p,.01$) and sensory-regulation impairment ($p<.001$), and parent stress ($p<.001$) compared to wait-list controls. Effect sizes were in the large range.

Conclusions: A parent-directed Chinese massage intervention for pre-school children was effective in reducing the severity of measures of autism, sensory regulation impairment, and parent stress relative to caring for their child.

105.084 84 Autistic Traits and Auditory Perceptual Discrimination. M. E. Stewart*[1], M. Grube[2] and T. D. Griffiths[2], (1)*Heriot-Watt University*, (2)*Newcastle University*

Background: The Enhanced Perceptual Functioning model (Mottron & Burack, 2001; Mottron, et al. 2006) suggests that persons

with ASD have enhanced low level processing of basic perceptual information. In the auditory modality enhanced discrimination for pitch is found in children (Bonnel et al. 2003; O'Riordan & Passetti, 2006). Jones et al. (2009) found a subset of an adolescent ASD group to have enhanced ability to discriminate frequency. Memory for basic pitch stimuli is enhanced in ASD (Heaton, 2003). Whether enhanced low level processing occurs in ASD for all basic stimuli, and whether this model holds across the broader autism phenotype has not been tested. Traits or features of ASD are present both in relatives of those with ASD and in the general population (Autism-Spectrum Quotient, AQ Baron-Cohen et al., 2001a; Dawson et al., 2007; Hurley, et al. 2007). These traits are predictive of behaviours similar to those observed in ASD (Bayliss & Tipper, 2005; Baron-Cohen et al., 2001b; Stewart et al., 2009).

Objectives: We assess whether autistic traits predict performance on basic, low level auditory perceptual discrimination tasks of pitch, timing and loudness, by measuring individual thresholds in a reliable, adaptive fashion.
Methods: Participants were recruited from a database who had completed the AQ in order to achieve a range of scores in the sample (Mean AQ Likert scoring total=114.0, range=77 to 150) from Heriot-Watt University (n=24; mean age=22.3, s.d.=3.9; 12 males, 12 females). Ethical approval was obtained from the Ethics Committee of Heriot-Watt University. Participants were asked to discriminate tonal stimuli based on frequency, intensity and timing. The frequency and intensity tasks used a fixed tone reference; the timing task was conducted with a variable and a fixed time interval reference. IQ was assessed by a shortened version of Raven's Advanced Progressive Matrices (Raven et al., 1998).

Results: AQ scores correlate with thresholds for pitch discrimination ($r=-0.51$, $p<0.05$) and the fixed timing task ($r=-0.45$, $p<0.05$); as AQ scores increase there is enhanced discrimination of pitch, and timing on the fixed interval task. No correlation was found between AQ and intensity discrimination thresholds or the variable timing task. There was no relationship with AQ and the Raven's task, nor was there any relationship between the Raven's task and any of the perceptual tasks.

Conclusions: Autistic traits are predictive of pitch discrimination in a similar way to ASD, suggesting that features normally associated with ASD are also present in the Broader Autism Phenotype. This is the first study to show this relationship, and to show a relationship with timing. This study gives some indication as to the locus of the enhancement, suggesting that a stable representation of the stimuli may be formed. Both timing and pitch are important aspects of understanding aspects of language such as prosody. The literature suggests that basic perceptual processing may be related to language processing (Jones et al., 2009; Heaton et al, 2008), it remains to be tested whether this is the case.

105.085 85 Altered Face Perception in Children and Adults with ASD. J. Martineau*, N. Hernandez, L. Roche, L. Hiebel, A. Metzger and C. Barthelemy, *INSERM U 930*

Background: Autism Spectrum Disorder (ASD)is a pervasive neurodevelopmental disorder associated with a unique profile of social and emotional behaviour. The core symptomatology of autism highlights lack of social or emotional reciprocity, failure to develop age-appropriate relationships and lack of interest in the human face. The ability to judge facial expressions and derive other socially relevant information from faces is a fundamental requirement for normal reciprocal social interactions and interpersonal communication.
Objectives: The aim of this work was to investigate typical development of gaze behaviour during face and emotional expression perception on a wide number of subjects, using an eye-tracking system, and to identify dysfunction in patients with autism.
Methods: The study was conducted in 52 healthy children (aged 4 to 15 years) and 44 healthy adults (aged 18 to 35 years) and in 27 children with autism (aged 4 to 15) and 7 adults with autism (aged 18 to 35 years). The measurement of various parameters of

visual path scans (fixation time, length of path scan, velocity of ocular path scan, exploratory strategy, pupil dilation) was performed during visual perception of neutral faces (with direct or averted gaze), emotional faces or virtual faces.
Results: Analyses of the path scan data revealed marked differences between groups. The autistic adults and children have spent less time on the core features areas of the faces (eyes, mouth and nose) than controls and more time on the rest of the face. No effect of emotion was evidenced. In all groups, the effect of ocular dominance had been shown on the exploratory strategy. This strategy was sensitive to the maturation for the normal children. The autistic groups (adults and children) presented atypical patterns of visual exploratory strategy of faces concerning fixation time, length of path scan, velocity, exploratory strategy and pupil dilation.
Conclusions: These results indicate disorganized exploration of face stimuli in autistic patients. These findings raise the possibility that altered visual exploration of faces may contribute to the social impairment that characterizes autism.

105.086 86 Music Perception and Musical Behaviors in Children and Adolescents with ASD. E. M. Quintin*[1] and A. K. Bhatara[2], (1)*Université du Québec à Montréal & Autism Research Training Program*, (2)*University of California, Los Angeles*

Background: Individuals with Autism Spectrum Disorder (ASD) exhibit above average auditory processing abilities including enhanced pitch memory (Heaton, Hermelin, & Pring, 1998) and discrimination (Bonnel et al., 2003; Mottron, Peretz, & Ménard, 2000). They can also recognize basic emotions in music (Heaton, Hermelin, & Pring, 1999; Heaton et al., 2008). Although a growing interest for music perception in ASD has fuelled studies over the past decade, most studies have assessed performance of participants with ASD on laboratory tasks and few studies have collected information on use of music in everyday lives of individuals with ASD. Allen and colleagues (2009) conducted a semi-structured interview with adults with ASD to investigate their musical habits. They found that adults with ASD respond to and appreciate music in a similar fashion as the typical listener. Objectives: The aim of this study was to assess responsivity to music and musical habits, experience and ability in children and adolescents with ASD. We also investigated sensitivity to sounds in early childhood. Methods: Children and adolescents (7-17 years old) with typical development (N = 32, FSIQ: 79-130) and ASD (N = 27, FSIQ: 65-133), with comparable auditory working memory (p = .05) and musical training and experience (p >.05) participated in the study. The Salk and McGill Musical Inventory (Levitin et al., 2004) was completed by parents and a semi-structured interview was conducted with the participants (Queen's University Music Questionnaire – Revised, based on Cuddy et al., 2005). Results: There were more participants with ASD than TD who showed unusual fright or sensitivity in response to certain sounds in early childhood (p < .001). Children with ASD were viewed as being generally more musical than children with TD (p = .01), however the amount of interest in music was greater for the TD group than the ASD group (p = .04). The number of weekly hours spent listening to music as well as the strength of positive reactions to upbeat music and negative reactions to sad music did not differ between groups. Conclusions: Though the parents of children with ASD in our study reported more frequent hypersensitivity to sounds than parents of typical controls, this hypersensitivity appeared to have no detrimental effect on the musicality of children with ASD. Musical responsivity in everyday life seems to be similar in ASD and TD. Although parent report bias may explain why parents of children with ASD view their children as more musical, possibly in comparison to other aspects of their profile, this result warrants future studies on the islets of abilities of children with ASD. The positive view of parents with regards to their child's responsivity to music can fuel ideas for therapeutic use of music in family therapies for ASD.

105.087 87 Difference in Auditory Evoked Potentials in Children with Autism Spectrum Disorder Using Magnetoenecphalography. K. Khatibi*[1], T. Kenet[2], M. Arroyo[1], A. M. Findlay[1], S. Honma[1], B. Siegel[3], S. Nagarajan[1]

and E. Marco[3], (1)*University of California, San Francisco*, (2)*Massachusetts General Hospital*, (3)*UC San Francisco*

Background: Communication deficits are a core clinical feature for individuals with Autism Spectrum Disorders. Consequently, understanding the integrity of the auditory cortex, beginning with early cortical activity in the superior temporal sulcus is essential. Evoked related potential studies of cortical processing suggest ineffective regulation of auditory sensory input and disruption in early hemispheric specialization. While there are contradictory findings in peak latencies/amplitudes depending on technique, developmental age, and diagnostic variation, several studies have reported diminished amplitudes of the early cortical peak.

Objectives: To determine if children with autism have atypical early cortical response (latency and amplitude) to simple repeated and deviant tones relative to healthy controls.

Methods: We assessed children with ASD (autism n=5, PDD, NOS n=2, Asperger's syndrome n=3) and 11 healthy controls. Subjects watched a silent movie while listening passively to an auditory paradigm: binaural presentation of a standard 1 kHz tone repeated with an intermittent deviant 1.2 kHz tone as deviant. Recordings were made using the whole head OMEGA 275-Channel Magnetoencephalography System (CTF Systems Inc.) Stimulus locked responses to the pre-deviant, deviant and post-deviant tones were analyzed for each hemisphere. These responses were band pass filtered (1-40 Hz), averaged over all the presented trial and root mean squared over parietal and temporal sensors. Two raters (KK and SN) choose M100 peaks. The latency and amplitude of these peaks were compared by diagnostic group using t-tests. In addition, the conditional and group effects were assessed using a mixed linear effects model.

Results: In accordance with previous reports, we see a diminution in amplitude in the ASD group relative to controls. This finding is limited to the right hemisphere but exists for the pre-deviant standard, the post-deviant standard and the deviant tone (all < p=0.01). We see a conditional effect across groups with the deviant having a larger amplitude relative to the standard tones in both hemispheres (LH p=0.002, RH p=0.008). However, this difference is primarily driven by the ASD group. The latencies also show a striking discrepancy between the ASD and HC groups with the ASD group showing earlier latencies in the left hemisphere ($p<0.05$). Conditional comparison revealed shorter latencies in the deviant condition relative to the repeated tones. This was also limited to the left hemisphere and largely dependent on the ASD group (p=0.04).

Conclusions: These data suggest atypical early cortical activity in children with ASD in response to repeated and novel tones. The early latencies may be related to heightened attention and auditory sensitivity that has been widely described in the literature. A deeper explanation may be that the temporal cortex has impaired inhibitory input, creating a hyper-excitable or "noisy cortex." In this state, the cortex would be prone to early, yet poorly coordinated (low amplitude) responses. The cross hemispheric findings are intriguing and may suggest atypical specialization of tonal processing as has been suggested for language processing in ASD.

105.088 88 A Cross Cultural Comparison of Sensory Behaviors in Children with ASD From the USA and Israel. K. Caron[1], R. Schaaf*[2], T. Benevides[2] and E. Gal[3], (1)*Scarborough School District*, (2)*Thomas Jefferson University*, (3)*University of Haifa*

Background: Evidence suggests that a person's cultural background has an effect on various facets of development, illness, and behavior. Sensory perceptual abnormalities in children with Autism Spectrum Disorders (ASD) are common (85-90%) (Klienz & Dunn, 1997; Rogers et al., 2003; Tomchek & Dunn, 2007) and have been described in the perception of sound, vision, touch, taste, and smell, as well as in kinaesthetic perception and proprioception. Sensory experiences are described by individuals with ASD as both a source of distress and anxiety as well as of

fascination and interest (Jones, Quigney, & Huws, 2003) that can have a profound effect on their quality of life by limiting full participation in home, school, and community activities (Kay, 2001; Baranek, David, Poe, Stone & Watson, 2006).
Objectives: The purpose of this study was to determine if differences exist in sensory behaviors of individuals from two cultures. This study examined differences in sensory modulation between children with ASD who live in the USA and in Israel and between typically developing children from the two countries.
Methods: Short Sensory Profile scores (McIntosh, Miller, & Shyu, 1999) were compared between a cohort of children with ASD and a cohort of typically developing children from Israel and the USA. A retrospective chart review of datasets from two separate, larger investigations was used to gather data. Subjects from both data sets who met the current study's inclusion/exclusion criteria for this study were entered into one database for group comparison.
Results: Parents of children with ASD from both cultures rated their children as having difficulties with sensory modulation (> -1.0 SD) on the Short Sensory Profile, but subjects from Israel were rated higher (less difficulty) in the auditory and visual domains. Typically developing subjects from both countries scored within the normal ranges, but subjects from Israel scored significantly higher (less difficulty) than those from the US on 4 of the 7 subdomains and on the total test score.
Conclusions: Parents from Israel reported less severe sensory modulation problems in the visual and auditory domains for their children with ASD. In addition, parents from Israel rated their typically developing children as having less problems in sensory modulation overall (total test score) in the tactile, auditory filtering, visual/auditory sensitivity; and under-responsive/seeks sensation domains. These findings have important implications for assessment and intervention. It is important that cultural differences are taken into consideration and that culturally sensitive assessments and interventions for problems in sensory modulation in the ASD population be developed.

105.089 89 Can Problem Eating Behaviors in Autism Be Explained by Sensory Subtype. A. E. Lane* and M. Geraghty, *The Ohio State University*

Background: Children with autism are commonly reported to experience eating difficulties. These difficulties range from picky eating to food refusal and disruptive mealtime behaviors. Recent studies have reported that children with autism are at-risk for nutrient deficiencies as a result of these problem behaviors. A number of theories have been proposed regarding the etiology of eating difficulties in autism. Sensory processing difficulties are assumed by many autism practitioners to play a role in problem eating behavior. To date, however, there is limited empirical evidence elucidating this relationship in children with autism.
Objectives: This study compared the eating behavior of children with autism presenting with different sensory processing subtypes.
Methods: Caregivers of children with autism (autistic disorder or pervasive developmental disorder – not otherwise specified) (n=30) aged between three and eight years participated in the study. Caregivers completed the Short Sensory Profile (SSP) and the Brief Autism Mealtime Behavior Inventory (BAMBI) about their child with autism. Model-based cluster analysis was used to determine the specific sensory processing subtype exhibited by each participant based on their standardized SSP scores. Participants' eating behavior scores were determined for each of the following categories: *limited variety* (a pattern of picky, selective eating), *food refusal* (a pattern of refusal of many foods and/or whole food groups accompanied by disruptive behaviors) and *features of autism* (a pattern of disruptive mealtime behavior)(Lukens & Linscheid, 2008). Higher scores indicate more problematic eating behavior. ANOVA and correlation analyses were then used to examine differences and associations between sensory processing subtype and eating behavior pattern.
Results: Children with autism in this study presented with five different sensory processing subtypes that aligned with autism-specific sensory subtypes reported previously (Lane, Young et al, 2009). Participants differed in sensory processing according to

their levels of taste/smell sensitivity and vestibular/proprioceptive function. Compared to a neurotypical sample provided by the BAMBI authors, our sample exhibited greater tendencies for all three problem eating behaviors. Correlation analysis revealed moderate-strong, significant relationships between parent-reported taste/smell sensitivity and eating behaviors characterized by limited variety (r=.73, p<.05) and food refusal (r=.46, p<.01). One-way ANOVA analyses with post-hoc Tukey tests revealed significant differences between sensory subtypes in patterns of eating difficulties. Specifically, children with the most severe parent-reported taste/smell sensitivity but intact vestibular/proprioceptive function had the highest (most problematic) scores in limited variety (p=0.02). Children with moderate levels of parent-reported taste/smell sensitivity and vestibular/proprioceptive dysfunction had the highest levels of food refusal (p=.006). No significant differences were observed between sensory subtypes in the category of features of autism which equates to general, disruptive mealtime behavior.
Conclusions: Children with autism display predictable patterns of sensory processing dysfunction that are related to some problem eating behaviors. In particular, parent-reported taste/smell sensitivity appears to be discriminative of both limited variety and food refusal eating behavior patterns. Vestibular/proprioceptive dysfunction further distinguishes those who refuse food from those who are picky eaters. Limitations of the study and directions for future research will be discussed.

105.090 90 Sensory Processing in Infants with and without Risk for Autism During the First Year of Life. K. Harpster*, V. Sloutsky and A. E. Lane, *The Ohio State University*

Background: The prevalence of sensory processing disorders in children with autism ranges from 69% to 95%. Sensory processing disorders manifest themselves as auditory under-responsiveness and restrictive and repetitive behaviors and are thought to contribute to the functional limitations experienced by children with autism. Behaviors related to sensory processing difficulties can be detected prior to diagnosis. . Retrospective videotape analysis suggests that infants later diagnosed with autism exhibit auditory under- and over-responsiveness, delayed response to name, excessive mouthing of objects and unstable visual orientation/attention more often than typically developing children or children with developmental delays. Several of these studies report that sensorimotor and social development features can be used to distinguish infants later diagnosed with autism from neurotypical and developmentally delayed infants. Further, early identification and treatment of sensory processing deficits in infants at-risk of autism may promote more typical developmental patterns thereby reducing the severity of core autism symptoms. Currently, identification of sensory processing disorders in infants is reliant on imprecise proxy-report measures. There is limited neurophysiologic research available regarding sensory processing of children with autism and no studies that link behavior to neurophysiologic findings.

Objectives: This paper will describe sensory processing function using a multi-modal assessment protocol in infants with and without known risk factors for autism in the first year of life. Performance of infants on neurophysiologic measures will be further compared with parent reports and clinical observations of sensory processing.

Methods: A total of 30 infants (4, 8, and 12 months of age) with and without risk factors for autism will be recruited to this preliminary cross-sectional study. Inclusion criteria: infants with no known risk factors for autism, infant siblings of a child with an autism spectrum disorder, and infants born prematurely. Participants will attend a single study visit at the Cognitive Development Lab at The Ohio State University. Participants will be administered the Autism Detection for Early Childhood and Bayley Scales of Infant and Toddler Development, Third Edition to establish early signs of autism and developmental status. Sensory processing function will be evaluated using: the Sensory Processing Assessment for Young children, the Infant/Toddler Sensory Profile, the Test of Sensory Function in Infants, Event Related

Potentials(ERP), and Heart Rate(HR). A mismatch negativity(MMN) protocol will be implemented with ERP and HR. MMN is a pre-attentive measure of sensory processing elicited by a speech or non-speech sound. Data analyses will describe sensory processing function in infants by age group and risk factor status. It is hypothesized that infants with known risk factors for autism will exhibit attenuated responsiveness to speech sounds.

Results: We are currently collecting data.

Conclusions:

This study will address a significant gap in scientific research specific to sensory processing in infants at-risk for autism. Utilizing a multi-modal assessment protocol including standard clinical instruments in addition to neurophysiologic measurements, this study will be the first to provide a comprehensive description of sensory processing function within the first year of life.

105.091 91 A Randomized Trial of the Effectiveness of Occupational Therapy to Address Sensory Behaviors in Children with Autism: Phase 1 - Feasibility. R. Schaaf*[1], T. Benevides[1], D. Kelly[2], J. Hunt[2], E. van Hooydonk[2], F. Patti[2], Z. Mailloux[3] and E. Blanche[4], (1)*Thomas Jefferson University*, (2)*Children's Specialized Hospital*, (3)*Pediatic Therapy Network*, (4)*University of Southern California*

Background: This session will present the findings from Phase 1 (Feasiblity) of a 3 year RCT designed to study a manualized protocol of occupational therapy to reduce maladaptive sensory behaviors and enhance participation and quality of life for children with autism and their family. Children with autism exhibit many behaviors that may have a sensory basis 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. Although it is clear that these behaviors significantly impact the child and families ability to participate in daily activities, and families report that they are among the most debilitating symptoms for their children, data supporting interventions to specifically address the behaviors from a sensory perspective are sparse and lack evidence to support their efficacy and impact on improving adaptive behavior and participation. Despite the lack of evidence, occupational therapy to address sensory behaviors is among the most often requested services by families of children with autism (Mandell, et al, 2005; Green, et al 2006).

Objectives: The primary objective of this phase of the RCT is to evaluate the feasibility of a manualized protocol of occupational therapy designed to decrease sensory behaviors and increase participation and quality of life for children with autism and their families. The program, entitled "SMART" Sensory Motor Activities in daily Routines and individually Tailored, follows a set of theoretically-based principles and clinical reasoning strategies.

Methods: During phase 1 of the study we conducted10 case studies. After careful characterization of subjects using the ADOS, the ADI-R and IQ testing, and pre-testing, we provided 6 weeks of the SMART intervention and evaluated progress toward individual goals using Goal Attainment Scaling, adaptive behavior (using the Vineland) and quality of life for the family (using the WHO quality of life scale). Therapist and families also completed feasibility ratings and parents provided data on changes in sensory behaviors in the home using a systematic rating form. Therapist's ability to carry out the intervention was assessed using a "Fidelity to Treatment" measure (Parham, et al, 2007).

Results: We found that it is feasible to carry out the intervention, that parents are satisfied with the intervention protocol and that there were changes in individual goals. We also noted that the therapists require additional training to develop fidelity on the intervention. Several additional findings related to outcome measures were of interest.

Conclusions: Our data supports the feasibility of the SMART intervention and supports the

initiation of Phase 2 of the RCT. Goal Attainment Scaling is a sensitive outcome measure but the procedure for developing goals will be adapted in the next phase to assure that the goals identified by the parents are feasible and realistic for the treatment period. Several additional methodological changes will be made for phase 2 based on Phase 1 data.

105.092 92 3D-Multiple Object Tracking in Autism. E. M. Hahler*[1], D. Tinjust[1], L. Mottron[2] and J. Faubert[1], (1)*Visual Psychophysics and Perception Laboratory, Université de Montréal*, (2)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*

Background: Multiple object tracking (MOT) is the capacity to allocate attention simultaneously to different areas in order to track multiple moving objects (Pylyshyn & Storm, 1988). Whereas there is evidence for superior visual search performance for static and dynamic targets in autism (O'Riordan et al., 2001; Joseph et al, 2009), autistic people display reduced perception in a subgroup of motion integration tasks (Bertone et al., 2003). The contribution of these contradictory abilities to the capacity to track multiple moving objects in autism is unknown.

Objectives: Evaluate 3D-MOT capacities in individuals with autism in a fully immersive virtual environment (with stereoscopic vision).

Methods: 10 autistic adults with typical intelligence and 10 matched control subjects tracked either 1 (single) or 3 (multiple) previously indexed target objects in a set of 8 moving spheres and verbally identified the sphere or the three spheres that they considered to be the targets. Performances were measured based on speed thresholds, which evaluate the greatest speed at which observers are capable to track the moving objects. A correct answer was considered as the identification of all the targets. All other responses were considered false. An adaptive staircase protocol (one down/one up) was used in order to adjust the speed of the moving spheres between trials relative to the subject's answer. Participants were matched on age (mean age of 23.6 years), gender (9 males and 1 female) and IQ (mean IQ of 106.5), based on the Wechsler Adult Intelligence Scale.

Results: Results showed that for both groups speed thresholds were higher, and thus reflected better performance, for the single-object tracking versus the multiple-object tracking condition. Autistics were capable of tracking a single sphere among a set of distractors as well as the comparison group. However, a significant group x condition interaction was found between groups in their multiple-object tracking capacities, showing that autistics, as a group, were less able to track multiple moving objects, and that they seem thus less capable to allocate their attention to different areas at the same time.

Conclusions: Autistic documented superiority in visual search may find its limit when targets are numerous and moving in unpredictable directions.

105.093 93 Can Common Genetic Factors Account for the Association Between Autism Symptoms and Sensory Abnormalities?. S. Lietz*, F. Rijsdijk, E. Colvert, E. Woodhouse, N. Gillan, V. Hallett, P. Bolton and F. Happé, *Institute of Psychiatry, King's College London*

Background: Elevated levels of sensory abnormalities, such as hypo- and hyper-sensitivity to sound, light, touch, and taste, are well-documented in autism (e.g. Leekam et al., 2007, Rogers & Ozonoff, 2005) as well as in Fragile X (Rogers et al., 2003). Since autism and Fragile X are both highly heritable, genetic factors may also be involved in sensory abnormalities. Studies so far indicate moderate heritability of sensory sensitivity in typically developing samples (e.g. Goldsmith et al., 1997), with some indication that the tactile domain might be more heritable than the auditory domain (Goldsmith et al. 2006). A sibling study of sensory abnormalities in ASD (Szatmari et al., 2006) examined the structure of the restricted, repetitive behaviours and interests domain in autism measured by the ADI. Using factor analysis, they found that this domain consists of 2 factors: 'insistence on sameness' (IS) and 'repetitive and sensory motor behaviours and interests' (RSMB). However, their analysis of sibling data did not suggest familiality of the RSMB factor. To

date, no twin study of autism has investigated the genetic and environmental contributions to individual differences in sensory responsivity.

Objectives: Using bivariate genetic model-fitting (adjusted to account for selection), this study aims to examine how much of the phenotypic association between sensory abnormalities and autism symptoms is due to genetic and environmental factors shared between each set of symptoms. Furthermore, the relative contribution of genetic and environmental effects to individual differences in sensory responsivity will be estimated.

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 60 ASD twin pairs (at least one twin with ASD) and 60 control twin pairs, aged 12-15 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 to confirm diagnostic status.

Results: Results show moderate phenotypic correlations between total Short Sensory Profile scores and ADI scores. Bivariate Liability Threshold model-fitting analyses will yield the heritability of sensory symptoms and the genetic/environmental correlations between autism symptoms and sensory abnormalities.

Conclusions: Finding genetic overlap between autism and sensory symptoms may indicate that sensory abnormalities are part of the core symptomatology for ASD, and thus could be used as early predictors of ASD as well as being included in diagnostic criteria.

105.094 94 Sensory Responses in Optimal Outcome Children with a History of Autism Spectrum Disorders. A. Orinstein*[1], K. E. Tyson[1], E. Troyb[1], M. A. Rosenthal[1], M. Helt[1], I. M. Eigsti[1], L. Naigles[1], E. A. Kelley[2], M. L. Barton[1], M. C. Stevens[3], R. T. Schultz[4] and D. A. Fein[1], (1)*University of Connecticut*, (2)*Queen's University*, (3)*Institute of Living, Hartford Hospital / Yale University*, (4)*Children's Hospital of Philadelphia and the University of Pennsylvania*

Background: A study is currently following children who have a history of autism spectrum disorder (ASD), but who no longer meet diagnostic criteria for the disorder. These children have achieved social and language skills within the average range for their ages and receive little or no school support. Several recent studies suggest that this small subset of children, once diagnosed with ASD, achieve an "optimal outcome" (Sutera et al., 2007, Kelley et al., 2006, and Helt et al., 2008).

Objectives: While not included in the ASD diagnostic criteria, abnormal responses to sensory stimuli are frequently noted in children with ASD. This study examines parent report of sensory responses in a group of children who have achieved optimal outcome (OO) as compared to children with high-functioning autism (HFA).

Methods: The Autism Diagnostic Interview-Revised (ADI-R) was completed by the parent of 18 HFA children (mean age = 13.06, mean IQ = 110.35) and 29 OO children (mean age = 12.93, mean IQ = 114.04). Item scores on the ADI-R range from 0 to 3, with a higher score indicating more severe and frequent behaviors. Three items on the ADI-R relate to sensory functioning: "Unusual Sensory Interests," "Undue General Sensitivity to Noise," and "Abnormal, Idiosyncratic, Negative Response to Specific Sensory Stimuli." The two groups were compared on both past and present parent report for each of the items, as well as on a past and present average of the three items.

Results: There were no significant differences between the HFA and OO children, currently or in the past, for "Unusual Sensory Interests" (Current: M(OO)=0.31, M(HFA)=0.56; Ever: M(OO)=0.86, M(HFA)=0.89) or "Undue General Sensitivity to Noise (Current: M(OO)=0.48, M(HFA)=0.72; Ever: M(OO)=1.14, M(HFA)=1.67)." There was a marginally significant difference between the HFA and OO children currently on "Abnormal, Idiosyncratic, Negative Response to Specific

Sensory Stimuli," with the HFA children scoring higher than the OO children, M(OO)=0.21, M(HFA)=0.67, p=.056. Additionally, on the past rating of this item, HFA children had significantly more abnormal responses to sensory stimuli than OO children, M(OO)=0.48, M(HFA)=1.28, p<.05. Forty-four percent of the HFA children received a rating of 2 or 3 on this item, compared to only ten percent of the OO children. Abnormal responses most commonly resulted from auditory stimuli, such as babies crying, vacuuming, or toilets flushing in the HFA children, and crowds or high-pitched laughing in the OO children. HFA children also exhibited more abnormal sensory responses than OO children, both currently and in the past, when compared on the average of the three sensory items (Current: M(OO)=0.33, M(HFA)=0.65, p<.05; Ever: M(OO)=0.83, M(HFA)=1.28, p<.05).

Conclusions: These preliminary results based on parent report suggest that OO children display significantly fewer abnormal sensory behaviors, both currently and in the past, than HFA children. HFA children specifically showed significantly greater "Abnormal, Idiosyncratic, Negative Response to Specific Sensory Stimuli" in the past than OO children. However, OO children still exhibited some abnormal sensory behaviors, particularly in the past. Further research including larger samples, particularly of HFA children, is needed to support this conclusion.

105.095 95 Sensory Sensitivities in Autism Spectrum Disorders: A Qualitative Analysis. A. E. Robertson* and D. R. Simmons, *University of Glasgow*

Background:

There is a variety of evidence (e.g. parent reports, first-hand accounts and experimental data) which suggests that individuals with ASD show atypical responses to sensory stimuli. Following on from our previous study (Robertson & Simmons, IMFAR, 2009), in which we found a strong positive correlation between score in the Autism Spectrum Quotient (AQ; Baron-Cohen et al, 2001) and score on a measure of the severity and frequency of sensory problems, we attempted to determine whether those with medium/high AQ scores reported being affected by sensory stimuli more than individuals with lower AQ scores. We were particularly interested in the effect that sensory sensitivities may have on accessibility – for example that issues with lighting, sounds or smells may restrict some individuals with ASD from accessing certain facilities within their communities.

Objectives:

· To determine whether individuals with higher AQ scores described issues involving sensory stimuli more frequently than those with lower scores (this was in response to all questions).

· To determine whether those with high AQ scores were more likely to have presentedwith hearing problems at a young age (e.g. displaying hypo-sensitivity to sounds).

· To discover which environments were most problematic for participants, and the effect that this had on their daily lives.

Methods:

Five questions, designed to examine the issues with sensory stimuli that participants experienced, were administered online to 212 individuals (68% female; 32% male). Participants also completed the AQ.

Results:

When the questions were coded for sensory content (this was performed blind to AQ score), the likelihood that sensory issues were mentioned increased as AQ score increased. Supermarkets were deemed the most sensory-noxious environment for the high AQ scorers in our sample, with 80% of respondents experiencing issues with sensory stimuli in that particular environment. However, only 3.8% of those in the low-scorers group and 13.8% in the medium-scorers group mentioned having difficulties with sensory stimuli in supermarkets.

Conclusions:

· Participants with high AQ scores were more likely to describe having issues with sensory

stimuli than the low- and medium-scoring groups. Also, when asked how they found it easiest to calm down when anxious, high-scorers were more likely to describe methods involving sensory stimulation (e.g. jumping on a trampoline or rocking back and forth).

· Our previous research (Robertson & Simmons, IMFAR, 2008) showed that children with autism were more likely to have been referred for potential hearing problems (despite clinically normal hearing) than those with PDD-NOS. However, there was no group difference found in the current sample.

· Problematic environments mentioned by those with a high AQ score were varied, but those that were indicated most frequently included supermarkets and strong-smelling shops. Some people said that they could not physically enter such environments, and therefore resorted to using the internet to do their shopping.

105.096 96 The Everyday Routines of Families of Children with Autism: Examining the Impact of Sensory Processing Difficulties in Children with Autism On the Family. T. Benevides*[1], R. Schaaf[1], S. Toth-Cohen[1], S. L. Johnson[2] and G. Madrid[3], (1)*Thomas Jefferson University*, (2)*Walter Reed Army Medical Center*, (3)*Therapy Services of Delaware*

Background: Family routines are used to organize activities, maintain cultural beliefs and values, and provide stability in everyday life. Children with autism tend to have behaviors that are ritualistic, nonfunctional actions that interfere with participation in daily routines. According to Larson (2006), "families of children with autism may experience more difficulty orchestrating smooth functional family routines", but little research has addressed how families choreograph their routines to address the needs of their child or children with autism. Family routines, including school and work, can be troublesome when the children are not flexible, and will not deviate from their own routines (Larson, 2006). Given that family routines provide a stabilizing force in the family, gives the family and identity, and promote health and well-being of family members (DeGrace, 2004), information about the impact of sensory-related behaviors on family routines can provide important information for professionals working with families.

Objectives: The purpose of this phenomenological study was to explore the lived experience of families living with a child with autism. The objective was to describe how sensory related behaviors in children with autism impact family routines and roles in order to better inform future treatments for both children and families.

Methods: A phenomenological qualitative design was used to explore the lived experience of four caregivers of children with autism. Purposive and snowball sampling were used to obtain primary caregivers of children with autism between the ages of 7 and 12 years of age. Following informed consent, participants were interviewed and tape recorded describing their experiences performing daily routines. Analysis of the transcripts followed van Manen's (1990) procedures. In order to ensure validity of the study, triangulation, member checking and an audit trail were used during data analysis.

Results: Several themes arose from the data, including the need for flexibility, performance differences in familiar space vs. unfamiliar space, difficulty completing family activities together, the impact of autism on siblings, the need for constant monitoring of the child with autism, and the importance of developing strategies to improve participation for the family as a whole. Although sensory related behaviors are not the only factor that influences family routines and participation in activities, the data from this study suggests that it is an important consideration when evaluating the child and family's health and well-being. The results indicate that families plan their participation in activities around the child with autism, but attempt to be flexible in how they accomplish their own family's goals. Environments and routines were changed to meet the child's sensory needs.

Conclusions: The findings of this study highlight the importance of consideration of the family routines, activities and coping strategies, as well as the child's sensory difficulties when working with families and children affected by autism. Findings also

identify specific areas that may be problematic for families and which should be included when planning interventions. Interventions should include a discussion of potential strategies for improving family participation and managing the child's sensory-related behaviors to improve participation in home and community activities.

105.097 97 A Preference for Geometric Patterns Early in Life as a Risk Factor for Autism. K. Pierce*[1], D. Conant[2], R. Hazin[1], J. Desmond[1] and R. Stoner[1], (1)*University of California, San Diego*, (2)*UCSD Autism Center of Excellence, University of California San Diego*

Background: Eye tracking technology holds promise as an objective methodology for characterizing the early features of autism. While patterns of eye gaze have been found to be abnormal in 2-year-olds with autism (Jones et al., 2009), a recent study suggests that eye scan paths may not be deviant in the first year of life (Young et al., 2009). The degree to which preference and motivation mediate normal and abnormal visual scan patterns is unclear. For example, Klin and colleagues (2009) utilized a preferential looking paradigm and found a reduced preference for biological motion in 2-year-olds with autism. Thus, what an infant prefers to look at may be a more clearly definable indicator of risk than how he looks at something. When given the direct choice, typically developing toddlers prefer to look at social images over non-social images. It is unknown if this same preference exists in toddlers at-risk for autism. At older ages children with autism are often superior in local processing of geometric patterns and prefer to visually attend to real world repetition such as the moving blade of a fan. Objectives: To determine if toddlers at risk for an autism spectrum disorder (ASD) prefer to look at dynamic geometric patterns over social images, the age at which such preference emerges, and the degree to which preferential looking patterns can discriminate toddlers at-risk for an ASD from those at-risk for a language delay (LD) and developmental delay (DD) as well as typically developing (TD) controls. Methods: Using a population based screening method, toddlers at-risk for an ASD, language delay (LD) and developmental delay (DD) as young as 12-months were recruited and tracked. Ninety toddlers ranging between 12-42 months with later confirmed diagnoses participated (33 ASD; 35 TD; 11 LD; 11 DD, mean age = 23 months). Toddlers viewed a movie consisting of simultaneous images of dynamic geometric patterns (GP) on one side and children in action on the other. Duration of fixation was determined using a TOBII eye tracker and preference was defined as looking time > 50% towards one movie type. Results: Overall, toddlers at-risk for an ASD spent significantly more time looking at GP than TD, $t(66) = 3.33$, $p < .05$ and toddlers with a LD $t(42) = 2.1$, $p < .05$. Thirty three percent of the ASD group spent more than 50% of their time fixated on GP movies in contrast to only 5% of typical, 9% of LD and 10% of DD toddlers. Of the ASD toddlers who preferred GP, over half spent > 70% of their time visually examining GPs, with several toddlers exceeding 90% GP viewing time, a pattern not found in any other group. Thus, when 70% GP viewing time is used as a cut off, the positive predictive value for ASD is 100%. Furthermore, a GP preference was found in the ASD group as young as 14 months. Conclusions: A preference for geometric patterns may be a risk factor for autism and is observable in some toddlers by 14 months in age.

105.098 98 The Systemizing Trait of Autism Is Associated with a Shift From Reliance On Global to Local Contextual Cues. C. A. Wiliamson* and P. Dassonville, *University of Oregon*

Background: The theory that autism is associated with a decreased reliance on contextual cues (Frith, 1989) had led to suggestions that individuals with autism might have a decreased susceptibility to visual illusions. However, direct evidence for this was mixed, at best (e.g., Happé, 1996; Ropar & Mitchell, 1999). Recent work, though, has shown that illusion susceptibility is negatively correlated with the autistic trait of systemizing, when measured across the general population (Walter, Dassonville & Bochsler, 2009). However, this relationship seemed to hold only for those illusions that were caused by global distortions of the observer's egocentric reference frame.

Objectives: Here, we tested the hypothesis that the relationship between illusion susceptibility and systemizing is limited to illusions that are caused by global distortions of the observer's reference frame, using an illusion (the Rod-and-Frame Illusion, or RFI) that is known to have two variants. When shown a large tilted frame, the observer's global perception of vertical is distorted, causing a misperception of the orientation of an enclosed rod. In contrast, a smaller tilted frame has no effect on perceived vertical, but causes a misperception of rod orientation via a local contrast effect between the rod and the nearby contours of the frame.

Methods: Typically developing college students with normal vision (n=54) performed three tasks involving the RFI in counter-balanced order. The *Perception task* was a measure of the overall effect of the RFI. Participants were asked to make a judgment ("clockwise" or "counterclockwise") about the perceived tilt of a rod presented within a tilted frame. The *Saccade-to-Vertical task* was a measure of the global distortion of the observer's reference frame. Participants were asked to make a vertical saccade, within the context of a tilted frame, to the top of an outer circle. The *Saccade-to-Target task* was a measure of the local contrast effect. Participants were asked to make a saccade, within the context of a tilted frame, to the point on the outer circle where they believed that an imaginary extension of the rod would intersect with the circle. Participants also completed the questionnaires of the Systemizing Quotient, the Autism Quotient, and the Empathizing Quotient.

Results: As hypothesized, the global distortions of perceived vertical associated with large frames were negatively correlated with systemizing, as well as the attention-to-detail subscale of the AQ. Surprisingly, systemizing was also found to be correlated with the local contrast effects associated with small frames, but here the correlation was a positive one: higher levels of systemizing were associated with an increased susceptibility to the local contrast effects.

Conclusions: In sum, these findings indicate that while autism is not simply associated with a decreased reliance on contextual cues, it is associated with a more complex shift from a general reliance on global contextual cues to an exaggerated reliance on local contextual cues. The complexity of these relationships in terms of illusion susceptibility may have confounded earlier attempts to understand the perceptual effects of autism.

105.099 99 Olfactory Functioning in the Autistic Spectrum. S. Galle*[1], J. Frasnelli[2], J. A. Boyle[3], V. Courchesne[1] and L. Mottron[1], (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*Centre de Recherche en Neuropsychologie et Cognition (CERNEC) de l'Université de Montréal*, (3)*Montreal Neurological Institute, McGill University*

Background: Starting with the first descriptions by Kanner and Asperger, atypical sensory processing has been recognized as an essential feature of the autistic spectrum. Considerable clinical and experimental evidence on atypical sensory processing and autistic strengths in low level perception has been gathered. The *Enhanced Perceptual Functioning* (EPF) model by Mottron and colleagues (2006) describes these phenomena by stating that higher-order processing which is mandatory in typically developing individuals is more optional in autistic individuals, while low-level perceptual processing, such as feature extraction, is intrinsically superior. The combination of these two principles results in enhanced detection, discrimination, and categorization of perceptual stimuli in the visual and auditory modalities and, to a lesser extent, in the tactile modality. Despite clinical indications pointing towards atypical chemosensory processing in autism, and the theoretical importance of investigating all sensory modalities, the chemosensory modalities have received little scientific interest. Conclusive data on olfactory functioning in autism are missing.

Objectives: We aimed to compare olfactory functioning in individuals with a diagnosis of autism or Asperger syndrome to typically developing control subjects. The investigated olfactory functions were odor detection, discrimination, and identification. Subjective ratings of perceived odor pleasantness, familiarity, and intensity, as well as self-reported chemical sensitivity, were collected

to investigate differences in subjective odor perception.

Methods: Participants were 5 Asperger, 5 autistic, and 5 non-autistic adult males, matched on age (18-35 years) and Wechsler IQ. To measure odor detection thresholds we used an adaptive 3-alternative forced-choice ascending staircase method for 2 different odors: phenyl ethyl alcohol and n-butanol. Both thresholds were measured 3 times. Odor discrimination was investigated with a same-different paradigm, using odors selected according to their rated similarity. The University of Pennsylvania Smell Identification Test was used to assess the identification of 40 common odorants, embedded in scratch and sniff labels, using a 4-alternative forced-choice method. Participants rated the perceived pleasantness, intensity and familiarity of 8 different odorants on a visual analogue scale with verbal labels ranging from very unpleasant, weak or unfamiliar to very pleasant, strong or familiar. Participants rated their sensitivity to odorant substances in daily life on the 21 statements of the Chemical Sensitivity Scale.

Results: Preliminary results suggest impaired olfactory identification in autistic spectrum individuals compared to typically developing controls. There were no indications of group differences in detection and discrimination of odors.

Conclusions: Preliminary results do not show evidence of superior olfactory perceptual traces in the autistic spectrum. Typical performance on odor detection and identification suggests functional integrity of the medial temporal lobe structures implicated in olfactory processing, whereas diminished olfactory identification either is suggestive of functional atypicalities of olfactory orbito-frontal structures, or points to difficulties in labeling subjective information in the autistic spectrum.

105.100 100 2-Year-Old Toddlers with ASD Are More Successful at Visual Search Than Typically Developing Toddlers. C. K. Kraper, Z. Kaldy, E. Blaser, A. S. Carter* and U. Eneh, *University of Massachusetts Boston*

Background: Studies by Plaisted, O'Riordan and colleagues have shown that older children and adults with Autism Spectrum Disorders (ASD) are faster at finding targets in feature conjunction search displays (Plaisted, O'Riordan & Baron-Cohen, 1998; O'Riordan, Plaisted, Driver & Baron-Cohen, 2001). Currently, there is very little known about the visual search skills of very young children (1-3-year-olds), both typically developing or with ASD. Objectives: Our goal was to test if very young children with ASD (within a year of being diagnosed) show superior performance in visual search compared to typically developing toddlers. In order to do this, we adapted the classic visual search paradigm to be suitable for toddlers. Methods: Our paradigm required no verbal instructions and was based on minimal nonverbal feedback, making the task naturalistic for toddlers who are pre- or nonverbal. We used a Tobii T120 eye-tracker to measure fixation patterns. We tested toddlers with ASD (N = 17, mean age: 29 months) and typically developing toddlers matched on age (N = 14, mean age: 30 months) and on the Visual Reception scale of the Mullen Scales of Early Learning (N = 13, mean age: 23 months). All participants saw one, two or three blocks of trials depending on their mood and motivation. Each block consisted of 4 familiarization trials and 13 test trials (a random mix of 4 single feature trials (4 or 8 distractors) and 9 feature conjunction trials (4, 8 or 12 distractors)). Each test display was presented for 4 seconds. At the end of each trial, the target started spinning back and forth: we hoped that this event is interesting enough for toddlers to look for the target even before the spinning has started. We compared Time to First Fixation and Fixation Length for the target to the average of the distractor items that were fixated in any given trial. Results: Toddlers with ASD were not significantly faster, but were more successful at finding the target in conjunction search displays than either age-matched controls or controls matched on Visual Reception. Search times and success rates for single feature displays (pop-out) did not differ among the groups. Conclusions: The developmental trajectories of visual attentional processes start to diverge as early as 1-3 years of age in

typically developing children vs. children with ASD.

105.101 101 Reliability and Validity of a Sensory Seeking Scale in the Sensory Processing Assessment. L. M. Little*[1], G. T. Baranek[1], D. Jackson[2], C. L. Wakeford[1] and M. Sabatos-DeVito[1], (1)*University of North Carolina at Chapel Hill*, (2)*Walden University*

Background: Sensory processing abnormalities have been found highly prevalent, although not universal, among young children with Autism Spectrum Disorder (ASD). The Sensory Processing Assessment (SPA; Baranek, 1999b) is a 20 minute semi-structured, play based observational tool designed to measure hyperresponsiveness (an exaggerated response to sensory stimuli) and hyporesponsiveness (a lack of response to sensory stimuli). Sensory seeking, a third construct of sensory processing, has been demonstrated by recent factor analytic models. Thus, a sensory seeking scale was added to the SPA. Previously untapped by observational measurement, sensory seeking is characterized by initiation and preoccupation with oneself, an activity, or object, and can provide strong visual, auditory, vestibular, tactile, proprioceptive, olfactory, or gustatory input. Engagement may be prolonged, repetitive, or stereotypical in its presentation, although repetition is not a sufficient characterization for sensory seeking.

Objectives: The purposes of this study were to measure the (a) inter-rater reliability and (b) "known-groups" discriminative validity of a sensory seeking scale in the Sensory Processing Assessment.

Methods: Construction of the sensory seeking scale drew from existing literature and clinical observations of behaviors related to sensory processing. The sensory seeking scale includes 8 items rated on a scale from 0 (none observed) to 2 (intense and frequent). The current sample included 52 children, aged 7 to 95 months, with ASD, developmentally delay (DD), or typical development (TYP). (Note: Total sample size will be 105 by May 2010). An ANCOVA was conducted to evaluate the relationship between diagnostic group (ASD, DD, TYP) and sensory seeking scores, while controlling for mental age.

Results: Preliminary data analysis revealed inter-rater reliability of the sensory seeking scale is ICC=.95. Results of the ANCOVA found significant main effects for group ($F= 8.482$, $p<001$). Follow up Tukey's LSD showed significant differences between the ASD group, and the DD and TYP groups, $p<.02$ and $p<.001$ respectively.

Conclusions: These preliminary findings suggest that the sensory seeking scale of the Sensory Processing Assessment is a reliable tool for measuring behaviors previously untapped by an observational assessment, with excellent inter-rater reliability. The sensory seeking scale distinguished the ASD group from the developmentally delayed and typically developing groups, suggesting that high levels of sensory seeking are unique to ASD, and a possible discriminating feature of the disorder. There are mixed findings suggesting that repetitive behaviors, often conflated with sensory seeking, distinguish DD from ASD. Follow up analyses will be completed to determine if specific types of sensory seeking behaviors are more likely to discriminate groups in order to further elucidate the sensory phenotype of children with ASD.

105.102 102 The Influence of Background Noise On the Intermodal Perception of Speech in Children with Autism Spectrum Disorders: An Eye-Tracking Task. L. N. Hancock*, J. M. Bebko, C. A. McMorris and M. Slusarczyk, *York University*

Background: Although information from the environment reaches us over several modalities, we perceive a unitary event. Newborn infants have been shown to integrate information reliably over two modalities and this automatic integration of auditory and visual information is necessary for the development of speech and language. One real-world situation that requires the integration of auditory and visual information is the understanding of speech in noisy social settings. In this situation, the difficulty in deciphering what is being said is routinely referred to as the cocktail party problem (Cherry, 1953). Individuals with

autism often exhibit ineffective sensory processing, and integration of information across auditory and visual modes appears impaired (Iarocci & McDonald, 2006). Deficits in this sensory processing may be related to some of the language impairments that characterize autism. Further, there is limited research investigating the effects of background noise on the processing of speech in persons with an Autism Spectrum Disorder (ASD). Objectives: The objectives of the current study are twofold. First, to distinguish if previously identified deficits in auditory-visual integration are specific to linguistic information. Second, to understand the impact of increasing levels of background noise on speech intelligibility. Methods: Fourteen children with an ASD were matched to fourteen typically developing (TD) children based on chronological age, verbal and non-verbal abilities. The present study used eye-tracking with a preferential looking design which involved displaying four identical videos, offset in time, with an auditory track synchronous to only one of the videos. Videos contained either linguistic (person telling a story) or non-linguistic (hand playing a piano) stimuli. Background noise was added to a portion of trials and the signal to noise ratio (SNR) was manipulated. Results: For the conditions with no background noise, group membership predicted performance for the linguistic trials only. The TD participants were more likely to show a preference for the synchronous screen compared to the ASD participants. Group membership did not predict performance in the non-linguistic trials. For the conditions with added background noise, rates of preferential looking decreased as the SNR increased for the TD participants only. There was no trend found for the ASD group. Conclusions: Typically developing children show enhanced perception for speech stimuli compared with the ASD group. These results suggest that 1) some features of intermodal perception are intact in individuals with ASD, and 2) the ASD group is impaired in some intersensory process(es) advantageous for language processing. The addition of background noise essentially equated performance for the two groups, suggesting the possibility that intersensory information is already "noisy" or degraded for children with ASD. Implications of these findings are discussed.

105.103 103 The Sensory Profile: An Investigation of Its Relationship with Experimentally Measured Sensory Thresholds in Adults with Autism Spectrum Conditions. T. Tavassoli*[1], K. Latham[2] and S. Baron-Cohen[1], (1)*University of Cambridge*, (2)*Anglia Ruskin University*

Background: Anecdotal reports suggest sensory differences in autism spectrum conditions (ASC) (Grandin, 2006; Chamak et al, 2008). In fact, the Sensory Profile, a questionnaire measure, finds differences in sensory processing in over 90% of children with ASC (Kientz & Dunn, 1997; Tomcheck & Dunn, 1997; Watling et al, 2001, Wiggins et al, 2009), adults with ASC (Crane et al, 2009, Kern et al 2007), and across cultures (Cheung & Siu, 2009). Scores on the Sensory Profile have been correlated with repetitive behaviours (Chen et al, 2009), stress levels (Corbett et al, 2009) and skin conductance (Brown et al, 2001). However no study to date has investigated the link between Sensory Profile scores and experimentally measured sensory thresholds.

Objectives: We aimed to test if a) adults with ASC differed in Sensory Profile scores or b) sensory thresholds, and c) to investigate whether the Sensory Profile scores show any relationship with experimentally measured sensory thresholds in vision, touch, hearing, taste, and smell.

Methods: 24 adults with ASC were matched to 30 control participants on age, sex and IQ. The Sensory Profile was administered, and scores calculated for the following subscales, both in sum and modality-specific: Low Registration, Sensation Seeking, Sensory Sensitivity and Sensation Avoiding. Sensory thresholds in vision were measured by a qualified optometrist assessing clinical visual functioning as well as experimentally tested visual acuity measured by the FrACT. Tactile spatial acuity was measured using the 'Domes gratings', and tactile sensitivity thresholds were measured using the 'Semmes Weinstein Von Frey Aesthesiometer' on both the fingertip and the arm. Hearing thresholds for low, middle and high frequencies were measured using the 'Audio-CD'. Taste thresholds were measured

by the 'Taste strips' for sweet, sour, bitter, and salty tastes. Finally, the smell threshold was measured using 'Sniffin sticks'.

Results: Adults with ASC showed differences on all subscales of the Sensory Profile. They had higher scores in Low Registration (U: 82.5, p=0.002), Sensory Sensitivity (U: 87.5, p=0.003), Sensation Avoiding (U: 36, p< 0.00) and lower scores in Sensation Seeking (U: 42, p<0.00). Regarding the experimentally measured sensory thresholds, the ASC group had higher taste thresholds overall (U: 146, p=0.002), but otherwise did not differ to controls. Correlations between Sensory Profile subscales and experimentally measured sensory thresholds were surprisingly few and are reported.

Conclusions: The current experiment confirms differences in the Sensory Profile scores between adults with ASC as compared to controls. However, the few relationships between Sensory Profile subscale scores and experimentally measured sensory thresholds suggest these two methods may measure different sensory constructs.

105.104 104 Sensitivity to Social Touch in School-Age Children with Autism Spectrum Disorders. M. J. Ackerman*[1], G. Ramsay[2], A. Klin[1] and W. Jones[2], (1)*Yale University School of Medicine*, (2)*Yale School of Medicine*

Background: Atypical sensitivity to touch has been described frequently in children with autism spectrum disorders (ASD), although these reports have been largely anecdotal. Existing reports cover a wide array of behaviors, including 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 few studies exist with direct, quantitative measurements of sensitivity to social touch in individuals with ASD.

Objectives: The aim of this study was to measure selective sensitivity and response to contingent social touch in school-age children with autism spectrum disorders in comparison with matched typically-developing peers. Control conditions measured sensitivity and response to mechanical (non-social) touch.

Methods: We designed and built a novel device for measuring haptic interaction between two individuals or between one individual and a pre-recorded signal. The device consisted of horizontal rollers, linked remotely, that could be turned by either of two participants. The rollers of each participant were coupled electromechanically, so that if one participant moved a roller, the other participant would feel that movement on his or her own roller; if both participants moved their rollers, the resulting motion of each roller would be proportional to the force applied to both. The force applied by the test participant in response to varying input signals (contingent social versus non-social, mechanical manipulation) served as the dependent variable for measuring haptic sensitivity.

Results: We compared the behavior of 20 children with ASD and of age- and IQ-matched, typically-developing controls during non-social, mechanical manipulation tasks and during haptic social interaction. The behavior of children with ASD was distinguished by stereotyped and repetitive movements and, in a subset of the children, by the favoring of select parts of the hand and forearm during task completion. These patterns were not observed in typically-developing children. In addition, children with ASD, in contrast to controls, showed little change in behavior between the haptic interaction condition and the non-social, mechanical manipulation condition.

Conclusions: These results quantify altered sensitivity and response to social touch in individuals with ASD, and serve as a platform for future studies of the development of haptic intersubjectivity: how typically-developing children, beginning in infancy, are highly sensitized to recognize certain kinds of touch as social, and to react and respond in kind. This will be an important part of understanding atypical behavioral and neural specialization in individuals with ASD.

105.105 105 High-Risk Infants' Behavioral and Neural Responses to Faces: An Eye-Tracking and Visual ERP Study. R. Luyster*[1], J. B. Wagner[1], T. Augenstein[2], L. M. Kasparian[3], H. Tager-Flusberg[4] and C. A. Nelson[2], (1)*Children's Hospital Boston/Harvard Medical School*, (2)*Children's Hospital*

Boston, (3)*Boston University School of Medicine*, (4)*Boston University*

Background: Studies of early development in children at risk for autism spectrum disorders (ASD) have revealed that behavior from a single task or activity does not necessarily predict outcome. This seems related to the inter- and intra-individual heterogeneity in early behavior, and these individual differences are thought to be useful in specifying developmental pathways. Therefore, the effort to better understand the complex endophenotypes associated with risk and outcome requires that we begin to address the role of individual differences, as well as children's responses across a range of tasks. Objectives: The present investigation works towards these goals by (1) employing measures of visual attention and electrophysiological response to faces, and (2) exploring the role of individual differences across these two measures. The aim is to improve our understanding of the relations between children's visual scanning of faces and their electrophysiological response to them. Methods: High-density event-related potentials (ERPs) and eye-tracking tasks were administered to infants at high risk for ASD (HRA, by virtue of having at least one older sibling with ASD), as well as low-risk controls (LRC). The data reported here were collected when the infants were 12 months of age. Eye-tracking data were collected when children were presented with side-by-side images of two faces: their mother and a stranger. ERP data were collected when children were presented a series of single images (their mother and a different stranger, shown in random order). Analyses included facial regions of interest (i.e., eyes, mother only) collected during eye-tracking and relevant components in the ERP (Nc, N290 and P400). These preliminary findings are based on 8 children in the HRA group and 4 LRC. Results: For the HRA group, there were associations between the Nc (a frontal component of attention) and children's visual attention to faces. Specifically, increased attention to mothers' eyes was associated with both larger (r=-.88, p=.004) and faster (r=-.80, p=.02) Ncs to mothers' faces (versus strangers' faces). No such relation was found in the LRC group. Similarly, the HRA group demonstrated associations between a face-sensitive occipital component – the N290 – and visual attention to mothers' faces, such that increased attention to eyes was marginally associated with larger N290s to stranger (r=.67, p=.07). This trend was not observed in the LRC group. Finally, greater attention to mothers' eyes was associated with a P400 (also an occipital, face-sensitive component) that was larger to mothers' faces (versus strangers' faces, r=.75, p=.03) but only in the HRA group. Conclusions: These results suggest that in infants at high risk for ASD, there are meaningful relations between patterns of looking to faces and electrophysiological measures of attention and face-processing. In light of previous findings that atypical face scanning is common in high-risk infants, these results indicate a need to understand better the role that very early visual attention plays in functional brain development.

105.106 106 Visual Search and the Broader Autism Phenotype: A Study of the Infant Siblings of Children with Autism and Typically Developing Infants. E. Goldknopf*, K. Gillespie-Lynch, T. Hutman, M. Sigman and S. P. Johnson, *University of California, Los Angeles*

Background: Visual search—detecting a single target among a large number of distractors—may be enhanced in people with autism, from 3 years of age to adulthood, possibly due to enhanced perceptual discrimination (O'Riordan et al., 2009; Plaisted et al., 1998). In typically developing infants, evidence of visual search has been found as early as 3 months (Adler & Orprecio, 2006; Amso & Johnson, 2006). Visual search has not yet been examined in the infant siblings of children with autism.

Objectives: To determine whether the infant siblings of children with autism have enhanced visual search relative to typically developing infants. Such an examination can enrich our understanding of the broader autism phenotype, and can help pinpoint when enhanced search abilities first emerge in autism.

Methods: We observed 22 infant siblings of children with autism (five 6-month-olds, nine 12-month-olds, and eight 18-month-olds)

and 24 typically developing infants (five 6-month-olds, nine 12-month-olds, and ten 18-month-olds).
Each stimulus consisted of a "plus" sign target among "L" distractors; targets were equidistant from the center. In the Random condition, 7, 13, or 26 distractors were distributed randomly around the screen; in the Circle condition, 4, 7 or 13 distractors were distributed in a circle. All Random condition stimuli were presented before Circle condition stimuli.
Before each 2 sec stimulus, an attention-getter attracted the infant's attention to the center of the screen. Infants' gaze (onset and duration of fixations) was measured with Tobii eye-trackers. ANOVAs and independent-samples t-tests were conducted on accuracy (number of targets found) and time-to-target (time before the infant fixated the target). Data from trials lacking an adequate central fixation were excluded.
Results: The ANOVAs found no significant differences between the groups; with a Bonferroni correction, the t-tests also did not find significant differences. For each group, accuracy in both Random and Circle conditions increased with age and with fewer distractors ($p < .01$). In an overall ANOVA with the groups taken together, in the Circle condition, time-to-target decreased with fewer distractors ($p = .009$). Accuracy in the Circle condition showed a trend towards interaction between age and risk category ($p = .07$), such that typically developing infants were worse than infant siblings at 6 months but better at 18 months. An unexpected result was a positive correlation in infant siblings at 12 months between average time-to-target in the Circle condition and total scores on the Autism Observation Scale for Infants (12month), $r = .718$, $p < .05$, N=10.

Conclusions: In this preliminary data, there were no significant differences between the two groups. This may be because enhanced visual search is specific to autism rather than to the broader autism phenotype, because it develops after 18 months, because it is not evident in implicit visual search paradigms or with the measures used, or because of the small sample size. Ongoing data collection will include 24-month-olds and additional participants in all conditions, data analysis will include additional measures such as latency to target when that is the infant's first fixation.

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105.107 107 Identifying Social and Non-Social Change in Natural Scenes: Comparisons Among Adults, and Children with and without Autism. B. R. Sheth*[1], J. Liu[1], O. Olagbaju[1], L. Varghese[1], R. Mansour[2], S. L. Reddoch[3], D. A. Pearson[2] and K. A. Loveland[2], (1)*University of Houston*, (2)*University of Texas Medical School at Houston*, (3)*Univ. of Texas Med. Sch. at Houston*

Background: Children use social cues as a major mechanism of learning about the world through "social referencing" that guides their attention. Therefore, attentional processes that are under the guidance of social referencing cues, such as gestural joint attention, observations of facial expression, gaze and so on, should be well developed in the typically developing (TD) child. In contrast, children with autism spectrum disorders (ASD) have early deficits in joint attention and impaired social skills.

Objectives: We employed the "change blindness" paradigm to compare how the presence, absence, or specific context of different types of social cues in a scene affect TD children, children with ASD, and typical adults in visually identifying changes in a pair of scenes. We hypothesized that i) Children with ASD would find it more difficult than TD children to discover changes in the scene that are related to social cues; ii) If social cues in the scene are unrelated to the target change or serve to direct attention away from it, children with ASD would discover the change more readily than TD children, whose attention would be misdirected by the social cues; iii) Because social cues continue to develop past early childhood, typical young adults would perform better on the change detection task than children with or without ASD.

Methods: Forty adults and forty children participated; 22 were high-functioning (IQ = 98 ± 4) children with ASD (autism: 12, Asperger's: 4, PDD-NOS: 6; 10.5 ± 0.5 years). The remaining 18 were TD children (10.8 ± 0.6 years; IQ = 107 ± 6). Change trials were categorized into one of six conditions, depending on the

presence/absence and nature of the social cues in the scene. On different conditions, the change was in an actor's facial expression or gaze, an object that an actor overtly pointed to or gazed at, an object connected with an actor in the scene, an object unconnected with any actors in the scene, an object while an actor pointed to a different, unchanging object, or an object in a scene containing no actors. Percent correct, response time, and inverse efficiency were measures of performance.

Results: No significant differences were observed on any performance measure between children with and without autism on any of the six conditions. Children (with and/or without autism) were worse than adults in identifying change while an actor pointed to an unchanging object, or change in an object, whether or not it was connected with an actor in the scene, but no worse when no actors were present in the scene, i.e. when there was no social cueing, or when an actor in the scene pointed to the change.

Conclusions: Children with autism use relevant social cues while searching a scene just as typical children do. Compared with adults, children with and without autism are over-reliant on social referencing cues in the scene, and are less able to disengage from them and use other kinds of cues. Social cues "capture" the child's attention.

105.108 108 Development of the School-Age Autism Screening Inventory for High-Functioning Students. C. T. Wormeli*[1], G. M. Robinson[1] and W. T. McKee[2], (1)*Provincial Outreach Program for Autism and Related Disorders*, (2)*University of British Columbia*

Purpose of the Project:Construction, norming and validation of a screening scale to be used by school psychologists to identify high-functioning students who may be appropriately referred for diagnostic assessment of autism.

Many individuals with ASD are diagnosed after beginning formal education, as they encounter social and academic expectations embedded in large-group instruction systems. Identification of students who have ASD but do not have a cognitive or language delay is particularly problematic, with the average age of diagnosis at 12 years. Most early screens for Autism miss students with milder forms of ASD, especially those without cognitive delay.

Background:

An 89-item rating scale was constructed to identify "high-functioning" students who might be usefully referred for diagnostic assessment of autism. A clinical sample of 102 students with ASD enrolled in public schools in the province of British Columbia was obtained. Teachers and parents were asked to rate students on a four-point likert scale to develop norms. The results were compared with data from a matched sample of non-referred students in the province to validate the inventory.

Objectives:

The principal investigators sought to develop a scale that could be easily completed by respondents, would contain content that reflected current knowledge of ASD (qualitative information describing characteristics from both the DSM and the literature on ASD students is expanded in the manual), could be easily scored and interpreted by qualified personnel and would discriminate between students with ASD and students without ASD.

Methods:

An initial item pool was constructed, based on criteria in DSM-IV-TR and on a review of literature. After review of items and instructions by several teachers, a pilot study of 164 items, grouped into 14 "characteristics" (clusters) involving 60 students (20 students diagnosed with ASD, 20 students from the same classes without a diagnosis of ASD and 20 students with behaviour problems) was performed. Seventy-four items were discarded. Ninety items, grouped into 13 characteristics, were normed on a provincial clinical sample.

Results:

A clinical sample, stratified by geography and age and ASD gender distribution, was identified. Teachers and parents were asked

to complete the revised scale. A matching sample of non-referred children was obtained (the participation rate for the NonASD sample was 66 % of the clinical ASD sample). One more item was deleted, leaving 89 items, grouped into 12 "characteristics." Internal consistency reliability for the total score exceeded .9 for both groups of respondents for the clinical sample. Discriminant function analysis showed for both groups overall correct classification rates that exceeded 90 %, using total scores. A small group of behaviour-disordered students was also rated by teachers. Analysis of variance showed significant differences between all three groups. Mean scores of parents and teachers differed significantly from each other. Separate norms were constructed for each.

Conclusions:

The principal investigators suggest that the inventory is a valid and reliable scale that may be used as part of a decision-making process to facilitate referrals for diagnostic assessment of school-age children who are suspected of having ASD.

105.109 109 Autonomic Responsiveness to Images with Social-Affective Content in Individuals with Autism. O. Olu-Lafe*[1], M. C. André[2], D. Plesa-Skwerer[2] and H. Tager-Flusberg[1], (1)*Boston University*, (2)*Boston University School of Medicine*

Background: Autism Spectrum Disorder (ASD) is characterized by a triad of deficit: impairments in social interaction, problems with communication, and repetitive and restricted behavior patterns. A number of studies have observed social perceptual abnormalities in ASD using explicit tasks. Recent work suggests overt measures may not be ideal for studying social perception in autism.

Objectives: To examine implicit processing of social-affective information in individuals with ASD using (1) magnitude and frequency of skin conductance responses (SCRs) and (2) pupil dilation.

Methods: Individuals with ASD, matched on age with normal controls (NCs), passively viewed static emotionally-laden images (from the International Affective Picture System, IAPS) based on their content: social threatening, non social threatening and angry and fearful faces. Skin conductance responses and changes in pupil diameter were collected using the BIOPAC MP150 Systems and Tobii-1750 eye-tracker, respectively.

Results: Overall the ASD group was more electrodermally responsive than typical controls; the ASD group had significantly more SCR's for all images than the NC group. In addition, greater pupil diameter changes were observed in the ASD group when viewing faces compared to social and non-social threatening images.

Conclusions: The ASD group's hyperarousal to faces is consistent with findings of (1) hyperactivation of the amygdala and, (2) social aversion, especially to direct gaze, in ASD. This work supports the notion that increased autonomic responsiveness may underlie impairments in face recognition observed in ASD. Further work is needed to elucidate what mechanisms underlie the hyperarousal to faces observed in ASD.

105.110 110 Activity Participation Patterns of Children with Asperger Syndrome: Implications for Health. R. L. Taylor*[1], T. S. Olds[1], K. Boshoff[1] and A. E. Lane[2], (1)*University of South Australia*, (2)*The Ohio State University*

Background: Optimal participation in activities by children is important as participation is thought to contribute to child development and health and well-being (Law 2002). Children with Asperger syndrome may be at particular risk of lower levels of participation due to difficulties in social interactions and repetitive and stereotypical behaviours (American Psychiatric Association 1994). An awareness of how the participation of children with Asperger syndrome differs to that of typically developing children will identify areas where health professionals can target support and interventions to maximize participation and health outcomes.

Objectives: This study compared the participation patterns of children with Asperger syndrome aged between ten and fifteen years to those of typically developing children using a computer-based use-of-time recall.

Methods: Children with Asperger syndrome (n=30) and typically developing children (n=42) aged between ten and fifteen years were administered the Multimedia Activity Recall for Children and Adolescents – Participation Edition (MARCA-PE) on two occasions, approximately one week apart. The MARCA-PE is an interviewer-administered, computer-based, twenty-four hour use-of-time recall which allows children to recall all activities they were involved in on the previous day in time slices as fine as five minutes and choosing from over 250 different activities. For each activity recalled, the child is also asked to report how much they enjoyed the activity and how difficult they found it. Data were collected for at least one school and one non-school day for each participant. One way analysis of variance (ANOVA) and Mann-Whitney U tests adjusted for age and sex were used to explore differences in participation patterns between children with Asperger syndrome and typically developing children.

Results: Analyses revealed differences between the participation patterns of children with Asperger syndrome and typically developing children, with two main areas of difference. First, the physical activity level (PAL) of children with Asperger syndrome was 5% lower ($p=0.01$) than that of typically developing children with 14 minutes less of sport involvement per day ($p=0.04$). Second, children with Asperger syndrome were shown to be involved in fewer activities (4 activities less per day, $p<0.00$) than typically developing children. There was a trend towards greater use of videogames (31 minutes more per day, $p = 0.12$). No differences were found between the two populations on overall reported levels of enjoyment and difficulty experienced.

Conclusions: This study demonstrates that children with Asperger syndrome are involved in fewer activities than their peers but overall they report experiencing the same levels of enjoyment and difficulty with their participation. Lower levels of physical activity (PA), combined with higher use of video games were reported by children with Asperger syndrome which may impact on their physical health in the long term. Literature focusing on typically developing children describes a linear relationship between the amount of PA completed and the child's health status (Warburton et al. 2006). In particular, a lack of PA has been linked to obesity (Trost 2005). It is therefore important that children with Asperger syndrome be supported and encouraged to be active.

105.111 111 Affective Internalizing Problems Related to Age in Children and Adolescents with High Functioning Autism. J. F. Strang*[1], L. Kenworthy[1], P. Daniolos[1], L. K. Case[2], M. Wills[1] and G. L. Wallace[3], (1)*Children's National Medical Center*, (2)*University of California, San Diego*, (3)*National Institute of Mental Health, National Institutes of Health*

Background: Clinical reports have suggested increased rates of affective internalizing symptoms among adolescents with autism spectrum disorders (ASDs). A recent study of children with ASDs and a broad range of intellectual functioning reported that age was positively related to anxiety symptoms. Another study documented a relationship between depression and intellectual and social functioning in a sample of high functioning adults with ASDs; depressed individuals had significantly higher IQ and significantly lower autism symptoms than non-depressed individuals. To the authors' knowledge, the current study is the first to examine the relationship between affective internalizing problems and age, IQ, and autism symptoms in a large sample of high functioning children and adolescents with ASDs. Objectives: Examine the relationship between parent reported affective internalizing symptoms (anxiety, depression, and withdrawal) and age, IQ, and autism symptoms in a high functioning cohort of children and adolescents with ASDs. Methods: Subjects were a clinically referred sample of 157 high functioning children/adolescents (mean age=8.5+3.2 years; verbal or nonverbal IQ > 75) diagnosed with an ASD based on the Autism Diagnostic Interview, Autism Diagnostic Observation Schedule (ADOS), and clinical impression. Subjects also received a comprehensive neuropsychological battery which included the parent report versions of the Behavioral Assessment System for Children (BASC) or the Child Behavior Checklist (CBCL) and an IQ

measure. Based on recommendations from the authors of the BASC, we computed an Affective Internalizing Problems (AIPs) composite (Anxiety, Depression, and Withdrawal) so as to include both BASC and CBCL data. Results were analyzed using correlations between BASC or CBCL AIPs and age, IQ, and ADOS symptoms (Communication and Social Domains). Additionally, overall AIPs for children (age 2-11) and adolescents (age 12-17) were compared. Results: Age was significantly correlated with AIPs, $r(155) = .35$, $p<.01$, so that older age was associated with greater AIPs. There was also a significant age group difference, $t(155) = 3.2$, $p<.01$, with adolescents experiencing higher mean AIPs than children. Mean adolescent AIP T-scores fell within the borderline clinical cutoff (mean AIP T-score=66+9.1, borderline clinical cutoff ≥ 65). IQ, Communication Domain symptoms, and Social Domain symptoms were not related to AIPs. Conclusions: In this large group of high functioning children and adolescents with ASDs, increased age is related to higher levels of AIPs. The adolescents fell on average in the borderline clinical range for AIPs, significantly above their younger counterparts. This finding may be significant clinically, as it supports accounts of increased risk for AIPs during adolescence. Unlike recent findings in a high functioning sample of adults with ASDs, IQ and autism symptoms were not related to internalizing problems among our high functioning children and adolescents.

105.112 112 Children Who Fail the M-CHAT but Do Not Have ASD: A Comparison of Younger Siblings with Pediatric and Early Intervention Populations. K. Carr*[1], J. Pandey[2], A. Verbalis[1], S. Hodgson[1], M. L. Barton[1], J. Green[1] and D. A. Fein[1], (1)*University of Connecticut*, (2)*Children's Hospital of Philadelphia*

Background: Children who screen positive on the Modified Checklist for Autism in Toddlers (M-CHAT) are at high risk for autism spectrum disorders (ASD) and other developmental disorders. Younger siblings of children with ASD (SIBLING) have higher rates of developmental disorders than the general population and are at risk for ASD and the Broader Autism Phenotype (BAP). Three groups of children were included: SIBLING, pediatrician-referred children (PED), and early intervention-referred children (EI). The EI and SIBLING groups are considered high-risk for ASD and other developmental disorders and thus might have elevated scores on the M-CHAT even without an ASD diagnosis. SIBLING children are more likely to have BAP symptoms and are hypothesized to fail a greater number of ASD-related items than PED and EI. Objectives: To compare M-CHAT scores of SIBLING, PED, and EI children, all of whom failed the M-CHAT and follow-up phone interview but did not have ASD; to determine whether positive screens are more likely to predict ASD and/or other developmental disorders for the high-risk groups; and to determine failed items for the groups. Methods: Sample sizes were: SIBLING = 27, PED = 56, EI = 55. All children failed the M-CHAT and phone interview, were evaluated, and received non-ASD diagnoses. Phone interview data were available for 20 SIBLING, 35 PED, and 34 EI. The M-CHAT has six critical items that best discriminate between ASD and non-ASD. Total and critical scores on the M-CHAT and phone interview, and the proportion of children failing each item, were compared among groups using univariate analyses. Using chi-square analysis, the number in each group with ASD, and the likelihood of having another developmental diagnosis and no diagnosis or typical development, was compared. Results: 67.1% of SIBLING, 43.8% of PED, and 75.6% of EI who failed the M-CHAT had ASD. SIBLING and EI were more likely than PED to have ASD ($p<.01$). PED was more likely than EI or SIBLING to have another specific disorder, such as global developmental delay or language disorder ($p<.001$). SIBLING and PED were more likely than EI to have no diagnosis or typical development than EI ($p<.001$). On the M-CHAT and phone interview, EI failed eye gaze, noise sensitivity, pointing, language comprehension, and staring items significantly more frequently than SIBLING. SIBLING did not fail any items more frequently than EI. On the M-CHAT, PED failed noise sensitivity and staring items more frequently than SIBLING. SIBLING failed directing attention and checking reaction items more often than PED. On the phone interview, PED failed no items more often than SIBLING, but SIBLING failed the

directing attention item more frequently than PED. EI had significantly higher total and critical scores on the M-CHAT and phone interview than SIBLING; there were no differences in these scores between SIBLING and PED. Conclusions: EI children likely have more global delays and are more severe as a group, meaning their increased social symptoms may be secondary to their overall delays. SIBLING exhibit social deficits on the M-CHAT more often than PED.

105.113 113 Early Childhood Predictors of Social Functioning in Adults with Autism Spectrum Disorder. L. Gomez*[1], L. Sepeta[1], K. Gillespie-Lynch[1], L. Sterling[2], T. Hutman[1] and M. Sigman[1], (1)*University of California, Los Angeles*, (2)*University of Washington*

Background: Low levels of adaptive social functioning in adults with Autism Spectrum Disorders (ASD) have been reported across a range of longitudinal studies (reviewed in Seltzer et. al, 2004). However, some adults with ASD achieve higher levels of social functioning (Kanner et al., 1972; Kobayashi et al., 1992). Identification of early predictors of differential adult social outcomes may inform intervention approaches. While early IQ scores and language skills (Howlin et. al, 2004, Lord & Bailey, 2002) are frequently indicated as the strongest predictors of adaptive outcomes in adolescents and adults with ASD, early joint attention skills predict subsequent language in middle childhood (Sigman & Ruskin, 1999) and adolescence (McGovern & Sigman, 2004). We hypothesized that joint attention, in addition to IQ and language skills, would predict adult social outcomes.

Objectives: This longitudinal study sought to identify developmental predictors of social functioning in adulthood and to relate our findings to prior studies (such as Howlin et al., 2004).

Methods: Participants included 20 adults (19-32 yrs) who were diagnosed with autism in early childhood. Social outcome ratings (based upon Howlin et. al, 2004) were used to differentiate between adults with good to fair social outcomes (some independence) and adults with poor outcomes (lack of independent work, living arrangements and friendships). The two groups were then compared on the following skills assessed in early childhood (3-6 yrs): initiation and response to joint attention, developmental intelligence quotient and developmental language quotient. Due to variability in age at first assessment, scores on the intelligence and language measures are developmental quotients (DQ) or age equivalent scores divided by chronological age.

Results: Independent samples t-tests revealed that those with good to fair social functioning in adulthood (n=9) differed from those with poor outcomes (n=11) on intelligence scores [M=69.9 vs. 49.6, $p < 0.05$], language scores [M=52.4 vs. 33.7, $p < 0.05$], responsiveness to joint attention [M=16.8 vs. 6.3, $p < 0.001$], and initiation of joint attention [M= 13.4 vs. 5.3, $p < 0.01$]. However, when all of the variables were entered into a single regression model, only language DQ was a significant predictor of adult social outcome ($\beta = .72$, $t(13) = 3.2$, $p < 0.01$).

Conclusions: These findings suggest that in early childhood, autistic individuals who will achieve higher levels of adult social functioning differ from those with poorer social outcomes across a range of measures. However, by 3 to 6 years of age, language skills may exert more influence upon adult outcomes than either nonverbal social skills or intelligence scores. These findings encourage continued focus on language skills in treatment programs targeting social functioning in individuals with autism. Improvements in characterization and treatment of children with autism in the 30 years since this sample was first evaluated suggests the need for further longitudinal research in order to continue fine-tuning treatment for children with autism on the basis of early symptom profiles.

105.114 114 Autistic Traits in ADHD: Is There a Case for a Co-Morbid Subgroup?. R. Grzadzinski*[1], A. Di Martino[1], M. Mairena[1], E. Brady[1], M. O'Neale[1], E. Petkova[1], C. Lord[2] and F. X. Castellanos[1], (1)*NYU Child Study Center*, (2)*University of Michigan*

Background: Current diagnostic criteria do not allow for a diagnosis of Pervasive

Developmental Disorder (PDD) and Attention-Deficit/Hyperactivity Disorder (ADHD) in the same individual. Although clinical anecdotes, case reports, and increasing empirical evidence suggest that autistic traits co-occur in some children with ADHD, the phenomenology of such co-morbidity remains unclear.

Objectives: To systematically characterize the occurrence of autistic traits in children with ADHD and their corresponding clinical features.

Methods: The parents of 78 typically developing children (TDC; 32 boys) and 75 children with ADHD (60 boys) between the ages of 7 and 17 years completed the Social Responsiveness Scale (SRS) to identify children with elevated autistic traits (T score = 60).To determine whether elevated SRS total score in ADHD is associated with items that probe specific aspects of PDD (versus items nonspecifically related to PDD), all SRS items were classified in four domains. Three domains mapped on PDD related symptoms: Social (S; 24 items), Communication (C; 8 items), Restricted/Repetitive Behaviors (R; 10 items), the fourth domain included SRS items not specifically related to PDD (23 items). Domain scores were computed as average of the items within a domain. The ADHD groups with and without autistic traits ($ADHD^{+}$ and $ADHD^{-}$,respectively), and the TDC were compared with respect to the four domains scores adjusting for ADHD severity ratings. Conners' Parent Rating Scale and cognitive testing were also collected.

Results: Within the ADHD group, 31% (n=23) presented with elevated SRS scores. This $ADHD^{+}$ subgroup scored significantly higher than the $ADHD^{-}$ subgroup on Conners' ratings of Social Problems, Oppositionality, Hyperactivity, DSM-IV Hyperactive-Impulsive, and DSM-IV Total but not on Inattention. Across the four domains of SRS items, statistically significant differences were observed with TDC

Conclusions: 1) we confirmed that a substantial number of children with ADHD have elevated parent ratings of autistic traits. 2) Elevated ratings of autistic traits are not accounted for by items that are not specifically related to autism. 3) The children with ADHD and autistic traits display a more severe pattern of behavioral abnormalities. Future work using multiple informants should address the clinical relevance of the co-occurrence of autistic traits in children with ADHD

105.115 115 Do Specific Difficulties in Social Development Relate to Generalized Social Challenges in Young Children with ASD?. L. O'Connell*, E. A. Kelley, K. Dunfield and V. Kuhlmeier, *Queen's University*

Background: Impairments in the ability of children with autism spectrum disorders (ASD) to engage in two fundamental social-cognitive skills (joint attention, imitation) are well documented (e.g., Charman et al., 1998). Whether these, and additional, forms of other-oriented behaviours are associated with generalized social challenges in this population is of importance. Moreover, determining which specific other-oriented behaviours most closely relate to socialization difficulties holds theoretical and clinical value.

Objectives: The current study examined the extent to which performance on specific social-cognitive and prosocial behavior tasks in a laboratory setting relates to the capacity of young children with ASD to maneuver in their social worlds more broadly. A measure of children's nonverbal mental age was also obtained to account for differences in cognitive ability.

Methods: Fifteen children with ASD (Mean Age: 48 months, Range: 28 to 68 months) were assessed for their propensity to engage in several social behaviours. Children participated in a series of play-based tasks designed to examine social-cognitive skills (joint attention, imitation of bodily movements and actions on objects). Participants were also presented with social scenarios in which they were evaluated for their tendency to provide different types of aid to the examiner (i.e., retrieving an out-of-reach object, comforting, and sharing). To obtain a measure of children's socialization skills beyond the laboratory, the *Vineland Adaptive Behaviour Survey* (*VABS*; Sparrow, Cicchetti, & Balla, 2005) was administered to primary caregivers. All diagnoses were

confirmed using the *ADOS-G,* which also provided an additional index of social abilities. To ensure that any associations between the various measures of social abilities could not be accounted for by children's level of development, all children were administered the *Mullen Scales of Early Learning* (*MSEL*; Mullen, 1995) from which an index of nonverbal mental age was obtained (Visual Reception Subscale).

Results: The extent to which specific early social abilities measured in a laboratory setting relate to broader socialization skills displayed by children with ASD was examined via a series of partial correlations. After controlling for nonverbal mental age, there was no relationship between any social behaviour observed in the laboratory and parent-reported daily socialization skills (*VABS*). Nonetheless, significant associations were revealed between the engagement of children with ASD in various helping behaviours and their *ADOS-G* Reciprocal Social Interaction (r=-.56, p<.05) and Play (r=-.64, p<.05) scores, after controlling for developmental level. This relationship was not observed with children's social-cognitive performance and their social abilities as measured by the *ADOS-G*.

Conclusions: Increases in the propensity of young children with ASD to engage in various prosocial behaviours (helping, comforting, sharing), but not social-cognitive skills, was associated with better *ADOS-G* reciprocal social interaction and play performance. Engagement in these rudimentary forms of other-oriented behaviours appears to hold significant value for broader social success during this age of increasing peer interactions. The absence of an association between experimenter-evaluated social-cognitive and prosocial skills of young children with ASD and their daily socialization skills reported by primary caregivers may reflect the complexity of the latter index of social behaviour and requires further investigation.

105.116 116 Construct and Criterion-Referenced Validity of the Pervasive Developmental Disorder(PDD) ASJ Rating Scale(PARS). I. Tani*[1] and M. Tsujii[2], (1)*Hamamatsu University School of medicine*, (2)*Chukyo University*

Background: In Japan, government legislated "Developmental Disorders Support Act" in 2004. We have tried to make assessment tools for not only screening people with Pervasive Developmental Disorder(PDD) but also grasping support needs of them.
Objectives: A behavior checklist, the Pervasive Developmental Disorder(PDD) ASJ Rating Scale(PARS), was developed as a screening questionnaire to determine Pervasive Developmental Disorder(PDD) and also as a rating scale to evaluate the severity of a wide range of PDD symptoms. PARS was constructed by two rating, 37 toddlerhood items are evaluated retrospectively and 36 or 37 items are used for current evaluation.
Methods: 317 PDD participants and 345 non-PDD participants were assessed using PARS, and 174 PDD participants were assessed IQ for these purposes.
The subjects were recruited via the medical, psychological or educational institution.
The study was described to the subjects and written informed consent was obtained.
Diagnoses of either Autistic Disorder were made by a child psychiatrist and based on DSM-IV criteria.
Results: In this study, the construct and criterion-referenced validity of the PARS was tested on PDD and non-PDD samples.
Interrater and internal reliability was found to be adequate. Both the retrospectively evaluation scores and the current evaluation items accurately discriminated PDD from non-PDD.
The correlation between PARS and IQ demonstrated validity.
Conclusions: Result suggested that the PARS may be a useful screening scale for a various clinical settings.

105.117 117 Arousal and Anxiety in Children with Autism Spectrum Disorders. T. P. Levine*[1], S. J. Sheinkopf[2], B. M. Lester[2], M. Pescosolido[3], A. Rodino[3] and G. Elia[4], (1)*Warren Alpert Medical School of Brown University*, (2)*The Warren Alpert Medical School of Brown University*, (3)*Women and Infants' Hospital*, (4)*Boston College*

Background: Many children with Autism Spectrum Disorders (ASDs) are diagnosed and treated for anxiety disorders. However, deficits in communication and decreased understanding of emotions, in others and in

one's self, make self-report of anxious symptoms difficult in this population. Some investigations have explored the psychophysiology of arousal in children with ASDs to better understand the manifestation of anxiety in this population. However, these investigations have not yielded conclusive findings and explore individual arousal mechanisms. We have developed a paradigm to explore multiple measures of arousal and data on anxiety in children with High Functioning Autism (HFA) undergoing a social stressor. Objectives: Short Term: To investigate preliminary, individual differences in physiologic response and self-reports of anxiety to a social stressor in a cohort of children with HFA and a group without HFA. Long Term: To relate these physiologic findings to parent and self-report of anxiety symptoms. Methods: We collected pilot data in 8-12 year old children with community diagnoses of HFA (n=19, 16 males) and those without HFA (n=12, 7 males) on measures of physiologic arousal at baseline, while undergoing a social stressor (The Trier Social Stress Test, TSST), and after a recovery period. The TSST consists of 3 tasks performed in front of 2 adult evaluators: 1) an oral story completion, 2) oral serial substractions, and 3) a tracing exercise done while looking through a mirror. The measures include electrodermal activity (EDA), salivary cortisol reactivity (CORT), and vagal tone (VT). Cortisol was measured at 3 points during the baseline, once following the TSST, and once at recovery. VT and EDA were averaged over multiple, coinciding 4 minute intervals during the 3 epochs. Each participant also rated his/her own anxiety during each activity on a 1-10 scale. Results: Both groups demonstrated an expected decrease in VT and increase in EDA during components of the TSST when compared to the baseline and recovery period. Preliminary analyses demonstrate children with HFA were less likely to have an expected cortisol level increase following the TSST while the non-HFA children were more likely to have an increase, although findings did not achieve statistical significance . For both groups, self-reported anxiety was higher during the TSST than during baseline and recovery. Within and between group differences in physiologic measurements and their relationship to self-reported anxiety will be described. Conclusions: We have developed an assay that incorporates psychophysiology and self-reported anxiety to better understand manifestations of arousal and anxiety in children with HFA and potentially other ASDs. While these results are preliminary and descriptive, with continuation of this study we will be powered to detect significant differences between the two groups. We will also incorporate parent reports of anxiety to analyze correlations between psychophysiologic measures of arousal, self-reports, and parent reports of anxiety.

105.118 118 Adaptive Behavior in Young Children with High and Low Functional Autism Spectrum Disorders. C. L. Chu*[1], Y. S. Huang[1] and C. H. Chiang[2], (1)*National Chung Cheng University*, (2)*National Chengchi University*

Background: Adaptive behavior in autism is highly variable (Burack & Volkmar, 1992). Researchers found that overall or sub-domain adaptive functioning was lower in children with autistic spectrum disorders (ASDs) compared to their same cognitive function controls. This adaptive functioning pattern that was different from those children with other diagnoses was called 'autism profile', could be observed when these children were very young (Stone et al., 1999). Furthermore, the profiles within domains of adaptive behavior skills might be different between higher and lower cognitive function individuals with ASDs. However, this finding has not consistently been reported.

Objectives: This study was to examine the development in adaptive behavior skills in young children with ASDs in Taiwan, comparing to children with developmental delay (DD) and typical development (TD). Furthermore, we explored variability in adaptive behavior within children with ASDs (high functional autistic spectrum disorders (HFASD) vs. low functional autistic spectrum disorders (LFASD)). Well-established and wide-used test, Vineland Adaptive Behavior Scales-Second Edition (VABS-II), was used to assess the adaptive behavior skills.

Methods: Participants included 116 individuals, 51 children with ASDs (41 autistic disorder and 10 children with Pervasive Developmental Disorder – Not Otherwise

Specified, age 2:4 to 5:1), 32 children with DD (age 3:6 to 5:0) matched on mental age (MA) and CA, and 33 children with TD (age 2:3 to 2:9) matched on MA, who were recruited to the study. Autism diagnosis was confirmed with the ADOS (Autism Diagnostic Observation Schedule) and clinical impression (DSM-IV-TR). Verbal mental age obtained from the Mullen Scales of Early Learning. VABS-II was assessed by interview with caregiver(s).

Results: Two-way mixed ANOVA was conducted to compare scores on adaptive behavior domains (Communication, Daily Living Skills, Socialization, and Motor Skills) between groups (ASDs, DD, and TD). There was a significant main effect for groups but not adaptive behavior domains. TD group had better adaptive functioning than ASDs or DD. The interaction effect reached statistical significance indicated that there was a different adaptive functioning profile between groups. Follow up ANOVAs showed that in three domains, communication, daily living skills, and motor skills, TD had higher VABS-II scores than ASDs and DD, but the latter two group did not show the difference. In addition, comparing to DD and TD, children with ASDs was significantly poorer function in socialization domain. The differences in VABS-II scores between children with high and low functional ASDs were also analyzed. There was a significant main effect for groups. HFASD group had better adaptive functioning than LFASD group. The main effect for domain and the interaction effect did not reach statistical significance.

Conclusions: Relative to children with TD, both young children with ASDs and DD had weaker adaptive behavior skills. But in socialization domain, children with ASDs were much poorer than children with DD, even though their MA and CA were the same. HFASD had better adaptive behavior skills than LFASD, but their profile of adaptive behavior skills was similar. In summary, children with ASDs, regardless of their cognitive function, showed similar weakness in adaptive functioning.

105.120 120 Changes in the Social Networks of Elementary School-Aged Children with and without Autism. J. Locke*, C. Kasari, M. Kretzmann and J. Bang, *University of California, Los Angeles*

Background: With the rise of inclusion for children with disabilities, in particular, autism spectrum disorders in regular education classrooms, typically developing children are more likely to encounter and have social experiences with children with a disability or an ASD. Despite frequent interactions with typically developing children, children with a disability or an ASD may not truly be fully included in their classroom social networks. Children with autism often select children who are the most salient in their classrooms as friends, and these relationships are usually unreciprocated. This phenomenon may be due to deficits in social skills, thereby placing them at risk for negative social experiences.

Objectives: This study aimed to determine if children's social networks and various friendship features were stable over time and whether there were any differences in the social network salience between children with an ASD, children with a non-ASD disability, and typically developing children over the course of one academic year.

Methods: A total of 440 children participated in this study and were recruited from 19 classrooms in the university lab school. Of the 440 total participants, 338 were typically developing children (47.6% male), mean age of 7.53 ± 2.32 years old, 76 students (56.5% male) were suspected of having a disability by the school psychologist, mean age 7.96 ± 1.93, and 26 students were diagnosed with or were suspected of having an autism spectrum disorder by the school psychologist, were fully included in regular education classrooms and were an average of 7.84 ± 2.17 years old. All children completed a friendship survey that was coded for children's friends, connections, rejections, and social network status following the methods outlined in Cairns and Cairns (1994).

Results: As a whole, social network salience increased for all students across one academic school year, $F(1, 425) = 16.65$, $p < .001$; where, children in the upper grades were increasingly more likely to have higher social network salience as the school year

progressed, $F(3, 425) = 16.04$, $p < .001$. Compared to children with a non-ASD disability and typically developing children, children diagnosed with autism or were suspected of having an autism spectrum disorder had significantly lower social network salience, $F(2, 425) = 11.02$, $p<.001$, received significantly fewer friendship nominations, $F(2, 425) = 9.94$, $p<.001$, and more rejections, $F(2, 425) = 18.00$, $p<.001$, averaged across one academic school year. In addition, children with autism and children with a non-ASD disability also had significantly lower best friendship reciprocity compared to typically developing children, $F(2, 366) = 5.34$, $p<.005$.

Conclusions: These are among the first longitudinal data to suggest that children's social networks and statuses are relatively stable over time. These results indicate that even some fully included high-functioning children with ASD struggle to find stable friendships and their niche in their classroom's social structure. Additionally, these data suggest that school-based interventions that foster social development are needed for children with ASD. Perhaps future studies should examine the important role that teachers and paraprofessional might play in facilitating friendship formation and maintenance at school.

105.121 121 Ecological Features of Preschool Environments That Support the Social Engagement of Children with Autism Spectrum Disorder. S. S. Reszka[1], S. Odom*[2] and K. Hume[3], (1)*University of North Carolina at Chapel Hill*, (2)*University of North Carolina*, (3)*Frank Porter Graham Child Development Institute, University of North Carolina, Chapel Hill*

Background: Ecobehavioral theory is based on the premise that children's development, in particular their social development, interacts with characteristics of their environment. We know children with ASD have difficulties socially engaging with adults and peers. The prototypical approach to remediate these difficulties is to directly teach the child appropriate social skills. However, researchers have consistently demonstrated that children do not maintain or generalize these skills when taught in separate environments (Bellini et al., 2007). One way to promote and support the social engagement of children with ASD is to examine features of their natural environment that increase the likelihood of social interaction (Boyd et al., 2008). This study provides an understanding of the ecological features that support the social engagement of preschoolers with ASD in their classroom settings.

Objectives: This study examined the (1) social engagement of preschoolers with ASD in classrooms with peers and adults, (2) ecological features of preschool classrooms that promoted social engagement, (3) relationships between social engagement and ecological features.

Methods: The *Code for Active Student Participation and Engagement Revised III*, an ecobehavioral observational system, was used to code data on the social engagement and classroom ecology of 68 preschoolers with ASD. Children in the study were between 3-5 years of age, enrolled in a public school-based preschool program, and had a clinical or educational diagnosis of developmental delay or ASD. The ADOS and/or SCQ were used to confirm diagnosis. Using a momentary time sampling approach, each ecological variable was coded every 10 seconds during a 30-minute observation of the classroom's center time. The ecological variables included: activity area, child behavior, group arrangement, adult behavior, and initiator of activity. We calculated the base rate of social engagement with peers and adults across the ecological features.

Results: We present preliminary descriptive data here; however, data analysis is ongoing and will be completed prior to the IMFAR conference. First, preliminary analysis indicated preschoolers with ASD were engaged in social behaviors with adults 5.06% of the time and peers 1.89% of the time. Second, during center time, children were mostly (a) in the manipulative/blocks center (33.84%), (b) involved in small groups (34.17%) with adult support (32.29%), and (c) the adult most often initiated the activity (72.89%).The classroom environments that most supported child social engagement with adults were working 1:1 with an adult (75%),

being in the story time/books activity area (75%), engaging in adult-initiated activities (100%), and participating in pre-academics (43.75%) The classroom environments that most supported engagement with peers were being in a large group that contained an adult and 3 or more peers (72.73%), engaging in snack/meal time (59.09%) or large motor (18.18%) activities, engaging in adult-initiated activities (80.95%), and not having adults direct the activity (90.91%).

Conclusions: This study provides a preliminary analysis of preschool classroom environments that promote the social engagement of children with ASD with adults and peers. Identifying features of the classroom that facilitate the social engagement of children with ASD can assist teachers in purposefully arranging those situations to promote ongoing interactions.

105.122 122 Frequency of and Risk Factors for Behavior and Emotional Problems in Siblings of Children Diagnosed with Autism Spectrum Disorder. T. E. Hemming*[1], F. Hurewitz[1] and D. S. Mandell[2], (1)*Drexel University*, (2)*University of Pennsylvania School of Medicine*

Background: Siblings of children with autism may be at increased risk for emotional and behavioral problems. The presence of a child with autism in a family may affect the siblings directly, or indirectly through stress or financial strain on the parents, or by reducing the parent's ability to devote time to the sibling. Previous studies of siblings of individuals diagnosed with autism spectrum disorders have found several demographic factors that increase risk for emotional and behavioral problems in these siblings — specifically being the older sibling, being male, having only two children in the family, and low socioeconomic status. The generalizability of these findings, however, is limited due to the small sample sizes in these studies. The current study identifies specific behaviors and emotional states among siblings of children with autism, including interpersonal conflicts, depression, and anxiety, and examines their associations with socio-demographic factors. Objectives: The purpose of this study is to identify factors that affect the needs, and emotional and behavioral manifestations of siblings of individuals with autism.
Methods: Survey data for this study currently is being collected from the Pennsylvania Autism Needs Assessment. A letter describing the survey was delivered to 30,000 Medicaid-enrolled individuals in Pennsylvania with a claim for autism-related services in 1999, 2004, or 2009. Individuals then could request a paper copy of the survey (in English or Spanish) or complete it online. The survey asked questions about services available to the siblings of the individual with autism (family counseling, sibling support groups, and sibling mental health counseling), behaviors of the sibling (aggression, anxiety and interpersonal conflicts), clinical presentation of the child with autism, and demographic factors (birth order, sex, parents' marital status and workforce participation).
Results: Data collection is ongoing. As of November, 2009, more than 2,000 surveys have been returned. Reported results will include an analysis of risk factors, both demographic and based on the functional level and needs of the child with autism, which contribute to increased risk of behavioral and emotional needs in siblings.
Conclusions: By identifying the factors that may place siblings of children with autism at risk, the field can begin to focus on how to improve the quality of life for these individuals, who act as caregivers, teachers, and advocates for their siblings.

105.123 123 A Longitudinal Study of Adaptive Abilities and Autistic Symptoms From Middle Childhood to Adulthood. S. L. Marshall*[1], K. Gillespie-Lynch[2], L. Sepeta[2], J. Barnwell[3], T. Hutman[2] and M. Sigman[2], (1)*UCLA*, (2)*University of California, Los Angeles*, (3)*University of North Carolina at Chapel Hill*

Background: Previous research has demonstrated greater improvements in cognitive and linguistic skills from early to middle childhood than from middle childhood to adolescence (McGovern & Sigman, 2005). However, autistic symptoms (social deficits and repetitive behaviors) reported on the ADI-R decreased and social and daily living skills increased from middle childhood to adolescence (Sigman and McGovern, 2004). While lower-functioning children and adolescents show a moderate relationship between social skills measured by the

Vineland Adaptive Behavior Scales (VABS) and social disability as measured by the ADOS (Klin et al. 2006), high-functioning individuals do not (Anderson et al. 2009). Thus, the relationship between social skills and autistic symptoms may vary with level of functioning.

Objectives: To identify continuity and change in autistic symptoms and adaptive behaviors of autistic individuals from middle childhood through adolescence and into adulthood, and to ascertain the relationships between these constructs.

Methods: Participants were 20 individuals with autism, first observed in early childhood (M= 3.9 yrs, SD= 1.1yrs). Using repeated measures ANOVAs, we assessed change on the VABS and the ADI-R from middle childhood (M=11.2 yrs, SD= 3.2 yrs), through adolescence (M=17.7 yrs, SD= 3.8 yrs), and into adulthood (M=26.5 yrs, SD=3.8 yrs). Correlations were evaluated between adaptive abilities measured by the VABS and autistic symptoms reported on the ADI-R. Applying a rating of adaptive social functioning (Howlin et al., 2004), participants' outcomes in adulthood were classified as "Fair/Good" (N=9) or "Poor" (N=11). Using T-tests, we compared VABS and ADI-R scores between outcome groups at all three time points.

Results: While symptoms of autism in nonverbal communication and repetitive behavior did not change significantly from adolescence to adulthood, social symptoms on the ADI-R improved from middle childhood (M=19.0) to adolescence (M=13.5) only to worsen from adolescence to adulthood (M=15.5) ($p<.001$). While adaptive social skills did not improve from adolescence to adulthood, daily living skills ($p<.001$) and communication skills ($p<0.05$) continued to improve from early childhood (M(DLS)=69.2; M(CS)= 68.0) into adolescence (M(DLS)=96.9; M(CS)=83.9) and adulthood (M(DLS)=121.6; M(CS)=95.0). Groups formed on the basis of social-functioning outcome differed at the 0.05 level on all sub-domains of the VABS at each time point, with the "Fair/Good" group reporting higher adaptive skills than the "Poor" group. At all time points, social skills and social symptoms were strongly correlated (p values < 0.001): middle childhood ($r= -.809$), adolescence ($r= -.812$), and adulthood ($r= -.806$).

Conclusions: Results suggest that daily living and communication skills in people with autism improve from middle childhood to adulthood. Social skills did not improve across these stages. Autistic symptomatology increased from adolescence to adulthood. VABS scores and social sub-domain scores on the ADI-R in middle childhood and adolescence were related to adaptive social functioning in adulthood. Regardless of social functioning rating in adulthood, all participants demonstrated a lack of development in adaptive social skills and an increase in autistic social symptomatology from adolescence to adulthood. These findings suggest a need for additional social skills training/intervention during this period of development.

105.124 124 Examining the Relation Between ESCS and Pre-Intervention Baseline Levels of Joint Attention. J. M. Londono*, J. S. Durocher, A. Gutierrez, M. N. Hale, S. Novotny and M. Alessandri, *University of Miami*

Background: Joint attention is a core deficit in children with Autism Spectrum Disorders (ASDs) (DSM-IV-TR; APA, 2000; Mundy, 2003). Joint attention is often quantified using structured assessment procedures that incorporate specific activities and prompts to elicit behaviors of interest (Roos et al. 2008). Existing research has almost exclusively focused on the use of the *Early Social Communication Scales* (ESCS; Mundy et al., 2003) to measure joint attention in children with autism; few research studies have compared rates of joint attention across different experimental contexts. The ability to measure joint attention behaviors in more than one context, particularly naturalistic contexts, may allow researchers to obtain more representative samples of behaviors (Roos et al., 2008).

Objectives: The aim of the present study is to determine the extent to which joint attention behaviors on ESCS are related to joint attention in pre-intervention baseline assessment conditions. It is hypothesized

that there will be a positive correlation between joint attention on the ESCS and the quantity of joint attention during pre-intervention baseline assessments.

Methods: The present study compared scores on the *Early Social Communication Scales* (ESCS) to those on pre-intervention baseline assessments. Ten (n=10) 2 to 5 year old children diagnosed with ASD were assessed using the *Early Social Communication Scales* (ESCS) to measure joint attention behaviors. Joint attention was then assessed in a structured pre-baseline assessment under 2 different conditions, lasting15 minutes each. Both baseline conditions were naturalistic contexts, where the child and examiner interacted with a variety of toy on the floor. Similar to the ESCS, during the first baseline condition (baseline1), the examiner did not initiate interactions, but responded appropriately to all child initiations. During the second baseline (baseline2) condition, the examiner attempted to engage the child in play, initiating interactions as well as responding to child initiations.

Results: Contrary to expectations, joint attention (JA) behaviors on the ESCS were not significantly correlated with either Baseline1 (r=.023, p=.949) or Baseline2 (r= -.009, p=.980) JA acts. Baseline1 and Baseline2 JA acts were also not significantly correlated with one another (r=.029, p=.936). Mean JA acts across context were lowest on the ESCS (M=5.36, SD=6.12), followed by Baseline1 (M= 6.60, SD= 7.21), and Baseline2 (M= 7.10, SD= 6.49). Correlations between ADOS joint attention variables and JA acts across the 3 contexts were also explored. There was a significant negative correlation between ESCS JA and ADOS Showing (r= -.680, p=.021) and Baseline1 JA and ADOS Pointing (r= -.906, p=.0001). In addition, Baseline1 showing was correlated with ADOS Showing (r= -.667, p=.035). There were no significant correlations between Baseline2 JA and ADOS variables.

Conclusions: Results indicate that joint attention behaviors among children with ASD may be quite variable across contexts, and may be somewhat higher with more naturalistic paradigms. This reinforces the idea of utilizing multiple measures of joint attention in order to obtain more representative samples of behavior. These findings have implications for research utilizing joint attention behaviors as predictor and/or outcome variables, as the context may impact the frequency of joint attention behaviors observed.

105.125 125 Enhancing Positive Emotion Sharing in Toddlers at High Risk for ASD. J. Brian*[1], I. M. Smith[2], T. McCormick[3], E. Dowds[4], W. Roberts[5], L. Zwaigenbaum[6] and S. E. Bryson[7], (1)*Hospital for Sick Children & Bloorview Kids Rehab*, (2)*Dalhousie University & IWK Health Centre*, (3)*IWK Health Centre*, (4)*Bloorview Kids Rehab and Hospital for Sick Children/ University of Toronto*, (5)*University of Toronto*, (6)*University of Alberta*, (7)*Dalhousie University/IWK Health Centre*

Background: With the increased activity of longitudinal studies examining earliest signs of ASD in high-risk infants/toddlers, the age of detection continues to decrease, begging the question of what role earliest intervention might play (and what form it should take) in enhancing the development of these toddlers. We have been examining this question through a parent-mediated intervention program using adapted principles of evidence-based Pivotal Response Treatment (PRT; Koegel & Koegel, 2006), together with effective parent training techniques used with other high-risk infants (e.g., Landry et al., 2001). The targets of our intervention focus on two core domains of development: positive emotion sharing and early social communication. Following the original claim of Kanner (1943), who viewed autism as a disorder of "affective contact", the literature is increasingly recognizing the fundamental role of emotion in the psychopathology of autism. Positive facial affect is thought to motivate earliest developing communicative skills, notably eye-to-eye gaze and reciprocal social smiling (Berger, 2006; Farroni et al., 2002; Messinger et al., 2001), both of which are fundamental to connecting with others emotionally (Hobson, 2004; Mundy & Acra, 2006). The putative significance of shared positive emotion to subsequent social development, also reflected in our preliminary infant sibling findings (Bryson et

al., 2007), argues for interventions that target these core domains as well as later developing communicative skills.

Objectives: To provide preliminary data on the expression of positive emotion in the child, the parent, as well as 'shared' positive emotion, in our first 9 cases, comparing pre- versus post-intervention rates. Methods: Participants include 9 families of toddlers (aged 14-24 months) with suspected ASD, as indexed by high total scores on the Autism Observation Scale for Infants (Bryson et al., 2008). Parents received our 12-week Social ABC's parent training program consisting of 14, 1.5-hour home visits with manualized instruction and in-vivo coaching and support. Using a pre-established coding scheme, incidents of child-, parent-, and shared positive affect (i.e., mutual smiling) were coded and averaged across three 10-minute video segments at each of two time points: baseline and post-training.

Results: Our preliminary (pilot) data on positive emotion sharing revealed limited changes from baseline to post-intervention, in contrast to strong gains in expressive language on standardized measures (gains of up to 22 T-score points on the Mullen) and analyses of video recordings (gains in responsivity of up to 24%). We attributed this to two possible factors: (1) low rates of positive affect in both the children and parents, and (2) the fact that our focus to that point had been on child expressive language communication skills. Pilot data underscored the need to revise our training module on positive emotion sharing and refine coaching goals and strategies to increase the emphasis on positive emotion, with a focus on both partners. This poster will provide data on the first 9 cases followed since our increased focus on positive emotion sharing.

Conclusions: Discussion will centre on the importance of enhancing positive emotion in both partners in an effort to increase positive emotion *sharing* in high-risk-toddler-parent dyads.

105.126 126 Baseline Autonomic State Predictive of Social Responsiveness in Children with Autism Spectrum Disorders. M. A. Patriquin* and A. Scarpa, *Virginia Tech*

Background: As noted in the diagnostic criteria of the Diagnostic and Statistical Manual for Mental Disorders-4th Edition (DSM-IV; American Psychiatric Association, 2000), children with Autism Spectrum Disorders (ASD) struggle with social interactions, including eye contact, vocalizations, and facial affect. Spurred by the minimal effects of social skill interventions (Bellini, Peters, Benner, & Hopf, 2007), the present study diverges from the common understanding of social skill deficits and introduces an autonomic nervous system circuit that may be one root of social problems. The Polyvagal Theory (e.g., Porges, 2005, 2007, 2008) outlines a Social Engagement System that consists of interconnected cranial nerves. According to the Polyvagal Theory and the Social Engagement System, social dysfunction as seen in ASD should be paired with physiological dysfunction (i.e., fight-flight state). Research finds children with ASD show a fight-flight state (i.e., high heart rate and low heart rate variability) to unfamiliar individuals and during baseline when compared to typically developing children (Ming, Julu, Brimacombe, Connor, & Daniels, 2005). Prior research has not indicated that physiological dysfunction is predictive of social dysfunction in children with ASD.

Objectives: We hypothesize that baseline autonomic state (i.e., heart rate and heart rate variability) is predictive of parent-reported social responsiveness in children with ASD. Specifically, a higher baseline heart rate (HR) should predict lower parent-reported social responsiveness, and lower baseline heart rate variability (HRV) should predict lower parent-reported social responsiveness.

Methods: Preliminary data analyses were conducted on eighteen children, aged 4-7, previously diagnosed with an ASD. Participants were administered a 3-minute baseline video while cardiac and respiratory measures were recorded with a LifeShirt®. During this time, the child's guardian completed the Social Responsiveness Scale (SRS; Constantino, 2002). The SRS measures: social awareness, social cognition,

social communication, social motivation, and autistic mannerisms.

Results: Initial analyses showed that baseline HR significantly predicted total SRS score, _ = .46, t(16) = 2.09, p < .05, with higher HR related to increased social dysfunction. Furthermore, baseline HRV (i.e., high frequency normalized units) significantly predicted total SRS score, _ = -.45, t(15) = -1.97, p < .05, with reduced HRV related to increased social dysfunction. One-tailed correlations for SRS subscales indicated that 1) increased baseline HR was associated with more dysfunction in social motivation, r(16) = .46, p = .03, autistic mannerisms, r(16) = .35, p = .075, and social cognition, r(16) = .33, p = .089, and 2) decreased baseline HRV was associated with more dysfunction in social cognition, r(15) = -.33, p = .098, and autistic mannerisms, r(15) = -.39, p = .062.

Conclusions: Initial results supported our hypotheses that higher baseline HR and reduced HRV were related to dysfunctional social responsiveness, particularly social motivation, cognition, and mannerisms. Our results support the tenants of the Polyvagal Theory and the Social Engagement System, suggesting that physiological dysfunction is reflective of an overactive fight-flight state that may increase the likelihood of social difficulties in the child. Future studies should identify strategies to calm this over aroused state to potentially improve social responsiveness.

105.127 127 Friendship and Emotional Function Among Children and Adolescents with ASD. S. M. Kanne*[1] and M. O. Mazurek[2], (1)*Thompson Center for Autism and Neurodevelopmental Disorders*, (2)*University of Missouri - Columbia*

Background: Given the high rates of comorbid anxiety and other internalizing problems among children with ASD, identifying factors that protect against those symptoms is important. Although social impairment is a hallmark feature of autism spectrum disorders (ASD), little is known about the relations between dyadic friendships and emotional outcomes among children with ASD. Among typically developing children, friendships serve a protective function. Specifically, having at least one friend is associated with better emotional outcomes among typically developing children (e.g., lower levels of anxiety, improved self-esteem). The results of such research could have implications for understanding social and emotional development among children with ASD, as well as informing the design of future interventions.

Objectives: The purpose of this study was to examine the relations among friendship, autistic symptomatology, and internalizing symptoms among children with ASD. First, the study examined whether symptoms of anxiety and depression were higher among children with ASD and whether ASD symptom severity was associated with higher levels of internalizing symptoms. Secondly, the study examined the relationship between ASD symptom severity and friendships. A final aim was to determine whether having friends was associated with lower levels of anxiety/depression among children with ASD.

Methods: The sample included 933 children between the ages of 6 and 19 who participated in the Simons Simplex Collection (SSC), a North American multiple site, university-based research study that includes families with only one child with an ASD. The following child measures were included: the Autism Diagnostic Interview-Revised (ADI-R), Autism Diagnostic Observation Schedule (ADOS), and Child Behavior Checklist (CBCL).

Results: Results indicated the level of anxiety/depression among the current sample was not in the clinically significantly range based on the CBCL normative sample. Results also demonstrated that higher levels of ASD severity did not predict greater symptoms of anxiety/depression. Regarding friendships, correlations between ASD severity and friendship were positive (r = .178**), indicating that increased severity of autism was associated with poorer friendships. However, counter to expectations, better quality friendships were associated with increased levels of anxiety/depression among the current sample (r = -.157**). Secondary analyses further examined the relations among these variables, taking into

account additional factors (including IQ, gender, and severity of ASD), with some indication that the rated quality of the friendship had a nonlinear relationship to the degree of reported anxiety.

Conclusions: The relations among ASD symptoms, internalizing symptoms, and dyadic friendship appear to be complex. Having friends, at least as measured in the current study, does not appear to protect against internalizing symptoms for children with ASD. However, the current study has a number of limitations that will be discussed more fully. In brief, future research is warranted in this area. More comprehensive assessment of dyadic friendships among children with ASD will be necessary to fully examine these issues. In particular, future studies should include specific measures that address number of friends as well as friendship quality (using parent-, child-, and peer-report whenever possible).

105.129 129 A Comparable Analysis of Emotion Recognition in Autism Spectrum Disorders (ASD) and Attention Deficit Hyperactivity Disorder (ADHD). K. L. Ashwood*[1], B. Azadi[1], S. Cartwright[1], P. Asherson[2] and P. Bolton[1], (1)*Institute of Psychiatry, King's College London*, (2)*Institute of Psychiatry*

Background: The ability to discriminate and recognise facially expressed emotions has been studied extensively in Autism Spectrum Disorders (ASD). Less research, however, has been conducted on individuals with Attention Deficit Hyperactivity Disorder (ADHD). Although emotion recognition deficits have been observed in both clinical populations, few studies have compared individuals with autism and ADHD or considered whether the co-occurrence of ASD traits in ADHD may be relevant.
Objectives: The current study aimed to compare facial affect recognition in autistic individuals with and without comorbid ADHD to a 'pure' ADHD group who have few ASD traits. This will help clarify whether emotion recognition deficits are specific to autism.
Methods: To date 34 male children and adolescents between the ages of 7 and 16 have taken part in the study. Included were individuals who, according to the DSM-IV, fulfilled the diagnosis of an ADHD (n=19) or an autistic disorder (Asperger syndrome, high functioning autism and atypical autism) with (n=7) and without (n=8) comorbid ADHD symptoms (ASD+/-ADHD n=15) with an IQ>70. Facial affect recognition was assessed using labeling and same/different discrimination computer tasks, with negative emotions (sad, angry, fear, disgust) from the Facial Expression of Emotion: Stimuli and Tests (FEEST) at three different intensities (25%. 50%, 75%).
Results: The mean percentage correct responses on the labelling task was not significantly different between the ASD +/- ADHD group (M=39.53, *SE*=7.70) and the 'pure' ADHD group (M=37.95, *SE*=10.85) By contrast, the ASD +/- ADHD group were significantly less accurate (M=51.15, *SE*=6.57) on the emotion discrimination task compared with the 'pure' ADHD group (M=55.44, *SE*=4.83; $t(29) = -2.10$, $p<.05$).
Conclusions: Preliminary results indicate that young children and adolescents with ASD perform as well as children with 'pure' ADHD when asked to label faces showing negative affect. By contrast, their accuracy on an emotion discrimination task was significantly reduced. Future research in an extended sample will examine the pattern of discrimination deficits by emotion and intensity and will determine whether ASD cases with and without co morbid ADHD show similar levels of impairment.

105.130 130 A Treatment Program Utilizing Multiple Evidenced-Based Components Promotes Acquisition, Generalization, and Maintenance Effects for Social Skills in Pre-School and Elementary Age Children with ASD. H. Block*, J. Hood, K. C. Radley, T. P. Gabrielsen, B. Springer, B. Jenson, E. Clark and J. Bowen, *University of Utah*

Background: Social skills research for youth with ASD focuses largely on single modality treatments typically employing various outcome measures to assess treatment effectiveness. Research often fails to investigate whether treatment effects generalize to environments outside of treatment settings or are maintained over time. Measures of treatment fidelity, consumer satisfaction, and social validity may also be lacking.

Objectives: Aims were to (1) assimilate previous research on effective social skills

treatments into a single program for children with high functioning ASD; (2) examine treatment fidelity, consumer satisfaction, and social validity variables; and (3) measure generalization and maintenance effects outside of treatment settings.

Methods: The program was piloted in three settings: a school for children with autism; a public elementary school; and an outpatient clinical setting. Twelve children with ASD participated. Inclusion criteria were (1) current educational classification or clinical diagnosis of ASD; (2) score at or above cutoff for ASD on multiple measures, including ADOS, GADS, and SRS; (3) verbal IQ at or above 69; and (4) parental consent. University, mental health agency and school district IRB approval was obtained. Typical peers were also included.The program has 18 units covering introductory, intermediate, and some advanced social skills taught weekly in two 30-45 minute sessions or one 90-minute session. Multiple components of the program included: (1) instruction delivered by original animated superhero characters rather than adult didactic instruction; (2) video modeling of social scripts by peers; (3) peer-mediated intervention; (4) self-management by tracking skill practice on individual superhero collectible cards; (5) parental involvement through reading comics and watching DVDs with children; and (6) naturalistic settings for skill practice via teachers and parents tracking on collectible cards in class and at home. Treatment fidelity was accomplished by using two-page lesson plans with consistent format.

Treatment effects were assessed through a direct observation system that measures social engagement skills and has been used in prior research (Bellini, 2007). Ratings of specific social behaviors during unstructured analogue free play and recess periods were gathered. The Autism Social Skills Profile (ASSP) and Social Responsiveness Scale (SRS) were completed by teachers and parents prior to and following treatment. The Behavior Intervention Rating Scale (BIRS) and other study-developed measures of consumer satisfaction and social validity were collected. Treatment fidelity was rated by observers after each session.

Results: Preliminary results indicate primarily large effect sizes (ES) across observation settings and clinical and preschool groups for social engagement (.74 to 1.47). Percentage of nonoverlapping data points (PND) showed a range from 16.67% to 100% across all measures with 1 outlier of 0%. ES by Parent Daily Report ranged from .25 to 3.05. Treatment fidelity, social validity, and consumer satisfaction variables are still being analyzed, as well as some of the data from the elementary school setting.

Conclusions: Multiple evidence-based components were shown to successfully integrate into a single program delivered in a specialized school for children with autism, a public school, and clinical settings. ES for social engagement were primarily large with some medium ES across settings.

105.131 131 Advanced Theory of Mind in Autism Spectrum Disorder: From Childhood to Adolescence. A. M. Scheeren*, S. Begeer and H. M. Koot, *VU University*

Background: Age is an important factor in the development of Theory of Mind (ToM) abilities in school-aged children with high functioning autism spectrum disorders (HFASD, Wellman, 1991). However, the development of advanced ToM capacities (Happé, 1994) from childhood to adulthood has been largely neglected in studies on HFASD. In this study we explore the age related change in advanced ToM with a large cross-sectional design (n=175), aiming to assess the validity and sensitivity of advanced ToM tests across a wide age range and examining whether ToM development shows a stagelike or linear change. Furthermore, we will delineate to what extent the advanced ToM test is associated with the severity of the autistic disorder.
Objectives: Our goal is to explore the influences of age on the advanced Theory of Mind abilities of a large sample of children and adolescents with HFASD and to examine the predictive value of advanced Theory of Mind abilities for the severity of autistic symptoms.

Methods: Participants were 175 children and adolescents with HFASD (aged 6 to 18 years). ADOS scores were obtained from all participants. A five stories version of the Stories of Everyday Life (Kaland, 2002) was used to examine whether the participants were able to infer the intentions or feelings of story characters. The test included stories on second order false belief, emotional display rules, double bluff, violation of a social rules, and irony. Severity of autism symptoms was assessed with the Social Responsiveness Scale (SRS). Verbal IQ was measured with the Peabody Picture Vocabulary Test-III.

Results: Preliminary linear regression analyses on a subsample of participants indicated that when both age and verbal IQ were entered as predictors of Theory of Mind abilities, only age had a (nearby significant) predictive value. This effect became significant when age was entered as a single predictor (_ = 0.37, $p < .05$, n = 37). Despite the wide age range of 6 to 18 years, no floor or ceiling effects were found in performances on the advanced Theory of Mind test. Surprisingly, Theory of Mind abilities were not predictive of symptom severity as indicated by scores on the Social Responsiveness Scale.

Conclusions: Preliminary results suggest age is an important predictor of advanced Theory of Mind abilities. Generally, adolescents perform better than school-aged children on an advanced Theory of Mind test. Yet, there must be other background factors that influence advanced Theory of Mind abilities, because large variance was noted within the age groups. These will be explored in the analysis of the full dataset. Furthermore, the low predictive value of advanced Theory of Mind abilities for symptom severity seems to indicate that as such advanced Theory of Mind abilities are of limited value for understanding social limitations within the group of children and adolescents with HFASD.

105.132 132 Friendship and Loneliness of Students with ASD: Influence of Social Skills. J. L. Birdwhistell* and L. A. Ruble, *University of Kentucky*

Background: The Individuals with Disabilities Education Act requires that students with disabilities be educated in the least restrictive environment. This has resulted in an educational movement towards the integration of students with disabilities into the general education classroom where they are educated alongside their typical peers (Simpson, Boer-Ott, & Smith-Myles, 2003). Particular attention is being given to the inclusion of students with autism spectrum disorder (ASD), and many argue that the level of social interaction of students with ASD will increase as a result of placement in the general education classroom (Boutot & Bryant, 2005). The development of friendships is an important component of the social structure because it can provide an invaluable context for forming interpersonal skills and developing self-concept (Chamberlain, Kasari, & Rotheram-Fuller, 2007). However, individuals with ASD often fail to develop adequate friendships and experience feelings of loneliness compared to typical peers (Bauminger & Kasari, 2000; Ochs, Kremer-Sadlik, Solomon, & Sirota, 2001). Friendship is a complex construct requiring adequate social skills including an ability to understand what others think and feel (Chamberlain et al., 2007). Therefore, the quality of social skills of individuals with ASD as reported by both parents and teachers is relevant to how these individuals might develop friendships or experience loneliness within the general education classroom. Objectives: The purpose of this preliminary study is two-fold: (a) to examine self-reported quality of friendships and feelings of loneliness of students with ASD in the general education classroom; and (b) to determine the association between self report of friendships and loneliness with parent and teacher report of quality of social skills. Methods: Data come from an archival data set obtained from a previous social skills group intervention for middle school students with ASD who were educated in the general education classroom. Data collected at baseline from approximately six children with ASD with student self-report on the Friendship Questionnaire and the Loneliness Scale as well as both parent and teacher reports on the Social Skills Rating Form will be used. Results: Data will be analyzed using

descriptive statistics to examine how students with ASD in the general education classroom report on their quality of friendships and feelings of loneliness. Additionally, bivariate correlation will be used to examine the relationship between report of quality of social skills of the student (as reported by the parent and also by the teacher) and the self-reported scores on friendship and loneliness. Conclusions: Results from this preliminary study will seek to replicate previous findings looking at the quality of friendships and feelings of loneliness as reported by students with ASD in the general education classroom. Further, results from this study will explore the relationship between social skills of children with ASD and their perception of friendship quality and feelings of loneliness. Because of the growing emphasis on social skills training, it will be important to know whether students with ASD with higher quality social skills report greater quality of friendships and lower feelings of loneliness.

105.133 133 Developmental Associations Between Gaze Shifting, Joint Attention, and Later Autism Spectrum Disorder (ASD) Severity in the Infant Siblings of Children with An ASD. L. Ibanez*[1], D. S. Messinger[1] and W. L. Stone[2], (1)*University of Miami*, (2)*Vanderbilt Kennedy Center*

Background:

Children with Autism Spectrum Disorders (ASDs) exhibit deficits in their ability to disengage visual attention and initiate joint attention. In similar fashion, the infant siblings of children with an ASD (ASD-sibs) engage in fewer shifts in visual attention and initiating fewer joint attention behaviors than the infant siblings of typically developing comparison children (COMP-sibs). Few studies have examined how these early deficits relate to one another and to later ASD severity in ASD-sibs.

Objectives:

To examine the developmental associations between early visual attention, joint attention, and ASD severity 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. The mean number of initiations of joint attention was calculated during the Early Social Communication Scales (ESCS) at 8, 10, 12, 15, and 18 months of age. Later ASD severity was measured as a calibrated score on the Autism Diagnostic Observation Schedule (ADOS) at 30 months (Gotham et al., 2007).

Results:

For ASD-sibs, there were strong associations between early frequency of gaze shifts and later initiating joint attention, and between initiating joint attention and later ASD severity. ASD-sibs' (n = 28) frequency of gaze shifts was significantly correlated with later initiating joint attention, r = .57, p <.01, such that higher frequency gaze shifting was associate with more initiating joint attention behaviors. For COMP-sibs (n = 19), that correlation was not significant, r =.09, p = .72. For ASD-sibs (n = 10) initiating joint attention was significantly correlated with ASD severity, r = -.64, p <.05, such that more initiating joint attention behaviors were related to lower ASD severity. For COMP-sibs (n = 10), that correlation was not significant, r = -.23, p = .51. There was no significant correlation directly between frequency of gaze shifts and ASD severity for either ASD-sibs or COMP-sibs.

Conclusions:

Among ASD-sibs, flexible attention allocation at and away from the parent's face at six months predicted later initiating joint attention, which in turn predicted ASD severity on the ADOS a year later. Comp-sibs did not show these associations, perhaps because attentional flexibility did not constrain initiating joint attention among typically developing children. Difficulties with flexible allocation of visual attention—an essential behavioral component of initiating joint attention-- may be an early index of

developing difficulties among infants at-risk for autism.

105.134 134 Comparing Preference and Reinforcer Assessment Methods for Children with ASD. A. J. Margol*[1], A. Gutierrez[1], M. Pawlowski[2], M. N. Hale[1], J. S. Durocher[1] and M. Alessandri[1], (1)*University of Miami*, (2)*Nova Southeastern University*

Background: Children with Autism Spectrum Disorders (ASDs) show impairments in social functioning, most specifically in relating to others (DSM-IV-TR, APA, 2000). For many children, social consequences may not function as reinforcers (Dawson et al., 2002). Therefore, assessing preferences for social consequences may be important in developing interventions for children with ASDs. Currently, two methods for assessing social motivation have recently been described: a forced preference assessment for adult attention (Dube et al., 2004) and a single operant reinforcer assessment (Smaby et al., 2007). These procedures have not been systematically investigated in independent laboratories.

Objectives: The purpose of this study was to compare results of these two social motivation assessment methods with one another; it was hypothesized that these measures would be positively correlated.

Methods: Participants included a sample of 2 to 5 year old children with previous diagnoses of an ASD; all met cutoffs for ASD or Autism on the ADOS and were part of a larger study on the effectiveness of an intervention targeting initiating joint attention skills. Children were administered a *Forced Choice Preference Assessment for Adult Attention* (Preference Assessment, based on Dube et al., 2004), and a *Single Operant Reinforcer Assessment for Social Consequences* (Reinforcer Assessment, based on Smaby et al., 2007). During the Preference Assessment, children are exposed to a forced-choice procedure whereby they must choose between spending time on the side of the room where an examiner is both interactive and playful or on the side where the examiner is not interactive. For this procedure, the coding was modified to include duration of time spent engaged with either examiner (vs. duration of time spent on the "interactive" side of the room as described in Dube et al.). During the Reinforcer Assessment, the child presses a micro-switch in order to access 5 different social consequences (e.g., tickles, hugs, clapping, etc.), which were previously selected by their caregiver. This procedure measures the frequency of micro-switch presses during a one minute session for each consequence (5 minutes total).

Results: Preliminary findings indicated that results across the 2 procedures were not significantly correlated, although results were in the expected direction ($r = .519$, $p = .062$). Findings further revealed variability across participants in their preference for adult attention, although a majority appeared to favor the non-engagement condition. Results from the Reinforcer Assessment also varied across participants.

Conclusions: The relationship between scores on the 2 procedures suggests that it may be particularly important to assess social motivation across different contexts for children with ASD, as results may vary depending on how assessments define and measure this construct. Further, results point to the importance of measuring the child's active "engagement," as this may be an important aspect of social motivation. Given the recent emphasis on developing and evaluating interventions aimed at improving core social symptoms of ASD (such as joint attention), measures of social motivation may play an especially important role as predictors of a child's ability to positively benefit from intervention, as well as outcome variables themselves.

Invited Educational Symposium Program
106 The Ethics of Communicating Scientific Findings of Autism Risk

Moderator: C. Newschaffer *Drexel University School of Public Health*

Research on the etiology of autism spectrum disorder (ASD) is increasingly focused on complex genetic and environmental mechanisms. Findings from major new initiatives have the potential to enrich understanding of ASD etiology. Given the intensity of public debate about causes for ASD, communication of scientific findings relating to its etiology presents significant challenges and demands

sensitivity. Further difficulties may arise because of challenges involved in communicating potential or realized environmental and genetic risks shown to be associated with ASD. This complexity demands an understanding of the ethical implications associated with scientific findings on autism. However, little attention has been given to the ethics of autism research and challenges involved in communicating complex findings of autism research to the public. In October 2009 a two-day meeting entitled "The Ethics of Communicating Scientific Findings of Autism Risk," brought together leading ASD stakeholders and leaders in relevant areas of risk communication, bioethics, children's health, and community welfare. This IES will provide a summary of key aspects presented and discussed in the October meeting that relate most directly to how research findings are communicated by autism scientists.

106.001 Overview. C. Newschaffer*, *Drexel University School of Public Health*

Dr. Newschaffer will offer a short overview of the meeting process, provide a brief report on findings from a survey done in advance of the workshop examining parental knowledge, attitudes, and beliefs towards autism research, introduce presenters and moderate discussion.

106.002 Ethical issues surrounding ASD risk communication. H. Tabor*, *University of Washington School of Medicine*

Dr. Tabor will discuss ethical issues surrounding ASD risk communication. In particular, Dr. Tabor will focus on the challenges specific to communicating information pm complex genetic and environmental mechanisms in disease etiology.

106.003 Funding and Advocacy Organizations. G. Dawson*, *Autism Speaks*

Dr. Dawson will be report on the role that funding and advocacy organizations can play in promoting clearer dissemination of information about autism risk factors.

106.004 Ethical and Risk Communication Guidelines. M. Yudell*, *Drexel University School of Public Health*

Finally, Dr. Yudell will discuss the ethical and risk communication guidelines developed by the speakers and stakeholders involved in this meeting that are most directly relevant to autism scientists. He will also share recommendations for translating these guidelines into policy and practice.

Brain Imaging Program
107 Brain Imaging 1

107.001 A Magnetic Resonance Spectroscopy Study of White Matter in Autism. T. W. Frazier*[1], J. Stanley[2], N. J. Minshew[3], M. S. Keshavan[4] and A. Y. Hardan[5], (1)*Cleveland Clinic*, (2)*Wayne State University*, (3)*University of Pittsburgh School of Medicine*, (4)*Harvard Medical School*, (5)*Stanford University School of Medicine/Lucile Packard Children's Hospital*

Background: Aberrant connectivity theory hypothesizes that autism results from abnormal brain connections with excessive connectivity of short distance connections and under-connectivity of long-distance white matter fiber tracts. Converging evidence from different imaging modalities have identified white matter abnormalities in autism. A large number of morphometric, diffusion tensor imaging, and functional studies have reported alterations in white matter supporting decreased functional connectivity in autism, particularly in frontal, temporal, and parietal regions. However, only two proton spectroscopy (1H MRS) studies have investigated metabolites levels in white matter in autism. The first study found no differences between youth with autism and healthy controls for any cerebral white matter region while the second reported on decreased N-Acetyl-Aspartate (NAA) levels in both the left frontal and left parietal white matter in the autism group.

Objectives: The primary goal of this investigation was to examine 1H MRS metabolite levels in white matter regions in children with autism. The relationship between metabolites levels and age was also investigated.

Methods: Multi-voxel 1H MRS scans were obtained from a group of 23 children with autism and 23 age-, and gender-matched healthy controls. Using a STEAM chemical shift imaging sequence, measurements from white matter structures in the left and right hemisphere were obtained to assess the levels of several metabolites including: Choline, NAA, Glutamate+glutamine, Myo-inositol, and Creatine+ Phosphocreatine.

Statistical analyses included a series of mixed-effects regression models with Group (Autism, Healthy Controls), Lobe (Frontal, Temporal, Parietal, Occipital), and Hemisphere (Left, Right) as the fixed effects factors; Age as a covariate, and metabolite concentrations as the repeated measures dependent variable. Regression models were computed separately for each metabolite.

Results: High quality 1H MRS scans were available on 17 boys with ASD (Mean Age = 12.5, SD=1.9, range=8-15) and 17 healthy control boys (Mean Age = 11.6, SD=1.2, range=9-15). The same pattern of results emerged for each metabolite with levels being lower in youth with autism when compared to controls (Group main effect - smallest $F(1, 196)=7.44$, $p=.007$). Metabolite levels tended to remain stable or decrease with age in healthy controls but increased with age in youth with autism (Group by Age interaction – smallest $F(1,196)=6.45$, $p=.012$).

Conclusions: Lower 1H MRS metabolite levels in the deep white matter observed in the present study is consistent with previous studies identifying structural white matter abnormalities in children and adolescents with autism. These results may reflect an alteration in maturation of deep white matter structure, supporting the existence of abnormalities in long-distance fiber tracts. Developmental increases in metabolite levels in autism may reflect an ongoing compensatory process or simply result from developmental consequences of early life white matter pathology. Findings from this study should also be examined in light of grey matter abnormalities since white matter alterations are closely related to those of grey matter and vice versa. Future longitudinal 1H MRS studies are warranted to elucidate the age-related changes in white matter structures in autism and their relationship with grey matter imaging measures and clinical features.

107.002 Abnormal Brain Response to Language Stimuli in Sleeping Infants and Toddlers with ASD. L. T. Eyler*[1], K. Pierce[2] and E. Courchesne[2], (1)*University of California San Diego*, (2)*University of California, San Diego*

Background: Delays and deviances in language acquisition are among the early signs of autism, but alone are insufficient to clearly identify risk for ASD in infants or toddlers. Recently, there has been great interest in identifying biological markers of early ASD to be used alone or in combination with behavioral markers to better characterize risk. Using sleep fMRI, our laboratory reported abnormal laterality and extent of brain response to language in 3 year olds with ASD (Redcay and Courchesne, 2009). We sought to replicate this novel finding, determine whether this neurofunctional abnormality occurs in ASD 1 year olds, and profile the autistic brain's response to language across early development.

Objectives: To utilize sleep fMRI to reveal similarities and differences in brain response to language in infants at-risk for ASD and typically developing controls.

Methods: During natural sleep, brain response to language was evaluated in N=30 ASD (ages 14 to 46 mos) and 14 typical (ages 13 to 41 mos) infants and toddlers using fMRI. Two language tasks were used: prosodic speech consisting of segments of children's stories as in Redcay and Courchesne (2009) and single word stimuli from a list of words familiar to each participant based on the MacArthur Bates CDI. AFNI software was used to detect and correct for head motion and carry out regression analyses that compared BOLD responses between language blocks and periods of no language stimulation while controlling for potential confounds. After spatial blurring and normalization to standard atlas space, maps of significant language-related response were created for ASD and typical groups and for between groups comparisons, each corrected for multiple comparisons.

Results: In response to prosodic speech, typical toddlers showed positive activation in the primary language processing region, the left superior temporal gyrus, and deactivations in several brain regions such as thalamus. In contrast, ASD toddlers showed activation in midline cuneus /lingual gyrus and in left middle occipital gyrus and bilateral

deactivation in angular gyrus and several right frontal regions. In a direct between groups comparison, ASD children had significantly less activation in the left superior temporal gyrus in response to prosodic speech. Single word and non-word stimuli were less potent activators in the typical group, with only subthreshold responses noted in superior temporal gyrus. Strong and widespread deactivations of midline cortical and subcortical structures were observed during this task in the ASD group. On direct comparison, bilateral superior temporal gyrus was significantly under-responsive in the ASD group. Within the ASD group, strong positive correlations were observed with age: Older ASD toddlers showed more widespread and cortical responses compared to younger ASD infants and toddlers.

Conclusions: The superior temporal gyrus is consistently recruited in response to both stories and single words in infants and toddlers that are typically developing but not in those with ASD. Thus, with suitable stimuli, it is possible to detect differences in the brain response to language in infants and toddlers at-risk for ASD and holds promise that fMRI may be used to evaluate risk for autism in the future.

107.003 Abnormal Fusiform Gyrus Response to Low but Not High Spatial Frequency Face Information in Autism. K. M. Curby*[1], M. Riley[2], D. W. Grupe[3], E. T. Hunyadi[2] and R. T. Schultz[4], (1)*Temple University*, (2)*Children's Hospital of Philadelphia*, (3)*University of Wisconsin-Madison*, (4)*Children's Hospital of Philadelphia and the University of Pennsylvania*

Background: Face recognition deficits and hypoactivation in classically face-selective fusiform cortex are widely replicated in ASD. However, little is known about the mechanisms underlying such deficits and whether they might be tied to specific abnormalities in the perceptual processing of face information. For example, electrophysiological studies suggest that there may be abnormal specialization of *spatial frequency* (SF) processing in the ASD visual system. Notably, low spatial frequency (LSF) information is thought to better support the holistic processing strategies recruited for face recognition among healthy populations, whereas high spatial frequency (HSF) information better supports more featural processing strategies not unlike those recruited for face processing in ASD.

Objectives: To test the prediction that fusiform hypoactivation in ASD stems from an abnormal response to the LSF, but not HSF, components within face stimuli.

Methods: Whole brain fMRI images were collected from 31 participants (16 ASD; 15 age-/IQ-matched controls) while they performed identity-matching judgments on simultaneously presented image pairs. To assess whether the ASD sample showed fusiform hypoactivation for unfiltered faces relative to non-face stimuli, participants completed a standard localizer run with unfilltered face and house images. To examine the neural response to different SF information, participants performed five runs of matching trials with face or shoe images that were either broadpass (BSF; i.e. containing the full spectrum of SF information) or filtered to contain only LSF (<8 cycles/image) or HSF (>32 cycles/image) information.

Analyses were performed on *a priori* ROIs functionally defined by contrasting BSF faces with BSF shoes for the data collapsed over group. The TAL coordinates for the peak voxels were as follows: right fusiform gyrus (RFG) = (39,-37,-17); left fusiform gyrus (LFG) = (-39,-37,-20). Volume-of-interest analyses were performed on the 100 most face-selective voxels in each region.

Results: As found previously, the ASD group, relative to the control group, showed right fusiform hypoactivation for unfiltered faces (compared to houses) in a location consistent with previous studies (uncorrected p=.005; TAL co-ordinates: 39,-52,-17).

There was a main effect of category in the RFG, and most notably a significant three-way interaction between category, SF scale, and group, $F(1,29)=4.70$, $p=.039$: the ASD group showed a similar advantage for HSF faces over HSF shoes as did the control group, but a reduced advantage for LSF faces over LSF shoes. No other effects reached significance.

There was also a main effect of category in the LFG, F(1,29)=13.92 p=.001, with greater activation for faces compared to shoes and an interaction between category and SF scale, F(1,29)=6.49, p=.016, with greater face-selectivity for HSF compared to LSF faces. No other effects reached significance.

Conclusions: Consistent with previous findings of hypoactivation to face stimuli in ASD, face-selective right fusiform activation for LSF images was reduced in ASD relative to healthy controls. However, face-selective activation for HSF images was comparable among the two groups. The ASD group's abnormal pattern of face-selective activity to SF filtered face images suggests that the fusiform gyrus in ASD may be abnormally tuned (relative to controls) to the perceptual information in faces.

107.004 Biological Motion Perception in Autism and Unaffected Siblings. C. M. Hudac*[1], S. Shultz[2], S. M. Lee[1], C. Cheung[1], D. Sugrue[1], A. Voos[1], C. A. Saulnier[3], B. C. Vander Wyk[1] and K. A. Pelphrey[1], (1)*Yale University*, (2)*Yale School of Medicine*, (3)*Yale University School of Medicine*

Background: Recent work by Klin et al. (2009) suggests that preferential attention to biological motion, an early-emerging and evolutionarily well-conserved mechanism, is disrupted in autism. Dysfunction in the posterior superior temporal sulcus (pSTS), a region implicated in biological motion perception, has been shown in adults with autism (Pelphrey et al., 2005, *Brain*). While pSTS abnormalities may underlie biological motion perception deficits in autism, it is possible that these brain abnormalities result from a lifetime of disruption in preferential attention to biological motion. Little is known of the developmental trajectory of these neural processes in children with an autism spectrum disorder (ASD) or unaffected siblings (UAS). Given the high heritability of autism, UAS children may be susceptible to similar neural deficits.

Objectives: We sought to characterize the neural mechanisms involved in biological motion perception in 6-18-year-old children comprising the following groups: ASD (n= 16), UAS (n = 16), and typically-developing (TD) (n= 11).

Methods: During an fMRI scan, participants viewed point-light displays of dynamic human biological motion and randomly moving point-light animations. Random motion animations were created with equivalent amount of motion. Each condition was presented five times in a block design, with each block lasting 24 seconds.

Results: We defined structural regions of interest including the right pSTS, a middle temporal/occipital cortical region sensitive to viewed motion (MT), the right fusiform gyrus (FFG), the right and left amygdalae, and the right ventrolateral prefrontal cortex (VLPFC). Children with an ASD exhibited hypoactivation (biological > nonbiological motion contrast) relative to the TD and UAS children in the right pSTS, and right and left amygdalae. *Both* the ASD and UAS children exhibited hypoactivation in the right FFG and right VLPFC relative to TD children. In contrast, we observed equivalent levels of activation in MT for all three groups.

Conclusions: In agreement with prior studies, we observed pSTS dysfunction in children with an ASD relative to TD children. We extend the prior results by revealing continuity in this aspect of brain dysfunction in ASD from childhood to adulthood. In addition, consistent with previous neuroimaging studies of individuals with ASD, we found reduced activation to socially meaningful stimuli in the amygdala. Hypoactivation in the pSTS and amygdala in response to biological motion was specific to individuals exhibiting the autism behavioral phenotype – no such dysfunction was observed in the UAS group. Our results from area MT indicate that neither generalized cortical hypoactivation or global deficits in the processing of motion are part of the neuroendophenotype of ASD. Strikingly, both the ASD and UAS groups showed reduced biological > non-biological activation in the FFG and the VLPFC, relative to TD children. This finding raises the intriguing possibility that hypoactivation in these regions represents a brain mechanism for vulnerability to developing an ASD, even in the absence of the behavioral phenotype.

107.005 Social Brain Abnormalities in Very Young Children with Autism. N. Chabanne*[1], C. Amiet[2], A. Bargiacchi[3], N.

Boddaert[4], L. Laurier[5], E. Duchesnay[6] and M. Zilbovicius[5], (1)*INSERM U797, Robert Debre Hospital, AP-HP*, (2)*Salpetriere Hospital, APHP*, (3)*U797 INSERM CEA*, (4)*Hospital Necker*, (5)*Research Unit U797 "Neuroimaging and Psychiatry", CEA - INSERM*, (6)*Research Unit U797 "Neuroimaging and Psychiatry", CEA - INSERM and NeuroSpin, CEA*

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. These results concern school aged children, adolescents and adults.

Objectives: Here, we investigated whether these abnormalities could be detected earlier, before the age of 5 years

Methods: Regional cerebral blood flow (rCBF) was measured at rest with positron emission tomography (PET) in 22 children with ASD (18 boys, mean age: 3.8 ± 0.6 years, mean IQ: 60 ± 15) and 11 non-autistic mentally retarded children (mean age: 7.2 ± 2.3 years, mean IQ: 52± 23). The ASD diagnosis was based on DSM IV-R and ADI-R criteria. rCBF was determined from the distribution of radioactivity measured with high-resolution PET camera (ECAT - Exact - HR+ - 962) after bolus intravenous injections of H_2O^{15}. Images were analyzed using SPM2 software (http://www.fil.ion.ucl.ac.uk/spm/).

Results: We found in children with ASD a significantly hypoperfusion in the right temporal lobe ($p<0.001$, corrected), centred on the superior temporal sulcus, associated to a less significant and less extended hypoperfusion in left temporal gyrus, cingular gyrus and bilateral inferior frontal gyri ($p<0.001$, uncorrected). In addition, temporal hypoperfusion was detected individually in 82% of autistic children.

Conclusions: PET and voxel-based image analysis revealed a dysfunction of temporal lobes and frontal and limbic regions in very young children with ASD (<5 years old). As these interconnected regions are important components in social cognition, we can postulate an early dysfunction of a social cortical network including temporal, frontal and cingular regions in autism

107.006 Neural Correlates of the Interaction of Gaze Direction and Facial Expression in Individuals with Autism. E. J. Carter*[1], D. L. Williams[2], N. J. Minshew[3] and K. A. Pelphrey[4], (1)*Carnegie Mellon University*, (2)*Duquesne University*, (3)*University of Pittsburgh School of Medicine*, (4)*Yale University*

Background: Gaze direction is a key component of understanding the import of others' emotions. For example, if a companion is making a fearful facial expression, the viewer must determine where he or she is looking in order to select a course of action. If the companion is looking away from the viewer, the viewer may be in danger. However, that is not the case if the companion is looking at the viewer. Individuals with autism have difficulty both with understanding gaze direction (e.g., Baron-Cohen, 1995, Mindblindness) and with identifying emotional facial expressions (e.g., Celani et al., JADD). It has previously been suggested that these individuals have dysfunction in the right posterior superior temporal sulcus (pSTS) wherein they do not differentiate between looking towards or away from a goal (Pelphrey et al., 2005, Brain).

Objectives: In this fMRI study, participants viewed a woman making a fearful expression towards or away from the viewer. We examined whether individuals with autism displayed a brain response that differentiated the two conditions (whether the observed woman shows fear toward the viewer or fear to something in the environment) and whether or not this pattern is the same as that of TD controls. The purpose of this study was to further examine the function of the right pSTS and other social brain areas in autism.

Methods: Participants were twelve individuals with autism (age: 11-21 years, mean = 16; FSIQ: 94-128, mean = 111) and twelve matched typically developing individuals (age: 12-23, mean = 19; FSIQ: 98-124, mean = 115). They passively viewed a video of an animated woman who periodically turned either towards or away from them while making a fearful facial expression. Images were collected using a 3T Siemens

Allegra magnetic resonance imaging scanner and analyzed with Brain Voyager.

Results: Both groups showed a greater hemodynamic response when viewing the woman directing her expression away from them than towards them in the bilateral pSTS ($q < .05$). The typically developing group showed greater responses in many social brain areas to both conditions than did the group with autism, including the bilateral STS and right fusiform gyrus ($q < .05$).

Conclusions: Despite having a lower level of activity in some social brain areas relative to the typically developing individuals, the participants with autism still showed pSTS differentiation between a woman making a fearful facial expression towards and away from them. This suggests that individuals with autism are sensitive to differences in gaze information during emotion assessment.

107.007 Complex Network Properties of Intrinsic Brain Functional Organization in Autism Spectrum Conditions. M. C. Lai*[1], B. Chakrabarti[1], D. Bassett[2], D. Meunier[3], M. V. Lombardo[1], A. Fornito[3], J. Suckling[3], S. Baron-Cohen[4], E. Bullmore[3] and M. R. C. AIMS Consortium[5], (1)*Autism Research Centre, Department of Psychiatry, University of Cambridge*, (2)*Department of Physics, University of California, Santa Barbara*, (3)*Brain Mapping Unit, Department of Psychiatry, University of Cambridge*, (4)*University of Cambridge*, (5)*University of Cambridge; Institute of Psychiatry, King's College London; University of Oxford*

Background:

Human brain structural and functional organizations have features of complex networks, such as modularity, scale-invariance, small-world network topology, and the presence of highly connected hubs. Recent methodological advances in sociology, mathematics and statistical physics have provided a variety of graph metrics for the description of complex network architectures. In parallel, recent neuroimaging evidence suggests that the brain architecture of people with autism is characterized by aberrant (both hyper- and hypo-) connectivity. However, to our knowledge, no study to date has directly examined the network organization of the autistic brain within the context of complex network science.

Objectives:

To characterize the complex network properties of the intrinsic functional organization of the brain in people with autism spectrum conditions (ASC), and to compare them to those of the neurotypical brain networks.

Methods:

30 right-handed adult males aged 18-45 with a clinical and ADI-R confirmed diagnosis of an ASC (ASC group), and 33 age-, sex-, handedness- and IQ-matched neurotypical adults (NT group) were scanned in a 3T MRI scanner by echo planar imaging in an eye-closed, awake, non-task resting state. Following motion and slice timing correction, the 4D images were linearly registered to a study-specific template (averaged by the high-resolution structural images of the whole 63 participants). The cortical and subcortical areas were parcellated into 118 regions (i.e., network "nodes") according to the Harvard-Oxford cortical and subcortical atlas. Averaged timeseries for each node were extracted and filtered by a wavelet decomposition to obtain the scale 4 low-frequency (0.024 - 0.048 Hz) correlation coefficients. Connectivity strength was first calculated for each node. After thresholding in the cost-efficient small-world regime (proportion of all possible connections 9-48%), network properties were described at both global and nodal levels using global efficiency, clustering coefficient, local efficiency, hierarchy, assortativity, and nodal degree and betweenness-centrality. Group comparisons were performed using permutation testing.

Results:

Brain networks for both groups showed small-world topology. At the global level, there were no group differences in network metrics except that the ASC group showed a trend of lower mean clustering coefficient (1-tailed $p=0.067$) and local efficiency ($p=0.086$). However at the nodal level, bilateral medial orbito-frontal and several temporal regions showed lower connectivity strength in the ASC group. The ASC networks had lower global

efficiency and nodal degree in left posterior parahippocampal and bilateral anterior temporal areas, but higher in right basal ganglia (particularly nucleus accumbens) and posterior supramarginal gyrus. ASC networks also had lower clustering coefficient and local efficiency at bilateral postcentral and right anterior middle temporal gyri. Moreover, although both networks characterized several overlapping hub regions (e.g. right precuneus and posterior parahippocampal gyrus), the ASC networks had significantly lower betweenness-centrality at left posterior parahippocampal and middle cingulate cortices.

Conclusions:

The autistic brain showed a comparable small-world network organization to the neurotypical brain networks, while having slightly more random network characteristics. Whereas most global network properties were conserved across both groups, regional properties showed significant group differences localized to various temporal, subcortical and mid-line regions.

107.008 Neuroanatomical Differences Between Autism Spectrum Young Adults with Typical Versus Delayed Speech Onset. K. L. Hyde*[1], F. Samson[2], A. C. Evans[3] and L. Mottron[2], (1)*Montreal Neurological Institute, McGill University*, (2)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (3)*Montreal Neurological Hospital and Institute, McGill University*

Background:

Autism exists across a wide spectrum and there is debate as to whether, autism spectrum individuals with average IQ and typical speech onset (''Asperger's syndrome'') should be considered a distinct subgroup from those with delayed speech onset ("Autism"). Apart from the clinical relevance of this issue, the history of language acquisition is an important factor when deciding whether or not to merge these two subgroups in brain structural and functional magnetic resonance imaging (MRI) studies of autism, and may contribute to the inconsistent findings across research groups.

Objectives:

We investigated whether brain structure (in terms of cortical thickness or CT) in young adults with autism can be distinguished based on whether they have typical or delayed speech onset.

Methods:

There were three subject groups: 1) 13 autism spectrum individuals (AUT) with delayed speech onset (DSO) (defined as first words after 24 months and/or first phrase after 33 months old), 14 AUT with typical speech onset (TSO), and 15 typically developing individuals (TYP). All groups were matched on Wechsler IQ measures (FSIQ, VIQ and PIQ), age (mean 22 SD 6.1 years), gender and manual preference. The AUT groups were also matched on their diagnostic measures (ADI-R - Social, Communication and Repetitive behaviours scores).

T1-weighted MR images were obtained for all subjects on a 3 Tesla scanner. CT maps were derived from these MRI data for each subject and between-group statistical analyses were then performed. Ethical approval for the present work was obtained in accordance with the National Institute of Health guidelines.

Results:

AUT-DSO adults had increased CT relative to AUT-TSO adults in several cortical areas including bilateral cingulate and tranverse temporal gyri, as well as left insula, superior marginal, occipital and frontal gyri, but decreased CT in only the left postcentral and fusiform gyri. One possibility is that these CT differences are related to differences in age of speech onset (and less likely due to differences in core symptoms of autism, since diagnostic measures were matched between groups). Support for this claim comes from the fact that age of first phrase was correlated with CT in several of these above brain areas. Consistent with previous findings (Hyde et al., 2009), CT differences were also found between AUT-DSO and TYP in distributed cortical areas, however no CT differences were found between AUT-TSO and TYP.

Conclusions:

The novel CT differences found here between autism spectrum adults with typical versus delayed speech onset suggest that history of language acquisition may be a marker that distinguishes heterogeneous brain phenotypes within the autism spectrum. Thus, future studies should consider the history of language acquisition as an important factor to refine investigation of aetiological factors and interventions in autism.

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108.001 Vocal Behavior in First Year of Life Is Associated with Autistic Symptoms in Infants at Risk for ASD. R. Paul*[1], K. Chawarska[1], Y. Fuerst[1], L. Berkovits[2] and A. Klin[1], (1)*Yale University School of Medicine*, (2)*Yale Child Study Center*

Background: Prelinguistic vocal behavior is known to be related to speech development in typical children (Oller, 1999; McCune & Vihman, 2001) and has been shown to be atypical in preschoolers with ASD (Sheinkopf et al., 2000). 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 (HR) for developing ASD as a result of having an older sibling diagnosed with ASD, and compared these to vocalizations of low risk (LR) infants who did not have a diagnosed sibling. Our aim was to determine whether HR infants show differences from typical development in terms of their production of speech sounds, syllable structures, and prosody in the prelinguistic period, and whether such differences were related to outcomes in the second year of life. 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 several times 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. Analyses included: Consonant inventory (Shriberg & Kwiatkowki, 1994) % 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: No significant differences were seen vocal behavior at 6 months. At 9 months HR infants produced significantly fewer consonants and less mature syllables than LR peers. At 12 months the HR group produces less speech and more non-speech vocal behavior than LR. HR participants who took part in the 24 month visit (n=25) were subdivided into two groups: 1) Those in whom clinicians observed some autistic symptoms (not all met full criteria for ASD), n=14; 2) Those in whom autistic symptoms were not observed, n=11. Discriminant function analysis suggested that the number of consonants produced by HR infants at each visit predicted membership in the groups based on symptom presentation at 24 months. At 6 mo., prediction is correct 74% of the time At 9 mo., prediction is correct 77% of the time At 12 mo. , prediction is correct 65% of the time Conclusions: These findings suggest that infants at high risk for ASD do show differences from low risk peers in vocal production in the first year of life. These differences are related to recognition of autistic symptoms in the second year and may be helpful in providing early identification and intervention.

108.002 Evaluating Intermodal Processing in Autism and Asperger Syndrome Using the McGurk Effect. J. H. Schroeder*, J. A. Weiss and J. M. Bebko, *York University*

Background:
Intermodal or intersensory perception involves the coordination of information from various senses, leading to a unified perception of an event. The McGurk effect is an audiovisual task that demonstrates how we integrate what we see and what we hear

during speech. The illusion involves a video of a person saying one syllable auditorily (e.g. /ba/), and saying a different syllable visually (e.g. /ga/). The listener usually integrates the two resulting in experiencing a percept that is an entirely different sound (e.g. /da/).
Children with autism have increased difficulty in intermodal speech perception. Weiss, Bebko & Schroeder (in preparation) found that children with autism were significantly less likely to show the McGurk effect relative to both typically developing children and a cognitively impaired control group. The authors concluded that children with autism may have difficulty with intermodal processing of speech information. The current study aims to extend this research by exploring these processes in individuals with Asperger Syndrome (AS).
Objectives:
This research will help to determine if impairments in intermodal processing of speech are related to ASDs in general, or if they are related specifically to cognitive level or the developmental language delays and difficulties in current language that characterize autism.
Methods:
The samples ranged in age from 6-16 years and consisted of children with Autism (n=15), AS (n=15), Down Syndrome (DS; n=15), and a typically developing comparison group matched on chronological age (TD; n=19).
Results:
Significant group differences were found, $F(3, 60) = 6.59$, $p = .001$, $\_^2 = .25$. Post-hoc contrasts revealed that the Autism group show significantly less intermodal speech perception compared to TD children, children with DS and children with AS. Children with AS show equal levels of intermodal speech perception compared to TD and DS controls. These differences remained after controlling for performance on the unimodal tasks. Speech-reading is positively correlated with McGurk performance and listening performance is negatively correlated with McGurk performance across groups.
Conclusions:
It is the first study to directly investigate intermodal speech processing abilities in individuals with Asperger Syndrome as a distinct sample from Autism. This is also the first study to examine the McGurk effect in children with Down Syndrome. The results of the present study indicate that there are basic cognitive perceptual differences between children with Autism and those with AS. The difficulties for Autism do not appear to be shared by children with intellectual disabilities, including those with Down syndrome, or typically developing children. Moreover the audiovisual integration skills involved in processing speech appear to be intact in Asperger Syndrome. These results suggest that children with Autism may have unique intermodal speech perception difficulties linked to their representations of speech sounds.

108.003 Acoustic and Perceptual Analyses of Expressive Prosody in Children with High-Functioning Autism: A Comparison of Speech From a Structured Task and Conversation. H. Shaw and A. Nadig*, *McGill University*

Background: Children with high-functioning autism (HFA) have communicative difficulties despite age-appropriate cognitive and languge abilities. Over time aspects of communication improve but difficulties with expressive prosody often persist, and these lead to negative perceptions on the part of listeners (Paul et al., 2005). Prosody, the melody of a person's voice, is conveyed through features such as pitch and speech rate. The literature reports varied and sometimes contradictory terms to describe prosodic abnormalities in HFA, such as monotonous or exaggerated intonation and a fast or slow speech rate.

Objectives: The aim of the study was to explore whether consistent acoustic markers of atypical prosody could be identified in school-age children with HFA, which could then be used to specify assessment and intervention plans. To this end speech samples were analyzed from two different settings: a structured communication task and unstructured conversation. In addition, perceptual ratings were collected on the conversation samples to investigate how listener judgments relate to acoustic differences.

Methods: Participants were 8- to 14-year-olds with HFA or typical development (TYP), matched on language level, age and gender. In Study 1 speech samples were collected from15 HFA and 11 TYP children via a structured communication task where they produced instructions for a listener (e.g. "Pick up the cup"). Recorded audio was analyzed using PRAAT software (Boersma & Weenink, 2008). Each participant's average pitch, pitch range, and speech rate were calculated. Study 2 examined the same three prosodic features in speech collected during an unstructured conversation with an adult. Conversation samples were collected from 15 HFA and 13 TYP children and an uninterrupted 10 to 13 second clip of each participant's speech was analyzed. In Study 3 thirty-two Speech-Language Pathology students, blind to group membership, rated the conversation speech samples according to a perceptual rating scale.

Results: **Structured communication:** HFA group had a higher mean pitch than the TYP group after controlling for age. There were no significant group differences in pitch range or speech rate. **Conversation:** acoustic analyses revealed significantly higher pitch range and a trend for higher average pitch in HFA group compared with the TYP group. Both groups produced a similar speech rate. These results are consistent with findings from narrative tasks, where children with HFA were reported to have increased pitch and/or pitch range (Diehl et al., 2007; Edelson et al., 2007). **Perceptual ratings of conversational speech:** blind raters reliably differentiated the HFA and TYP groups on the basis of "overall impression"of prosody, giving the HFA group more atypical scores. However, no individual prosodic feature reliably differentiated between groups. Moreover a multiple regression analysis revealed that acoustic differences did not significantly predict ratings of overall impression of normal/atypical prosody.

Conclusions: Acoustic analyses of speech in school-age children with HFA reveal higher mean pitch in structured communication and increased pitch range/sing-songy speech during conversation, rather than the stereotype of monotone intonation.

108.004 Comparison of Children with Autism Spectrum Disorders and Developmental Language Disorders On Processing of Affective Information in Face, Voice, and Situational Contexts. J. van Santen*, L. M. Black, J. de Villiers, R. Coulston, B. Langhorst, M. K. August and R. Sanger-Hahn, *Oregon Health & Science University*

Background:

Impairment in social interaction is a core symptom of autism spectrum disorders (ASD), and reported weak processing of nonverbal affect may play a critical role. Children with developmental language disorders (DLD) are considered to have intact processing of social-affective information.

At IMFAR 2009 we reported weaker performances of children with ASD vs. typically developing (TD) children on vocal affect, situational affect, and facial affect. Here, we report for the first time results for children with DLD.

Objectives:

To compare children with ASD and DLD on processing social-affective information conveyed in face, voice, and situational contexts.

Methods:

Classification into the ASD group (N=29) utilized the Social Communication Questionnaire (SCQ); the revised algorithm of the ADOS; and DSM-IV-TR-based clinical diagnosis of ASD, via independent ratings and consensus agreement by a team of licensed psychologists and language pathologists. Classification into the DLD group (N=19) following an equally rigorous process, utilized Tomblin's Epi-Sli criteria (Tomblin et al., 1997) or a CELF index score at -1 s.d. plus a spontaneous language measure at -1 s.d.; and DSM-IV-TR-based clinical consensus diagnosis. ADOS scores were not used to make or rule out a diagnosis of DLD.

The DLD and ASD groups were well-matched on nonverbal IQ and age.

Affect measures included computerized tasks where participants touched an "affect button" that matched the emotion on a person's face

(Facial Affect; Fein, et al., 1985; 1992), a person's feeling in a conventional social situation (e.g., birthday party; ibid) (Situational Affect), or the emotion of a recorded voice (Vocal Affect).

Results:

The DLD group performed significantly better than the ASD group on Situational Affect, marginally better on Vocal Affect, and similarly on Facial Affect.

The lack of significant differences between groups on Vocal and Facial Affect, and the significant differences between ASD and TD groups found on all affect measures (IMFAR 2009), suggest that the DLD and ASD groups are both impaired in the ability to process affect in faces and vocal prosody.

Given these striking findings suggestive of a possible overlap between ASD and DLD, an analysis was conducted in which we removed a DLD subgroup with ADOS algorithm scores at criterion for ASD (this did not affect IQ and age matching). Results then showed significant differences on Situational Affect and Vocal Affect, but not Facial Affect.

Conclusions:

Results indicate that children with DLD understand the affective import of conventional social situations better than children with ASD; however, this may be less, if at all, the case for vocal and facial affect. When children with DLD, who on the ASD-DLD continuum (e.g., Bishop, 2000) are maybe closer to the ASD "border," were removed, significant differences between groups emerged in vocal affect. These findings indicate the importance of further exploring areas of overlap between the disorders in social cognition and competencies, as Leyfer et al. (2008) have discussed. Perhaps these are some of the characteristics of the broader range of DLD children that may be responsible for recently discussed diagnostic substitution of ASD for DLD (Bishop, et al., 2008).

108.005 Acoustic Differences in the Imitation of Prosodic Patterns by Children with Autism Spectrum Disorders. J. J. Diehl*[1] and R. Paul[2], (1)*University of Notre Dame*, (2)*Yale University School of Medicine*

Background: Atypical prosody production is a characteristic feature of autism spectrum disorders (ASD), regardless of the child's level of functioning. To date, however, many of the studies of prosody performance have not captured the full extent of the deficits that are observed clinically. Although behavioral studies have given us some insight into the nature of differences between children with ASD and other children, acoustic measures of speech are often more sensitive to more subtle differences between populations. Moreover, most studies just focus on the functional use of prosody (e.g., to communicate affect, intent in discourse, syntactic structure). It is possible that deficits in basic abilities, such as imitation, could offer some insight into patterns of prosody performance in ASD.

Objectives: Our objective is to examine acoustic differences in prosodic patterns produced in imitated speech.

Methods: Participants were 24 children and adolescents (ages 8-16) with ASD and average general language functioning, 22 typical controls (ages 8-17), and 16 children with language impairment (ages 9-17). All groups were matched on chronological age and gender. Participants were given two prosody imitation tasks from the Profiling Elements of Prosodic Systems in Children (PEPS-C), a norm-referenced measure of prosody perception and production for children. One task involved imitating prosodic patterns in single words, and the other task involved imitation across whole utterances. Speech data were also acoustically analyzed using PRAAT, a program for speech analysis and synthesis. Speech data were analyzed for the following acoustic measures: average pitch, pitch range (maximum pitch minus minimum pitch), pitch variance, duration, and intensity.

Results: Participants with ASD exhibited a significantly longer duration of utterances when imitating single words than the typically developing controls, $F(1,44)=6.47$, $p<.05$, and children with language impairment $F(1,38)=3.49$, $p<.05$. Participants with ASD

also had longer utterance durations than the other groups for whole phrases, although these differences did not reach significance. There were no other acoustical differences (pitch range, pitch variance, average pitch, intensity) between participants with ASD and typical controls. Children with language impairment showed significantly more pitch variance than participants with ASD and typical controls on both tasks. This finding, however, is likely qualified by the fact that the sample of children with language impairment had a higher average pitch overall (higher voice) than children with ASD, $F(1,38)=3.23$, $p<.05$, and typical controls $F(1,36)=5.87$, $p<.05$, because children with a higher voice also tend to have greater pitch variance.

Conclusions: This study found that children with ASD produce longer utterances than children with language impairment and typically developing controls when imitating speech. This suggests that fundamental deficits in the speech production system might contribute to some of the prosody production deficits seen in ASDs.

108.006 Predictors of Expressive Language Gain in Toddlers with ASD Enrolled in Early Intervention. A. Dubin*, L. Kalb and R. Landa, *Kennedy Krieger Institute*

Background: Delay in or absence of expressive language (EL) development is a core deficit of autism spectrum disorders (ASD) which is predictive of later adaptive functioning. While predictors of EL gain, such as gestural joint attention (Mundy, Sigman, & Kasari, 1990), have been identified in preschoolers with ASD, validating and expanding upon these findings for toddlers enrolled in very early intervention is vital to tailoring intervention to children's individual needs.

Objectives: To identify predictors of expressive language (EL) gain in 2-year-olds with ASD enrolled in early intervention.

Methods: Forty-seven toddlers with ASD (23-33 months of age at enrollment) participated in a 6-month nursery school-based comprehensive early intervention for 10 hours per week. A validation sample was included, consisting of the next 28 children enrolled into the program. Pre- and post-treatment assessments included the Mullen Scales of Early Learning (MSEL), Autism Diagnostic Observation Schedule (ADOS), and Communication and Symbolic Behavior Scales Developmental Profile (CSBS). Multiple linear regression models were employed to examine which ADOS items independently predicted pre-post EL gain on the MSEL in both samples while controlling for pre-test EL and nonverbal cognitive level. The identified items were summed to create an 'EL predictor' algorithm score. A non-parametric Receiver Operator Characteristic (ROC) procedure was then used to determine the most efficacious cutoff score that predicts children who gain in EL at a rate commensurate with increasing chronological age (gain of >6 months in age equivalent score on the MSEL Expressive Language scale between pre- and post-treatment assessments). The strength of the relationship between this novel algorithm and gains in functional EL was examined using an independent measure of EL gain: diversity of words used communicatively (CSBS word inventory score).

Results: Four predictors of EL gain were identified from the ADOS for the first sample: requesting, hand-finger complex mannerisms, functional play, and spontaneous joint attention (SJA) ($p<.05$). Analyses with the validation sample revealed that Requesting and SJA remained significant predictors ($p<.05$). Using a cutoff score of two (max=6), in the first sample, our EL algorithm accurately identified 94% of children who met our criteria for age-commensurate EL gain (sensitivity) and 56% of those who did not (specificity); ROC=.74. In the validation sample, this algorithm score accurately identified 84% of those with age-commensurate EL gain and 72% of those who did not meet our criteria for such gain (ROC=.78). Correlations revealed a strong to moderate ($r2=.45$-$.53$, $p<.05$) relationship between gains in requesting and SJA and the CSBS word inventory score.

Conclusions: These data provide strong evidence for the ability to communicate intentionally, albeit nonverbally, as a robust predictor of EL gain in toddlers with ASD

enrolled in a classroom-based comprehensive early intervention. While the literature has indicated that social communicative intent is a predictor of EL gain, we offer evidence that imperative communicative ability is also an important predictor of such gain. Thus, a child's awareness of his/her ability to effect and engage with others may be a vital goal for the earliest stages of intervention and, establishing readiness for linguistic acquisition.

108.007 Perspective Taking Abilities in Children with Autism: The Influence of Working Memory and Theory of Mind On Shared Knowledge. J. Schuh*[1], D. Mirman[2] and I. M. Eigsti[1], (1)*University of Connecticut*, (2)*Moss Rehabilitation Research Institute*

Background:
Pragmatic impairments in autism spectrum disorders (ASD) are significant. The skill known as *common ground* (Clark, 1992), involving the ability to track what information is known by both participants in a conversation, is likely relevant to pragmatic skills, and is to date unexplored in ASD. Common ground skills could draw on Theory of Mind (ToM) as well as, potentially, working memory (WM) skills. This study assesses (1) the ability of individuals with ASD to maintain and update their representations of what knowledge is shared between conversational partners, and (2) the contributions of Theory of Mind (ToM) and WM skills to such representations.

Objectives:
The current study examined pragmatic language in ASD within a cooperative problem-solving task, drawing on both explicit responses and eye-tracking data to explore the relative contributions of ToM and WM load to perspective-taking abilities. We hypothesize that WM abilities contribute significant variance in task performance, over and above the contributions from ToM.

Methods:
This study utilized a cooperative problem-solving task in which participants move shapes onto a computer display according to a trained partner's spoken instructions. Some shapes are "unknown" to the partner. Studies of *eye movement data* in typical development suggest significant competition from such "secret" shapes. Children with ASD (n =17) and typically developing controls (n =22) matched on age (range 9-16; mean 12.9 years), IQ, and language completed the computer-based puzzle game while their eye movements were tracked. As a manipulation of WM load, the number of secret shapes varied from 1 to 4. The relationship between task performance and standardized measures of WM and ToM was also examined.

Results:
Participants were accurate in their behavioral responses (91%), with slower reaction times across groups when competing "secret" information was present during high WM load conditions, $p<.02$. Eye-tracking data indicated that all participants were slower to process a partner's instruction when there were competing secret shapes, $p<.02$. This delay interacted with WM load, as participants were even slower to disambiguate target (correct) shapes from secret competitors under high WM loads, $p<.001$. The ASD group was slower to disambiguate the target, $p<.001$, was more influenced by the secret competing shape, $p<.001$, and had greater difficulty disambiguating the target in the presence of a secret competitor under high WM loads, $p<.02$. Across groups, performance errors were associated with language and WM, all $p's<.05$, and in the ASD group errors correlated with symptom severity, $p<.05$. There was a trend towards an association between ToM ability and the ability to take secret shapes into account, $p<.06$.

Conclusions:
Differences in performance for low versus high WM conditions suggested that WM modulates the ability to incorporate shared information, across all groups, with the ASD group particularly susceptible to WM load. Eye fixation patterns suggested that children with ASD were more influenced by "secret" information. Language and WM abilities were related to performance in this perspective taking task; TOM was weakly associated with task performance. Results are consistent with previous studies suggesting taking another

person's perspective requires additional processing capacity.

108.008 Responding to and Learning Joint Attention: A Comparison of Infant Siblings of Children with Autism and Typically Developing Infants. K. Gillespie-Lynch*, T. Hutman, S. Gaither, A. Navab, D. Beck-Pancer, M. Sigman and S. P. Johnson, *University of California, Los Angeles*

Background: Regardless of whether they are subsequently diagnosed with autism, infant siblings of children with autism (IS) may attend differently to faces and objects, and to social cues linking faces and objects, than typically developing (TD) infants (McCleery et al., 2009). The ability to follow another's gaze to an object, or responsiveness to joint attention (RJA), is often impaired in autistic children and may be atypical in infant sibs by 15 months of age (Presmanes et al., 2007; Sigman et al., 1999). However, autistic preschoolers who demonstrated limited spontaneous RJA exhibited more joint attention after a training period when a model's gaze was predictive of the activation of a toy (Leekam et al., 2000).

Objectives: We examined responsiveness to social cues and spontaneous and learned RJA in a cross-sectional sample of IS and TD infants.

Methods: Each infant watched a video of a model turning to 1 of 2 objects on either side of her. Eye movements were recorded with an eye tracker. Each trial consisted of a baseline phase, an infant directed greeting and smile, and the model turning and fixating an object for 5 seconds. Direction of turn was counterbalanced across trials. There were 4 "spontaneous RJA" trials with identical legos, 4 "spontaneous RJA" trials with non-identical objects, and 6 "learned RJA" trials in which the attention getter moved and emitted music for the last second of the model's fixation. Proportion of time attending to the face relative to the objects was calculated and RJA was indexed by proportion of time the infant attended to the object the model was looking at relative to the other object. After the eye tracking session, infant sibs also participated in the ESCS. Once ESCS scores have been calculated, we will correlate RJA scores on the ESCS to those on the eye tracking measure to test the external validity of the eye tracking measure.

Results: At 6 months, TD infants spent proportionally more time looking at the face relative to the objects than IS infants, $t(36)= 2.21$, $p=.046$ (TD n=26, M=.92, SD= .16; IS n=12, M=.72, SD= .31). No differences in this measure were observed at 12 months, and no differences in spontaneous RJA were observed at either age. At 6 months IS infants exhibited more learned RJA when the model's gaze was predictive of the subsequent motion of the rattle, $t(16)=-2.48$, $p=.024$ (IS n=7, M=.82, SD=.37; TD n=11, M=.36, SD=.39). At 12 months the reverse pattern was observed: TD infants demonstrated more learned RJA than IS infants, $t(14)=2.88$, $p=.012$ (TD n=9, M=.73, SD=.39; IS n=7, M=.22, SD=.29).

Conclusions: These preliminary results suggest that early in development infant sibs may be more interested in objects and predictive contingencies than typically developing infants. This is consistent with previous work demonstrating that infant sibs looked away from their mother's faces during a still face paradigm more than typically developing infants at 6 months and showed quicker neural responses to objects than faces at 10 months (Ibanez et al., 2008; McCleery et al., 2009).

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109.001 Texture Segregation in School-Aged Autistic Children: A Visual Evoked Potential (VEP) Study. J. Bertrand-Rivest*[1], A. Bertone[1], M. McKerral[2], M. Lassonde[2] and L. Mottron[1], (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*Centre de Recherche en Neuropsychologie et Cognition (CERNEC), Université de Montréal, Canada*

Background: Whereas local luminance perception relies mainly on primary visual cortex (V1) functioning, texture perception implicates recurrent neural interactions between V1 and higher visual areas (V2, V3). Recent studies on low-level visual perception in autism have revealed processing strengths for local luminance changes across an image, concomitant with weaknesses in processing

texture (Bertone et al., 2005; Vandenbroucke et al., 2009; see also Kemner et al., 2007 for a non- significant trend). Although these findings suggest atypical connectivity within the visual cortex, the type of neural alteration remains unknown. Furthermore, these studies have focused on autistic adolescents and adults. Because these visual functions mainly develop in infancy and childhood (Arcand et al., 2007; Bertone et al., 2008), studies focusing on younger individuals are needed to define the developmental trajectories of perceptual abilities in autism.

Objectives: The aim of this study is to investigate, using visual evoked potentials (VEPs), the neuronal correlates of local luminance and texture perception in school-aged autistic children.

Methods: Autistic and typically developing children, aged 6 to 10 years, were matched on handedness, gender, chronological age and intelligence based on Raven's Standard Progressive Matrices. All children had normal or corrected-to-normal vision. In a texture segregation task based on orientation, children were presented with four high contrast visual stimuli on a display while their brain activity was being recorded using a high-density electrophysiological system. Stimuli were shown 120 times each in a block sequence. Children were not required to respond to stimuli. To only record trials where the child was attending, one experimenter present in the testing room signaled the child's behaviour (via button press) to the adjacent control room. Testing sessions were also video recorded for later verification. Two stimuli were low-level orientation patterns (ORI) defined by homogeneous oblique lines oriented either to the right or left. Two stimuli were segregated texture patterns (TEX) composed of the same oblique lines but presented in an orientation-defined checkerboard (90º line gradients), oriented either concentrically or outwards. A texture segregation VEP (tsVEP) was isolated by subtracting the ORI- from the TEX-VEP response. The tsVEP reflects neuronal integration between V1 and V2/V3, mainly via feedback from V2/V3 to V1. Early VEP components (P1, N2) at occipital sites were examined for latency, amplitude and scalp distribution across all conditions.

Results: Preliminary results indicate that compared to controls, the P1 component in the autism group shows delayed but larger and sustained activity at occipital sites (Oz, O1, O2) for both ORI and TEX conditions. In the control group, the tsVEP appears as a negative deflection at around 194ms post-stimulation, as expected from the literature. In contrast, autistic children demonstrate reduced amplitude of this negative deflection.

Conclusions: Autistic children appear to process low-level orientation and segregated texture patterns differently from typically-developing children, and both low-level and texture processing contribute at altering texture segregation mechanisms. These findings will be discussed within the framework of the enhanced perceptual functioning model (Mottron et al., 2006) and the complexity-specific hypothesis for perceptual information processing in autism (Bertone & Faubert, 2006).

109.002 Atypical Electrophysiological Response and Lateralization to Speech Stimuli in Infants at Risk for Autism Spectrum Disorder. A. Seery*[1], V. Vogel-Farley[2], T. Augenstein[2], L. Casner[1], L. Kasparian[1], H. Tager-Flusberg[1] and C. A. Nelson[2], (1)*Boston University*, (2)*Children's Hospital Boston*

Background: Converging research suggests that individuals with autism spectrum disorder (ASD) often show atypical neural language lateralization including reversed asymmetry of frontal language areas. This atypical lateralization has been shown in individuals with ASD as young as 24 months (Coffey-Corina, Padden, and Kuhl, 2008); however, it remains unclear at what age this atypical pattern manifests. Additionally, while language delays and abnormalities are common in young children with ASD, it is unknown the extent to which these impairments may be due to early atypicalities in acquiring basic underlying building blocks necessary for language development, such as the ability to selectively perceive the phonemes relevant to one's native language.

Objectives: Here, we employ an electrophysiological method to look

developmentally at the perceptual narrowing of native language phonemic contrasts in infants at risk for ASD. This firstly allows us to determine whether phonemic perceptual narrowing occurs atypically, and secondly whether auditory stimuli evoke an atypical neural response in these at-risk infants.

Methods: As part of a larger longitudinal study, we compared high-density event related potentials (ERPs) of infants at risk for ASD (HRA) against low risk control infants (LRC) at 6 months (19 HRA, 18 LRC), 9 months (28 HRA, 22 LRC), and 12 months (30 HRA, 17 LRC). In a double-oddball paradigm, we presented infants with consonant-vowel syllable stimuli that were either phonemic or non-phonemic in the infants' native language (English).

Results: Over the frontal and temporal/central regions, we found an initial positive inflection (150-300ms) that was sensitive to the type of syllable heard and which revealed a significant atypical developmental trajectory of responses in HRA infants. Analysis of a later slow wave (300-700ms) revealed that LRC infants showed lateralization beginning at 9 months but that HRA infants failed to develop this lateralization even by 12 months. These atypical patterns remained even when excluding infants who met preliminary diagnostic criteria for ASD at 18 months.

Conclusions: Our data suggest that by 9 months, the development of HRA infants begins to diverge from that of typically developing infants regarding response to auditory stimuli. The HRA infants show an atypical trajectory of perceptual narrowing in addition to a failure to develop a lateralized response to auditory stimuli. Consideration of preliminary outcome data suggests that these differences are indicative of the overall autism endophenotype rather than the clinical-level disorder itself.

109.003 The Utility of ERP Measures as Putative Intermediate Phenotypes in Infancy. M. Elsabbagh*[1], E. Mercure[1], K. Hudry[2], T. Charman[3], S. Baron-Cohen[4], P. Bolton[5], A. Pickles[6], M. H. Johnson[1] and .. The BASIS Team*[7], (1)*Birkbeck, University of London*, (2)*Department of Psychology and Human Development, Institute of Education*, (3)*Institute of Education, University of London*, (4)*University of Cambridge*, (5)*Institute of Psychiatry, King's College London*, (6)*University of Manchester*, (7)*BASIS*

Background: Increasingly, researchers have advocated the use of dimensional intermediate phenotypes, viewed as more closely aligned to the genotype than complex clinical characterization. Specifically, measures of quantitative traits associated with ASD are though to be better candidates for gene mapping relative to diagnostic classification. The assumption here is that diagnosed forms of ASD, which are themselves highly variable, are extremes of what is otherwise typical individual variation. While this research has overwhelmingly focused on stable behavioral characteristics of children and adults, such intermediate phenotypes may not be static in early development, the period when dynamic gene-environment interactions are still unfolding. As such, studying infants at-risk for ASD, where manifestations of risk may be observed particularly in early brain functions, provides the opportunity for developing and validating intermediate phenotypes within the infancy period.

Objectives: The aim of the study was to examine the utility and feasibility of event-related potentials (ERP) within the first year of life as prospective measures of quantitative autism characteristics in toddlers followed longitudinally at 2-years of age. We focused on the neural correlates of gaze processing as the hypothesized developmental precursors to a wide range of emerging social and communicative skills.

Methods: Participants were from the British Autism Study of Infant Siblings (BASIS). One hundred infants (51 high-risk sibs and 50 low-risk controls) were included in the analysis. When aged between 6 and 10 months, ERPs were recorded while the infants viewed dynamic images of females shifting their gaze towards (directed) or away from (averted) the infant. At a 24-month follow-up visit, caregivers completed the Quantitative CHecklist for Autism in Toddlers (Q-CHAT), a measure of autistic traits that is normally distributed in the general population.

Results: Relative to the control group, the high-risk siblings group showed both

similarities and differences in the amplitude and latency of components related to gaze processing. Variation in individual infant's ERP response characteristics was correlated with Q-CHAT scores at 24-months. Dimensional associations between the infant ERP and later emerging behavioral characteristics included ERP components that distinguished the group of siblings at high-risk of ASD from low-risk controls, but also encompass components where the groups did not differ in infancy.

Conclusions: As a group, infants at-risk for ASD show differences in certain neural components related to the processing of eye gaze. Moreover, individual differences in the infant ERP could be mapped onto behavioral characteristics of the same infants at 2-years of age, as measured by parent-report. These findings emphasize the utility and feasibility of developing individually-sensitive and dimensional brain functioning measures as intermediate phenotypes within the infancy period.

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109.004 Pupillary Light Reflex as New Biomarker for Autism. E. J. Hessler[1], J. H. Miles*[1], T. N. Takahashi[1], X. Fan[2] and G. Yao[2], (1)*University of Missouri*, (2)*Univeristy of Missouri*

Background: Biomarker detection is crucial to the discovery of biologically homogeneous ASD subgroups. We found that children with ASD demonstrate a significantly different pupillary response (PLR) to a transient light flash (Fan & Yao, 2009). The latency of the pupil's response from light flash to the beginning of pupillary constriction discriminated ASD children from typically developing controls with a cross-validated success rate of 89.6%, which increased to 92.5% when constriction amplitude was considered. Since the PLR parameters (latency, constriction amplitude and constriction & redilation velocity) represent different biological functions, study of PLR may provide a number of distinct ASD biomarkers.

Objectives: 1) To identify the clinical and etiologic variables that correlate with variance in the PLR parameters. 2) To characterize the subgroups of children with ASD who demonstrate the various PLR variances. 3) To analyze the neurologic bases of the phenotypes of each subgroup in order to understand the biological mechanism for each PLR parameter change in ASD.
Methods: Phenotypic features including physical (dysmorphology, head size, growth), clinical course (age & type of onset, clinical improvement with fever), medical and neurologic symptoms (seizures, toe walking, sleep disturbances, etc.) and genetic indicators (gender, family history of ASD and related disorders, recurrence in sibs, parental ages), outcome measures (IQ, language, adaptive scores) and ASD symptoms (ADI-R) were compared with PLR data for 22 children with ASD and 43 age matched typically developing control children. Subject characteristics were 20 male:2 female, mean age 12 +/- 4 years, diagnoses: 9 Aspergers, 8 Autistic disorder and 5 PDD-NOS and mean IQ = 87.2 (SD=24).
Results: Two neurologic features correlated with PLR parameters. Children who showed an improvement in ASD symptoms during fever had a significantly larger constriction amplitude compared to those whose parents did not report improvement (P=0.006). The group with improvement in autistic behaviors during fever has constriction amplitudes closer in value to the TD controls than those who do not improve during fever. Second, children who toe walked during development showed a longer PLR latency compared to non-toe walkers (p=0.01). The group who toe walked had the longest latency, i.e. the greatest variance from the typically developing control group.
Conclusions: The clinical features, improvement with fever and toe walking that correlate with the PLR variances observed in ASD are both neurologic. Pupillary constriction is regulated by parasympathetic stimulation. Finding greater pupillary constriction in children who improve with fever suggests greater parasympathetic or less sympathetic tone in that subgroup. Thus, PLR constriction amplitude may be a biomarker for autonomic dysfunction in autism, possibly related to modulation of the locus coeruleus-

noradrenergic system which stimulates sympathetic effects. Increased latency is considered a measure of interference with nerve conduction or cerebellar modulation (Rinehart et al. 2006). Our finding of increased PLR latency in almost 90% of our ASD study group is consistent with either one ubiquitous mechanism or may be the result of a number of systems that effect nerve conduction efficiency. These correlations will guide ongoing studies designed to provide insight into biological mechanisms underlying ASD subgroups.

109.005 Neurophysiological Correlates of Treatment Outcomes. J. Stieben*, S. Shanker and D. Casenhiser, *York Univeristy*

Background:

There is a substantial body of evidence from both electrophysiological and neuroimaging studies showing face processing impairments in adults and children with autism. Most of this research has focused on high functioning subjects with very few studies carried out on low functioning samples and still fewer studies assessing preschoolers. Additionally, very few studies have examined the neurophysiological changes in face processing as a result of intervention.

Objectives:

The goal of the present study is to fill this gap in the literature by assessing brain changes in face processing associated with treatment. We assessed the N170 event-related potential (ERP) from faces to assess the change in N170 amplitude, latency and cortical location after one year of intervention using DIR/floortime (Developmental Individualized Relationship model developed by Greensan and Wieder, 2007). Given that previous research has identified smaller N170 amplitude ERPs, longer N170 latencies and source activations in areas outside of the fusiform gyrus (e.g., inferior temporal gyrus and middle temporal gyrus), it was hypothesized that successful treatment would be related to increased N170 amplitude, shorter component latencies and a shift in activation from compensatory regions to activation in the region of the fusiform gyrus.

Methods:

Dense-array (128 channel - EGI) data was collected from twenty-three, two to five year old children who met criteria for a diagnosis of autism based on ADOS and ADI and twenty-six typically developing age-matched controls. Participants were provided with an EEG net desensitization training protocol until they tolerated wearing the net for 30 minutes. Face stimuli were presented using Eprime (PST). An eye-tracker (Tobii) integrated in real-time with the EEG data stream was used to ensure that trials contained correct face gaze at stimulus onset. Faces were presented for 1500 milliseconds. Data were analyzed using Netstation (EGI) and inverse modeling was carried out using Loretta in Geosource (EGI). Behavioural changes associated with treatment success in the domain of social interaction were assessed using the Child Behaviour Rating Scale (Mahoney). Behavioural and electrophysiological assessments were carried out before and after 12 months of intervention using the DIR/Floortime method.

Results: The N170 showed a significant increase in amplitude and a decrease in component latency across the one year treatment period. Source estimation for the N170 revealed a shift in activation in the clinical group from middle temporal gyrus and inferior temporal gyrus at pre-treatment to greater activation in the area of the right fusiform gyrus at post-treatment. Controls showed a pattern of activation similar across time points with greatest activation in the region of the fusiform gyrus. Behavioural results mirrored changes in ERP activity with a significant increase in social involvement, attention to social activity, initiation of joint attention and overall enjoyment of interaction.

Conclusions:

Results from this study provide support for the proposal that successful treatment in young children with autism is related to changes in areas of the brain associated with social information processing.

109.006 Impaired Word Processing in Children with Autism Spectrum Disorders as Revealed by Mismatch Negativity. A.

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Background: Sensory dysfunctions are frequently reported in children with autism spectrum disorders (ASD). It has been suggested these symptoms are associated with their difficulties processing language as well as with social isolation observed in people with autism. It is speculated that impaired feature extraction in early sensory processing could result in poor quality of speech sound properties and could thus contribute to problems in communication.

Objectives: To investigate auditory (semantic) language processing in children with ASD and typically developing children in order to determine electrophysiological correlates of brain activity during automatic language processing. The aim was also to establish any behavioural and clinical indicators as well sensory abnormalities in ASD children which correlate with specific parameters of brain activation.

Methods: 11 high functioning boys (mean age 13years) with a diagnosis of autism spectrum disorders and 11 typically developing boys (mean age 13 years 7 months) participated in an auditory oddball task using words, nonwords and phonemes. Both groups were matched for age, gender, verbal and nonverbal IQ and handedness. All children with ASD completed the Adolescent Sensory Profile. Children engaged in a mismatch negativity task, a widely used ERP paradigm to test automatic auditory and semantic processing (see Endrass et al, 2004, Shtyrov and Pulvermüller, 2007). Participants were seated in front of a computer screen watching a silent film of their choice and were instructed to ignore the stimuli. Words and pseudowords were presented auditorily while mean ERP amplitudes and latencies for each stimulus type was calculated. EEG activity was measured from 32 electrodes.

Results: A significant interaction on amplitude response was present between the two groups of children and the words and pseudoword conditions. Further analysis revealed significantly reduced MMN responses to words in ASD children compared to typically developing children but no differences were found for pseudowords. Furthermore, the autism group showed similar amplitude responses across words and pseudowords. In addition, evidence of reduced attentional orienting to sound changes involving frequency and loudness was present. Behavioural data revealed auditory over-responsiveness to be the most common and pervasive form of sensory behaviour within the ASD group and key differences were observed in low registration, sensory sensitivity and sensory avoidance. The mean ERP amplitude for both, words and pseudowords was highly correlated with sensory sensitivity scores.

Conclusions: It is likely that the children deliberately avoid or prevent exposure to sensory stimuli (sensory avoidant) and the preventative strategies which they use may be related to impairments in language processing. We discuss how the expression of sensory behaviours (actively withdraw from environment) may modulate the degree to which sounds are detected and missed in the environment.

109.007 Gamma Band Oscillopathy: An Electrical Signature of Language Impairment in ASD That Impairs Active Listening.

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Background: It is often assumed that language impairment in autism spectrum disorders (ASDs) is secondary to an inability to develop a "theory of mind" necessary for social communication. An alternative is that children with ASD do not develop social communication due to an impairment of auditory processing that degrades the ability to understand spoken language. As clinical electrophysiology does not easily lend itself to understanding cellular mechanism, intracranial microelectrode array recordings of the primary auditory cortex (A1) in awake and behaving rats were compared to magnetoencephalography (MEG) of the A1 in children with ASD administered an auditory test that had no social or language content. The goal was to elucidate the circuit

mechanisms responsible for language impairment in ASD (ASD+LI).

Objectives: To determine auditory disturbances in real-time processing in children with ASD+LI using a trans-species approach that lends itself to understanding electrophysiological correlates of language impairment and circuit abnormalities.

Methods: Electrophysiology was carried out using whole-cortex MEG in children, and with intracranial arrays of microelectrodes in rats targeting A1. Children and rats received sequences of 2 tones presented with a 200 ms intertone interval. Seven rats were either: a) trained to actively listen to the tone pairs and report when they heard the second tone or, b) passive listeners with no prior experience with the tones. For rats, local field potential recordings (LFPs) and single-unit spikes were obtained with a computer-guided microelectrode array from at least 8 sites within the left A1 (128 sites total). Ten children with ASD+LI and 25 typically-developing (TD) control children passively listened to the tone pairs while watching a movie (soundtrack off). ASD in the children was confirmed by ADOS and SCQ, and language function quantified using the CELF-4. In the children, MEG data were decomposed from sensor to source space, and activity in left and right superior temporal gyri (STG) examined.

Results: During silence, passively-listening rats showed dominant delta activity (0.7-3.9 Hz). In contrast, during silence, actively listening rats showed dominant beta activity (12-30 Hz). During active listening, identification of the second tone was associated with the magnitude of resting gamma activity (30-130 Hz) during the period immediately prior to the tones, as well as with the occurrence of gamma bursts following the second tone. In the children with ASD+LI, an electrical signature of active listening was not observed at STG sources. Specifically, in the baseline period, the ASD+LI children had greatly reduced gamma activity and elevated delta activity compared to the language-intact children. Moreover, children with ASD+LI had a virtual absence of an induced gamma response to tone pairs despite obvious ERPs. In contrast, the baseline and tone-evoked activity of TD children approximated that of actively-listening rats.

Conclusions: An unexpected pathophysiology underlying ASD+LI is an inability to transition from passive to active listening due to an inability to generate gamma oscillation within A1. The relative absence of resting and evoked gamma activity in A1 suggests an oscillopathy that can be used to assess ASD severity and monitor treatment efficacy.

109.008 Neural Correlates of Social Rejection in Autism Spectrum Disorder. J. McPartland*[1], M. J. Crowley[2], P. Molfese[1], D. Perszyk[1], A. Klin[3] and L. Mayes[1], (1)*Yale Child Study Center*, (2)*Yale University*, (3)*Yale University School of Medicine*

Background: Social impairment is a defining characteristic of autism spectrum disorder (ASD), but recent behavioral research suggests individuals with ASD report typical levels of distress in response to social exclusion. During a virtual ball-tossing game with ostensibly real partners (Cyberball), when children with ASD were excluded from play, self-report of self-esteem, belonging, control, and meaningful existence was impacted similarly to typical controls. Neuroimaging research in typical individuals suggests this social "pain" activates a circuit encompassing anterior cingulate cortex (ACC) and ventral prefrontal cortex (VPFC), regions also theorized to contribute to social dysfunction in ASD. The relationship between neural response and behavioral experience of social exclusion in ASD remains unexplored.

Objectives: To compare electrophysiological and behavioral indices of social exclusion and corresponding distress in children with ASD and typically-developing peers.

Methods: Event-related potentials were recorded using 128-channel Geodesic Sensor Nets while children with ASD and typically developing controls (matched for age, sex, handedness, and cognitive ability) played Cyberball. Participants proceeded through an inclusion phase, in which virtual partners played fairly, and a subsequent exclusion phase, during which virtual partners ceased throwing the ball to the player. ERP

responses were compared across three stimulus conditions: inclusion (receiving the ball), omission (another's turn to receive the ball during fair play), and exclusion (virtual players throwing exclusively to one another). Each group's ERPs were contrasted with respect to a mid-latency slow wave (MSW) and a late slow wave (LSW) over medial frontal and posterior scalp regions. Minimum Norm source localization using GeoSource software (EGI) estimated activation in ACC and VPFC. A self-report questionnaire measured ostracism-related distress.

Results: Consistent with previous behavioral research, children with ASD displayed typical levels of ostracism-related distress across domains of social need. However, ERPs revealed distinct temporal processing across groups. Typically developing children differentiated between conditions at both the MSW and the LSW, but children with autism did not exhibit neural differentiation of conditions until the LSW. Source data indicated a pattern of distributed hyper-activation in the ACC-VPFC circuit in children with ASD and diminished sensitivity to inclusion versus exclusion.

Conclusions: This is the first exploration of the temporal dynamics of brain activity associated with social exclusion in ASD, revealing dissociation between behavior and neural response. Children with ASD displayed typical levels of distress in response to social exclusion; however, electrophysiological brain activity revealed distinct temporal dynamics. Compared to typical peers, brain responses did not distinguish between social inclusion and exclusion until late stages of processing. These findings indicate that, in children with ASD, normative overt behavior may be subserved by atypical processing mechanisms. These results are hypothesized to reflect differentially preserved function within ACC regions supporting rule violation and experience of social pain.

Lifetime Achievement Award and Presentations Program

110 Forty Years along the Research Trail

Speaker: E. R. Ritvo *UCLA*

I shall describe my research career, which has focused on understanding the nature of Autism Spectrum Disorder for forty years. I began my child psychiatry residency at Harvard Medical School in 1957, joined the faculty of UCLA as an instructor in 1962, retired there as Full Professor. I now conduct research from my home office. Over the decades I have recruited colleagues from many disciplines to help study my autistic patients, and have published research papers in the areas of; neuro-physiology, neuro-biochemistry, pharmacotherapy, epidemiology, genetics, neuro-radiology, neuro-pathology, as well as on clinical issues. My writings also include three books on autism. I have alwys been an outspoken advocate for my patients and their families, will describe some of the controversies that engulfed the "autism world" as the decades unfolded.

111 Clinical Phenotype

111.001 1 ASD and ADHD: Alternate Phenotype or Common Issue Etiopathology. R. Delorme*[1], P. Chaste[2], C. Moreau[3], C. Paredes[4], F. Amsellem[3], M. Leboyer[5] and E. Herbrecht[5], (1)*INSERM U 955, IMRB, Psychiatry Genetics, Créteil, France; department of child and adolescent psychiatry, Hôpital Robert Debré*, (2)*INSERM U 955, IMRB, Psychiatry Genetics, Créteil, France; Department of Child and Adolescent Psychiatry, Paris, France*, (3)*Child and Adolescent Psychiatry, Robert Debré Hospital*, (4)*Department of Psychiatry, A. Chenevier Hospital, Créteil, France*, (5)*INSERM U 955, IMRB, Psychiatry Genetics, Créteil, France; Fondation FondaMental*

Background: Although attention-deficit/hyperactivity disorder (ADHD) is frequently comorbid with autism spectrum disorder (ASD), it is unclear whether they have a common genetic etiology.
Objectives: Familial relationships between DSM-IV ADHD and ASD are studied in ASD+ADHD and ASD-only.
Methods: Direct-interview family study of 170 first degree relatives of ASD (119 parents and 51 siblings) with or without a comorbid ADHD (n=30 and n=32 respectively) collected between 2008 and 2009. Age-corrected prevalence rates of ADHD among relatives are estimated from blinded best-estimate diagnoses using survival Kaplan-Meier.
Results: The prevalence of ADHD in both group were relatively high (20%) when compared to its prevalence in general population. However, we were unable to detect any significant difference in age-corrected prevalence rates of ADHD in the ASD-only group when compared to ADHD-ASD group. There was a slight trend for relatives

in the ASD-only group to have more attentive ADHD subtype.
Conclusions: ASD and ADHD seem to be not alternate phenotypes of a single underlying genetic cause. There is an increased risk of comorbid ADHD and ASD in ASD families, possibly reflecting some overlapping neurobiology or pathophysiology. However, the size of our sample and the absence of a control group limit the pertinence of our results.

111.002 2 Atypical Sensory Processing in Individuals with ASD and Their Relatives: An Intermediate Phenotype?. I. L. J. Noens*[1], W. De la Marche[2] and J. Steyaert[2], (1)*Katholieke Universiteit Leuven*, (2)*UPC-K.U.Leuven*

Background: Genetic heterogeneity (e.g. copy number variants, single nucleotide polymorphisms) and additive effects are likely to contribute to the liability for ASD in a majority of cases. As a consequence, most parents and siblings of a child with ASD should be carriers of some of those risk factors without having ASD themselves, but possibly resulting in subclinical traits. Although they are not part of the diagnostic criteria, sensory symptoms are quite common in individuals with ASD. The Adolescent/Adult Sensory Profile (Brown & Dunn, 2002) is a self-report questionnaire for individuals aged 11 years or above, that results in scores on four sensory quadrants: Low Registration, Sensation Seeking, Sensory Sensitivity and Sensation Avoidance.

Objectives: 1) To replicate the findings that individuals with ASD show atypical sensory processing.
2) To find out whether first degree relatives of individuals with ASD show atypical sensory processing, in-between ASD subjects and controls. If so, atypical sensory processing may be an intermediate phenotype candidate.

Methods: We requested children with ASD as well as parents and siblings to fill out the Dutch version of the Adolescent/Adult Sensory Profile as a part of a larger family study. We calculated Z-scores for the quadrant scores based on the normative means and standard deviations as described in the manual. Z-scores of participants with ASD were compared with those of the relatives and Z-scores of both groups were compared to 0 (as to compare with the normative scores).

Results: 96 subjects with ASD (79 male, 17 female; 89 adolescents, 7 adults) and 277 relatives (119 male, 158 female; 217 parents, 60 siblings), from 123 different families, filled out the questionnaire. Mean Z-scores for the ASD subjects on the 4 quadrants were .33, -1.28, .47 and .48, and for the relatives -.58, -.68, -.26, -.48. All calculated differences (ASD versus relatives, relatives versus normative data, ASD versus normative data, for each AASP quadrant) were significant at $p<.001$ (except ASD versus normative data quadrant 1 $p=.0084$). Most of the differences remained significant if we analysed the results of males and females separately.

Conclusions: These results demonstrate that individuals with ASD show atypical sensory processing: they register more stimuli, are more sensitive to them, seek less sensations and avoid them more than control participants. Since the Sensation Seeking quadrant results in in-between scores for first degree relatives (between ASD cases and controls), this might be an intermediate phenotype candidate. The results for the other three quadrants were not conform our expectations: normative data were in-between scores of ASD participants and their relatives. One major drawback of this study is that we used the normative data from the American manual, the Dutch version of the AASP has not been standardized yet.

111.003 3 Autism Spectrum Disorder Characteristics in Smith-Lemli-Opitz Syndrome. I. Bukelis*[1], E. Tierney[1], J. Teng[1], C. Wheeler[1], Y. Chen[1], S. K. Conley[2], F. D. Porter[3] and W. E. Kaufmann[1], (1)*Kennedy Krieger Institute*, (2)*NICHD/ NIH*, (3)*National Institutes of Health/NICHD*

Background: Smith-Lemli-Opitz syndrome (SLOS) is an autosomal recessive disorder of impaired cholesterol metabolism with an estimated incidence among individuals of European ancestry of 1 in 20,000 to 1 in 60,000 births [Kelley and Hennekam, 2001]. We demonstrated that approximately 50% of individuals with SLOS meet the Diagnostic and Statistical Manual for Mental Disorders,

4th Edition (DSM-IV) criteria for autism [Tierney et al, 2001]. Furthermore, approximately three-fourths of the children with SLOS have some variant of ASD suggesting the most consistent relationship with ASD of any single gene disorder [Sikora et al, 2006].

Objectives: The purpose of this study was to determine (1) whether the individuals with SLOS+ASD have distinctive autistic profiles as measured by the Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observation Schedule-G (ADOS-G), (2) whether the individuals with SLOS+ASD have distinctive profiles in terms of IQ and adaptive behavior, and (3) which components of the ADI-R and ADOS-G contribute most to the ASD diagnosis.

Methods: Twenty-three participants (mean age 7.8±3.3 years) with SLOS were assessed by measures of autism features, IQ (Stanford Binet, 4th Edition (SB-IV) or Mullen Scales of Early Learning), and adaptive function [Vineland Adaptive Behavior Scales (VABS)]. We divided the SLOS subjects according to their summary diagnoses from the ADI-R/ADOS-G/DSM-IV and the Non-Verbal Mental Age (NVMA) into 3 groups: SLOS+ASD, NVMA >24 months (n=9), SLOS+ASD, NVMA<24 months (n=7), and SLOS+None, NVMA>24 months (n=7). Descriptive statistics were used for overall assessment of the sample. Characterization of autistic behaviors was performed by non-parametric and regression analyses.

Results: 52% of youths with SLOS met criteria for autism and 70% met criteria for ASD. Cognitive and adaptive profiles of individuals with SLOS+ASD, NVMA<24 months were significantly more impaired than SLOS+ASD, NVMA>24 months and SLOS+None groups. Despite differences in cognition, common patterns emerged among the two SLOS+ASD groups: (1) they both were significantly different from the SLOS+None group on ADOS-G Play/Imagination and (2) they were different at a trend level on Peer Relationships (A4) subdomain of the ADI-R Social. Logistic Regression analyses showed that ADOS-G Play/Imagination (p=0.0019) and A4 of the ADI-R Social (p=0.0005) were the most significant predictors of the ASD diagnosis.

Conclusions: Our findings demonstrate distinct autistic patterns that separated individuals with ASD from the rest of the SLOS cohort. Furthermore, our results indicate that selective impairment in more complex behaviors (i.e., peer relationships) differentiated autism related behaviors in SLOS. Further investigation of this phenomenon in a larger sample and its implications to ASD in general is suggested.

111.004 4 Autism Symptomatology and Psychopathology in Girls and Boys with Autism Spectrum Disorders. M. Miller*[1], M. Solomon[2], S. P. Hinshaw[1] and C. S. Carter[2], (1)*University of California, Berkeley*, (2)*MIND Institute, Imaging Research Center*

Background: The male predominance of autism spectrum disorders (ASDs) is thought to be 4:1 (Frombonne, 2003). Consequently, there has been relatively little research on girls with ASDs, and existing findings about the female ASD phenotype are complex and difficult to interpret. Given the greater incidence of internalizing disorders in adolescent girls than boys (e.g., Kessler et al., 1993), and the demonstrated increase in internalizing psychopathology in individuals with ASDs in general (Lainhart & Folstein, 1994), it is important to determine whether girls with ASDs are at an elevated risk for internalizing psychopathology because of combined gender and diagnostic influences.

Objectives: Primary aims included examining similarities and differences in ASD symptoms in a sample of high functioning boys and girls with ASDs, and determining differences in internalizing psychopathology between girls with ASDs, boys with ASDs, and typically developing (TYP) girls. We hypothesized that ASD girls would show fewer symptoms of social behavior impairments than ASD boys; that ASD boys would have more restricted and repetitive behaviors than ASD girls; and that ASD girls would show higher levels of internalizing symptoms than ASD boys and TYP girls.

Methods: ASD symptomatology (assessed via ADOS-G, SCQ, SRS, CCC, RBS-R) and internalizing psychopathology (assessed via

parent-reported BASC2; self-reported CDI, RCMAS) were examined in a sample of 60 age-matched children ages 8-18: 40 with ASDs (20 girls, 20 boys) and 20 TYP girls. Boys and girls with ASDs were matched on IQ. One-way ANOVAs with Tukey post hoc tests for multiple comparisons were used to examine group differences on each measure of autism symptomatology and psychopathology. VIQ and PIQ were covaried if associated with dependent measures.

Results: Girls and boys with ASDs did not differ in terms of autism symptomatology, except that boys had more restricted interests (p < .05). In adolescence, ASD girls had higher rates of parent-reported internalizing symptoms than ASD boys and TYP girls based on BASC2 anxiety, depression, and internalizing scores (p's < .05). The percentage of participants who fell in the "at risk" or "significant" range for depression based on self-reported CDI significantly differed by group, $\_^2$ (2, N = 60) = 10.91, p < .05, with ASD girls showing elevations in depression.

Conclusions: We found no support for the idea that being a girl is protective against developing ASD traits, nor did we find support for the notion that girls with ASDs are more severely impaired than boys with ASDs, but we did find that ASD boys have more restricted interests than ASD girls. Furthermore, in adolescence, girls with ASDs were at greater risk for internalizing symptoms compared to boys with ASDs and TYP girls. These results provide an initial platform on which to base future studies of high functioning girls with ASDs and suggest the importance of carefully evaluating internalizing symptomatology in this high-risk population.

111.005 5 Behavioral Profiles of Premature Infants: Similarities and Differences to Infant Siblings Later Diagnosed with Autism. C. Roncadin*[1], M. Rourke[1], S. Jilderda[1], J. Brian[2], S. E. Bryson[3], A. Niccols[4], W. Roberts[5], I. M. Smith[6] and L. Zwaigenbaum[7], (1)*Peel Children's Centre*, (2)*Hospital for Sick Children & Bloorview Kids Rehab*, (3)*Dalhousie University/IWK Health Centre*, (4)*McMaster Children's Hospital-Chedoke Site*, (5)*University of Toronto*, (6)*Dalhousie University & IWK Health Centre*, (7)*University of Alberta*

Background: The Autism Observation Scale for Infants (AOSI; Bryson et al., 2008), a direct rather than parent-report measure, reliably distinguishes autism spectrum disorder (ASD) from typical development at 12 months of age in one risk group: infant siblings of children with ASD (hereafter, 'high-risk siblings') compared with low-risk controls (i.e., no family history of ASD). Premature infants are another group at increased risk for ASD, although they are also at risk for other developmental disorders, which may complicate assessments of early ASD signs. **Objectives:** To examine early behavioral signs of ASD on the AOSI in a group of premature infants relative to groups of high-risk siblings later diagnosed with ASD and low-risk controls. **Methods:** Behavioral signs of ASD at 12 months of age, as indexed by AOSI total score (where higher values indicate increasing deviation) and total marker count (i.e., items with non-zero scores), were compared among premature infants (n=49; mean gestational age=32.18 weeks; tested at 12 months corrected age), high-risk siblings later diagnosed with ASD (n=53; ASD diagnoses made at 3 years of age based on the ADI-R, ADOS, and expert clinical judgment using DSM-IV, blind to prior study data), and low-risk controls (n=89) using independent-samples Kruskal-Wallis tests. We then examined the frequencies of behavioral signs exhibited on the AOSI by each group. **Results:** AOSI total scores and total marker counts differed among the three groups ($H_{(2, N=191)}$=70.35, p<.001 and $H_{(2, N=191)}$=66.34, p<.001, respectively). Post hoc pairwise comparisons showed that premature infants and high-risk siblings with ASD had significantly higher scores and counts than low-risk controls, although the former two groups did not differ from each other. A significant proportion of premature infants and high-risk siblings with ASD showed a lack of imitation skills (33% and 34%, respectively), variable orienting to name (27% and 40%, respectively), and decreased social behaviors (23-57% and 30-51%, respectively). Only the high-risk siblings later diagnosed with ASD had, in addition, reduced eye contact and response to a change in another person's facial emotion, as well as more extreme reactivity, difficulty with transitions, and atypical sensory and motor

behaviors (23-42% compared to 0-16% of the premature group). **Conclusions:** At 12 months of age, premature infants exhibit behavioral signs of ASD on the AOSI at similar overall rates to high-risk siblings later diagnosed with ASD, although AOSI scores may be higher in premature infants for reasons other than ASD. The AOSI behaviors these two groups have in common may be considered non-specific early signs, whereas only high-risk siblings later diagnosed with ASD also show specific early signs of ASD. In so far as the two groups share some but not all early ASD signs, it will be important for future research to identify the early behavioral markers that are most predictive of ASD, and to distinguish these from less or non-specific signs. We plan to continue our longitudinal investigation of high-risk siblings, premature infants, and controls in order to appraise the AOSI as an early detection and/or screening technique for use beyond empirical investigations of ASD.

111.006 6 Stability of Autism Spectrum Disorder in Children Diagnosed by Age 24 Months. L. H. Shulman*, M. D. Valicenti-McDermott, K. Hottinger, R. M. Seijo, D. J. Meringolo and N. Tarshis, *Albert Einstein College of Medicine*

Background: Early diagnosis of autism spectrum disorder (ASD) has become an important clinical and public health goal. By age 2 to 3 years (yr), an ASD diagnosis has been found to be stable. Long-term stability of a diagnosis of ASD in children younger than 2 yr has not been determined.

Objectives: To examine the stability of a diagnosis of ASD made in children by age 24 months (mo) and to explore characteristics at presentation and interventions associated with best outcomes.

Methods: Retrospective chart review of 44 children presenting by age 24 mo to a University Affiliated Early Intervention program from 2003 to 2008 who received an ASD diagnosis based on multidisciplinary evaluation and who had follow-up at least 1 year later. Data from initial evaluation included: age, demographics, cognition, autistic features based on the DSM-IV criteria, Childhood Autism Rating Scale (CARS) and, in some, the Autism Diagnostic Observation Schedule (ADOS). ASD diagnosis at follow-up was based on CARS (76%), DSM-IV (29%), ADOS (16%), and Board of Education classification/autism-specific class placement (93%). Type/hours of intervention received by each child per week (applied behavioral analysis, speech, occupational and physical therapies, family training) were tabulated. Data of those who retained ASD diagnosis and those who did not were compared. For children with multiple follow-up visits, the most recent data was utilized for follow-up analysis. Statistical analysis included chi-square, t-test and nonparametric testing.

Results: Mean age of the sample was 19.7 ± 2.8 mo (12-24 mo); 63% were male; 20% had cognitive standard score ≥70. Fourteen (32%) were diagnosed with autism and 30 (68%) with ASD; At follow-up, mean age was 51 ± 18 mo (29-117 mo). ASD diagnostic classification of the sample at follow-up was as follows:

ASD Diagnostic Classification at Follow-up

	Diagnosis at Follow-up		
Diagnosis at Presentation	Autism	ASD	No ASD
Autism (N=14)	12 (86%)	2 (14%)	0
ASD (N=30)	7 (23%)	15 (50%)	8 (27%)

Children who no longer met criteria for ASD were more likely initially to have lower CARS score (32.2± 2 vs. 35.5± 5, p=0.006), higher cognition (Standard Score: 62± 1.2 vs 50.3± 3, p=0.005), and evidence of conversational ability on the DSM-IV (29% vs 0%, p=0.03) suggestive of more language.There were no differences in age at initial evaluation, length of time between original diagnosis and follow-up, and type/hours of intervention between those who retained an ASD diagnosis and those who did not.

Conclusions: In this sample, the diagnosis of ASD made in children under 2 years of age was quite stable. A diagnosis of autism was more stable than ASD. The likelihood of

moving off the autism spectrum was increased for those children with milder autistic symptomatology, higher cognition, and more language at presentation.

111.007 7 The Electroretinogram in Adults with ASD. P. A. Constable[1], D. A. Thompson[2] and D. M. Bowler*[3], (1)*City University*, (2)*Great Ormond Street Hospital*, (3)*City University, London*

Background: Neurotransmitter receptors relating to GABA and glutamate have been implicated in the pathogenesis of ASD. The retina also utilises GABA and Glutamate as neurotransmitters, and the Electroretinogram (ERG) is able to record the response of retinal neurons to light. Therefore, the ERG may offer another clinical tool for investigating ASD.

Objectives: A reduction in the scotopic b-wave has been previously reported in approximately 40% of the study groups' participants (Ritvo et al, 1988). Our aim was to extend this finding by using an extended luminance series and to investigate if any SNPs associated with ASD may help explain any differences seen in the ERG waveforms.

Methods: Participants (N=10 comparison and N=6 ASD) 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. ERGs were recorded monocularly using a mini Ganzfeld. Participants were dilated and dark adapted for 20 minutes. Scotopic and photopic luminance functions were recorded between (-2.35 and 1.5 log cd.sec.m). A Naka-Rushton function was fitted to the scotopic limb of the luminance function and the parameters , K and R calculated by linear regression analysis using log[(R/R)-1] = -log L + *n* log K. In this case, R was set at 1% greater than the maximal b-wave response (R) for a given luminance (L). The parameter *n* represents retinal homogeneity, R as retinal responsiveness and K as a measure of retinal sensitivity. Additionally, 30 Hz photopic flicker, scotopic oscillatory potentials were recorded.

Genotyping was performed by KBioscience (http://www.kbioscience.co.uk). SNPs were genotyped using the KASPar chemistry- a competitive allele specific PCR SNP genotyping system using FRET quencher cassette oligos (http://www.kbioscience.co.uk/genotyping/genotyping-chemistry.htm). SNPs for the glutamate receptor (GRIK2, rs2235076); GABA A receptor subunits (_1, rs2351299, _4 rs2280073, rs1912960); Aspartate/Glutamate exchanger(SLC25A12, rs2292813); Neural cell adhesion molecule (NRCAM rs2300045); Disrupted in Schizophrenia 1 (DISC, rs1322784) and Neuroligin 4 X-linked (NLGN4X, rs12836764). Currently N=12 ASD and N=10 genotypes are available for (rs2292813, rs2235076, rs2280073, rs2300045 and rs1322784). Further will be performed on the final group of participants which we anticipate a size of 20 in each group.

Results: The ASD group 3/6 participants displayed a reduced luminance response function which is consistent with previous reports. Student's t-test for the parameters R_{max} representing retinal responsiveness ($p=0.03$), K representing retinal sensitivity ($p<0.001$) and *n* retinal homogeneity ($p=0.01$) were all significantly reduced. No difference was observed in the 30Hz ($p=0.51$) or oscillatory potentials ($p=0.95$). Preliminary analysis of SNP data using Chi-squared shows no difference in either allele or genotype frequency between the groups. <

Conclusions: We present preliminary findings that the scotopic retinal sensitivity and responses are altered in ~ 50% of adults with ASD. Genotyping of the individuals may offer insights into the contribution of SNPs associated with ASD in explaining the changes in the retinal luminance response function.

111.008 8 The Home Situations Questionnaire-PDD Version: Factor Structure and Psychometric Properties. M. Chowdhury* and M. G. Aman, *The Ohio State University*

Background: The original Home Situations Questionnaire (HSQ; Barkley & Edelbrock, 1987)) is a caregiver-rated, 16-item scale designed to assess noncompliance in

everyday settings. Despite its use in several studies in typically-developing children and children with Attention Deficit Hyperactive Disorder, few investigations have reported on the factor structure of the HSQ. In addition, *no* prior studies have examined its use in children with Pervasive Developmental Disorders (PDDs). This is unfortunate, because children with PDDs frequently present with behavioral problems related to noncompliance.

Objectives: We examined the factor structure of the HSQ, modified for use with children with PDDs by the Research Units on Pediatric Psychopharmacology (RUPP) Autism Network. We also assessed its correspondence with indices of disruptive behavior (which would be suggestive of convergent validity) and adaptive behavior (suggestive of divergent validity).

Methods: Investigators from the RUPP Autism Network modified the HSQ by adding 5 situations where many children with PDDs have particular difficulty (for e.g., making transitions from one setting to another). This modified scale (HSQ-PDD) was used as the outcome measure in a clinical trial evaluating improvements in compliance as a function of pharmacological and behavioral treatment. In the current study, we analyzed HSQ-PDD data for the 124 subjects who participated in this 24-week, three-site RUPP clinical trial. Key inclusion criteria for the trial were presence of PDDs, and serious behavior problems as indicated by high scores on the Irritability subscale of the Aberrant Behavior Checklist (ABC).

Results: Exploratory factor analyses with oblique Crawford-Ferguson (CF) quartimax rotations were used to derive two-to-five factor solutions. The number of factors retained was based on information gained from eigen values, scree plots, measures of model fit, and clinical content. The 2-factor solution appeared to be the most parsimonious and interpretable. Factor 1 (n = 14 items) consisted of situations characterized by "Socially-Inflexible" behaviors. These included social situations where the child's lack of adaptability becomes most prominent, such as deviation from an expected schedule, or adjusting to people or places outside the child's immediate comfort zone. Factor 2 (n = 6 items), which we named "Demand-Specific", consisted of situations where a direct demand was placed on the child and required effort. Item content of both subscales appeared to fit well with the rubric of PDDs. Internal consistency, using Cronbach's alpha, was 0.90 for "Socially-Inflexible", and 0.80 for "Demand-Specific." These derived subscales showed moderate correlations with subscales of the ABC, Child and Adolescent Symptom Inventory, and Children's Yale-Brown Obsessive Compulsive Scale, and low negative correlations with the Vineland Adaptive Behavior subscales.

Conclusions: The HSQ-PDD appears to be well suited for children with PDDs, and use of its two subscales will likely result in more refined interpretation of ratings than the more global total score. However, since participants were selected for the presence of behavior problems, it may not be appropriate to generalize results to *all* children with PDDs. Additional data from a broader range of children with PDDs would be helpful for confirming subscale content and developing norms.

111.009 9 The Implementation of the M-CHAT Follow-up Interview in a Community-Based Autism Screening Program in Italy: Preliminary Results. E. Salomone*[1], F. Muratori[2], A. Narzisi[2], A. Pitanti[3], C. Grassi[3], R. Tancredi[2] and P. F. M. Molina[1], (1)*University of Turin*, (2)*University of Pisa – Stella Maris Scientific Institute*, (3)*USL 1 Massa e Carrara*

Background:

Investigations have established that ordinary pediatric check-ups and general surveillance on child development are not sufficient to guarantee an acceptable identification rate for Pervasive Developmental Disorders. General guidelines in pediatrics therefore strongly recommend screening programs for autism at a general population level by means of standardized checklists. Despite this knowledge, there is still a need for a wide implementation of such early detection practices in Italy. To date, the care for autism in Italy has been characterized by late diagnosis (mean age at diagnosis is 4-5 years) and related negative clinical outcomes in social communication and cognitive

domains. Investigations have shown that the M-CHAT screening checklist associated with a Follow-Up Interview designed to reduce the false positive rate has good psychometric properties and is effective in early detection; however no data are available on an Italian population. The M-CHAT Checklist and Follow-Up Interview are currently being introduced in a screening program in the Tuscany region of Italy. Both tools are currently being translated, culturally adapted and tested among an Italian population at 18 months and fall within a wider screening process including the administration of the First Year Inventory at 12 months of age.

Objectives:

The purpose of this investigation was to determine to what extent failing the M-CHAT Checklist was associated with a misunderstanding of the checklist items as measured by the number of items which needed clarification in the Follow-Up Interview among an Italian population.

Methods:

The M-CHAT was administered to a preliminary ongoing sample of 108 parents during the pediatric visit at 18 months. Subjects failing the M-CHAT were given a follow-up phone call to receive the M-CHAT Follow-Up Interview. Of the 13 subjects who screened positive on the Checklist, 11 completed the Interview. One subject continued to show risk for autism and is currently under clinical evaluation. For all subjects, failed or missed items at the Checklist that resulted in a "pass" at the Interview were noted and then analyzed by trained independent raters in order to determine whether change in scores was due to child maturation or misunderstanding of the items. Raters had to unanimously agree for final categorization.

Results:

Preliminary results indicate that most frequently failed items were those related to atypical sensory responsiveness and gaze monitoring. In both domains parents had more difficulties in judging their child's behavior and considered typical patterns of behavior as unusual or abnormal. Lack of concrete examples in the wording of the checklist's items was considered to be the most likely reason for this misunderstanding.

Conclusions:

Further testing is needed which can establish the efficacy of early screening process including a follow-up in order to reduce false positives cases and addressing the resources to early diagnosis and treatment which is sorely needed in Italy given current practices. Investigations of this type will provide further evidence to multiple level screening processes and will specifically contribute in defining a culturally sensitive screening protocol for the Italian context.

111.010 10 A Family of Origin Scale in Mothers of Children with ASD. P. Gorczyca*[1], A. Kapinos-Gorczyca[2], M. Kapinos[3], J. Sobis[1], A. Leksowska[1] and R. T. Hese[1], (1)*Medical University of Silesia*, (2)*NZOZ FENIKS*, (3)*Psychiatric Hospital of Rybnik*

Background: The influence of the family of origin is often described in the aetiology of different psychiatric disorders. The majority of papers concerning the families of autistic children concentrate on theirs quality of life.

Objectives: To compare the experiences from the family of origin of mothers of children with ASD and mothers with healthy children.

Methods: In our study a Family of Origin Scale (FOS) by Hovestadt et al. was used. This scale consists of 10 constructs: clarity of expression, responsibility, respect for others, openness to others, acceptance of separation/loss, range of feelings, mood and tone, conflict resolution, empathy, trust. It was a pilot study. The examined group consisted of 9 mothers of children with ASD, the control group - 7 mothers of healthy children.

Results: Both group differed in a statistically significant way as for the construct called responsibility.

Conclusions: Our research was a pilot study and it requires further investigations.

111.011 11 A Novel Measure of Joint Attention for Use with Older Children and Adolescents: Evidence for Clinical Utility and

External Validity. J. L. Bean*, J. Casares and I. M. Eigsti, *University of Connecticut*

Background:
Joint attention (JTAT), the ability to share a mutual focus of attention with another person, is an essential developmental milestone; deficits in JTAT are one of the earliest symptoms of autism spectrum disorders (ASD). JTAT is thought to directly influence language acquisition and social development. It is effectively assessed in young children (e.g., with the ESCS, Mundy, 1982, and Modules 1-2 of the Autism Diagnostic Observation Schedule, ADOS). However, only limited research examines JTAT at later developmental periods and whether skills continue to distinguish ASD populations; research may be limited in part by lack of assessment measures.
Objectives:
To investigate JTAT skills in older individuals, we designed a measure consisting of six prompts for the initiation of and response to JTAT. The current study tests this measure's ability to discriminate between individuals with ASD and typically-developing (TD) controls. We also report reliability and external validity (e.g., correlations with the Social Communication Questionnaire, SCQ; ADOS; Childhood Behavior Checklist, CBCL; and Social Responsiveness Scale, SRS).
Methods:
Participants included 18 children with ASD and 24 TD controls, ages 7 to 17. Groups were matched on age, FSIQ, and PPVT (p's > .29). The JTAT measure consisted of three verbal and three nonverbal naturalistic prompts, interleaved with a standardized testing situation. Prompts were designed to elicit initiation of and response to joint attention, and included the experimenter searching for a lost item, calling attention to an interesting object, introducing the participant to another experimenter, etc. Scores were based on response characteristics (making eye contact, making an appropriate verbal response, and providing the socially-appropriate action).
Results:
As expected, the ASD group's JTAT scores were lower than for controls, $p < .01$. In addition, within the ASD group only, JTAT scores were correlated with the SCQ Communication scale, $r = -.61$, $p = .02$; SRS Social Awareness scale, $r = -.71$, $p = .02$; and (as a trend) with ADOS scores, $r = -.46$, $p = .05$. In contrast, for the TD group, JTAT scores were associated with SRS Social Motivation, $r = -.41$, $p = .04$; the SCQ (total), $r = -.46$ $p = .03$; and Social Withdrawal scale on the CBCL, $r = -.38$, $p = .05$. Twenty percent of JTAT assessments were coded by two raters for reliability; Cohen's kappa will be reported.
Conclusions:
Results indicate that this novel measure of JTAT, which requires no special equipment and is administered during a typical evaluation, is highly reliable and useful in capturing joint attention skills in older individuals with ASD. Further, scores were associated with parent-report and interviewer assessments of social awareness and ASD-specific behaviors, indicating high external validity. Individuals with TD showed a wide range of scores (14 - 22) and associations with social motivation and withdrawal, suggesting this measure captures meaningful variability in joint attention. Given the powerful developmental sequelae of JTAT and the numerous interventions targeting these skills, this measure offers a novel approach to assessing JTAT development longitudinally.

111.012 12 Autism and Autistic Traits: The Clinical Validity of the SRS and the SCDC. S. Bölte*, *Central Institute of Mental Health*

Background: Research indicates that autism is not a discrete disorder, but the extreme end of a continuously distributed trait. The Social Responsiveness Scale (SRS) and the Social and Communication Disorders Checklist (SCDC) aim to assess trait autism.

Objectives: To compare the clinical validity of the SRS and the SCDC in the same sample.

Methods: Diagnostic (sensitivity/specificity) and convergent validity with established clinical autism scales (ADI-R, ADOS, SCQ) were determined in a sample of $n = 148$ participants with idiopathic autism spectrum disorders (ASD), $n = 255$ clinical, and $n = 77$ neurotypical controls.

Results: The SRS showed sensitivities of .82/.72 and specificities of .75/.84 for ASD on recommended cut-offs. Sensitivities were .90/.87 and specificities .41/.47 for the SCDC. Correlations with the ADI-R, ADOS and SCQ were higher for the SRS than for the SCDC.

Conclusions: The SCDC seems superior to the SRS when screening for unspecific social and communicative deficits including autism. The SRS appears more suitable than the SCDC in clinical settings and for specific ASD screening.

111.013 13 Autism Spectrum Disorder Phenotype Profiles in Probands From Simplex Versus Multiplex Families. J. Gerdts* and R. Bernier, *University of Washington*

Background: Twin and family studies find that the risk of developing autism spectrum disorder (ASD) rises dramatically as the level of shared genes increases. However, most children with ASD are the only individuals in their family with the diagnosis. These simplex families have recently received attention from genetic researchers. Sebat and colleagues (2007) examined genetic markers in ASD families and found that de novo copy number variant mutations were significantly more likely to occur in simplex than in either multiplex or control families. Together, these findings suggest that the genetic etiologies of ASD may vary between single-incidence and multiple-incidence ASD families.

Objectives: Given the potential differences in genetic etiologies for ASD, it is plausible that differences in phenotype exist as well. The current study seeks to compare phenotype profiles in probands within multiplex versus simplex families.

Methods: Probands from simplex families were ascertained from the ongoing Simons Simplex Collection (SSC) project and The Autism Simplex Collection (TASC). Probands in these studies are carefully screened for a family history of ASD and families are excluded if any immediate biological family member has or is suspected to have a diagnosis of ASD. 154 probands from simplex families in the UW studies were included in these analyses. Data for the multiplex family sample was obtained from the Collaborative Programs of Excellence in Autism study. Multiplex families were included if two or more children in the family had a diagnosis of ASD, as assessed by study clinicians. One proband from each multiplex family was selected at random to participate in this study, resulting in 226 probands eligible for analysis. Diagnosis of ASD for both samples was based on meeting cutoffs on the ADI and ADOS as well as a clinical diagnosis made by experienced clinicians. Measures analyzed included the Aberrant Behavior Checklist (ABC), the social domain of the Vineland Adaptive Behavior Scales (VABS), ADOS severity score (Gotham et al, 2009), and either the Wechsler scales or the Differential Abilities Scale to assess IQ.

Results: Preliminary results suggest that multiplex probands scored significantly lower than simplex probands on both verbal, $t(344) = 8.23$, $p < .001$, and full scale IQ, $t(356) = 6.77$, $p < .001$. Given that IQ often correlates with social deficits in ASD, we controlled for IQ when analyzing scores on the social domain of the VABS. After controlling for IQ, multiplex probands scored lower than simplex probands on this domain, $t(336) = 3.90$, $p < .001$. Scores did not differ between the groups on any composite of the ABC nor on the nonverbal IQ composite. Analyses concerning the ADOS severity scores are ongoing.

Conclusions: Phenotypic differences between probands from multiplex versus simplex families were found in a number of areas, including IQ and social skills. These findings lend further support that different genetic mechanisms underlying simplex and multiplex families may have demonstrable effect on phenotypic presentation. Such findings may be important in further examinations of genetic risk markers potentially specific to each family-type.

111.014 14 Autism Spectrum Disorders: A Dimension or Sub-Categories?. T. W. Frazier*[1], R. Embacher[1], P. A. Law[2] and

J. N. Constantino[3], (1)*Cleveland Clinic*, (2)*Kennedy Krieger Institute*, (3)*Washington University School of Medicine*

Background: Our group has recently found that many cases of autism spectrum disorders (ASDs) represent a category, qualitatively distinct from typical (non-autism) behavior in clinically ascertained samples (Frazier et. al., in press). The next question concerns whether a broad autism category is composed of sub-categories or is best characterized as a dimension of symptom severity when only autism-affected youth are examined. A recent study addressing this question identified unique sub-categories based upon dysmorphology/head circumference, social communication, and verbal/non-verbal ability scores (Ingram et al., 2008). However, interpretation of these findings is complicated by the aggregation of two different samples, a design feature which may bias toward category identification.

Objectives: The present study examined whether autism symptoms would identify sub-categories or a dimension of symptom severity, consistent with the notion of an autism spectrum. This distinction is relevant to future DSM nosology, screening and diagnosis, genetic and neurobiological study design, and identification of differential treatment effects.

Methods: Data were obtained from the Interactive Autism Network (IAN) and Autism Genetic Resource Exchange (AGRE) samples and analyzed separately to determine whether results replicate across samples and indicator sets. IAN preferentially recruits families with at least one affected child who has been diagnosed with an ASD. In the IAN sample, caregivers reported autism symptoms using the Social Communication Questionnaire (SCQ) and the Social Responsiveness Scale (SRS). In the AGRE sample, parents were interviewed using the Autism Diagnostic Interview – Revised (ADI-R). Autism symptom indicator sets were derived from each measure in each sample. Taxometric and latent variable models evaluated whether 1-group (dimensional) or 2-group (categorical) models fit the data better across indicator sets, demographic sub-samples, and IAN/AGRE samples. These models are "blind" to diagnostic status and thus provide an empirical test of whether sub-categories or a dimension best describe the data.

Results: In the IAN sample, 6875 and 2575 autism-affected participants had SCQ and SRS data, respectively. In the AGRE sample, 889 autism-affected individuals had ADI-R data. Results indicated that dimensional models fit the data better than categorical models. This was true across all taxometric and latent variable procedures, indicator sets, demographic sub-samples, and IAN/AGRE samples.

Conclusions: Previously, our group found that ASDs are best conceptualized as a category distinct from typical behavior. The present findings suggest that this broad category includes a continuum of symptom severity. Together, these findings suggest that ASDs may be conceptualized as a single, discrete entity that is distinct from typical behavior but that shows large variation in symptom severity. This conclusion does not rule out the possibility of autism sub-groups. However, the results imply that indicators beyond autism symptoms, such as cognitive or biological indicators, will be needed to identify autism sub-groupings.

111.015 15 Challenges in the Diagnoses of Autism Spectrum Disorders in the Community. S. E. Levine*, A. Y. Hardan, M. Boettcher-Minjarez and C. Feinstein, *Stanford*

Background: Autism spectrum disorders (ASD) are very complex and heterogenous disorders. Making these diagnoses in children and adolescents can be very challenging for practitioners in the community with limited resources and training in this field. The diagnostic step is important since it allows for the implementation of early specific interventions and appropriate allocation of public funds. Objectives: To examine the rate of agreement between diagnoses of Autism Spectrum Disorder (autistic disorder (AD), Asperger's disorder (ASP), and pervasive developmental disorder, not otherwise specified (PDD, NOS)) made by practitioners in the community and a comprehensive evaluation using gold-standard instruments.

Methods: Children and adolescents between the age of 5 and 17 years with a previous diagnosis of an autism spectrum disorder (ASD) made by a community provider were recruited to participate in this study. Participants were identified from an autism specialty clinic after being referred for mostly treatment purposes. Evaluations were completed in an autism specialty clinic and included the Autism Diagnostic Interview-Revised, Autism Diagnostic Observation Schedule and Whechsler Abbreviated Intelligence Scale. The Social Responsiveness Scale, Child Behavior Checklist and Sensory Profile Questionnaire were also obtained. Consensus diagnosis was based on DSM-IV criteria and was generated by a committee of 3 investigators with two members with extensive experience in working with children and adolescents with autism spectrum disorders. Results: To date, 9 subjects have been evaluated. Of these 4 were previously diagnosed with ASP, 2 with AD, 1 with PDD NOS. These diagnoses were made by neurologists (2), child psychiatrists (5), child psychologists (2). One participant had received two different ASD diagnoses by two different psychiatrists and the most recent one was considered. The consensus diagnoses conference revealed that 5 out of 9 met criteria for an ASD with all participants being diagnosed with PDD, NOS after comprehensive review of clinical research data including videos observation. Conclusions: These preliminary observations suggest that community providers continue to face challenges in the diagnosis of ASD with a tendency to over diagnose to possibly allow these children to receive optimal treatments. However, final conclusions cannot be made before a larger number of children are evaluated. As this study is ongoing, additional data and analyses will provide more insight into the significance of these findings especially that recent epidemiologic studies are relying on community providers for diagnoses.

111.016 16 Sensitivity and Specificity of Original and Revised ADOS Algorithms in a Clinical Setting. D. Murray*, C. A. Molloy, R. Akers, S. L. Bishop and P. Manning-Courtney, *Cincinnati Children's Hospital Medical Center*

Background: The Autism Diagnostic Observation Schedule (ADOS) was developed as an observational component of a diagnostic assessment for autism spectrum disorders (ASD) that includes a thorough history and other developmental tests. Because administration is relatively brief relative to other ASD assessments, the ADOS has come into routine use for diagnostic classification in many clinical and educational settings. In 2007, the algorithms for Modules 1 - 3 were revised for improved comparability and measurement of severity across modules.
Objectives: The aim of this study was to examine the sensitivity and specificity of both original and revised ADOS algorithms when used as part of the standard clinical evaluation of children referred to a specialty center to rule out ASD.
Methods: Records of new visits to the Division of Developmental and Behavioral Pediatrics (DDBP) at Cincinnati Children's Hospital Medical Center in 2008 were reviewed. Records of children referred for evaluation with ADOS Modules 1 - 3 were more closely examined for comparison of final clinical diagnosis to ADOS classification on the new and original algorithms. All ADOSs at Cincinnati Children's are administered by speech-language pathologists specializing in autism who have met and maintain research reliability standards on the instrument. Final clinical diagnosis is made by a developmental pediatrician following a multi-disciplinary team assessment. Final diagnosis and ADOS classification were collapsed into Spectrum (autism and ASD) and Not Spectrum for comparison in 2x2 tables.
Results: In 2008, approximately 2200 children were seen for the first time in DDBP for concerns about developmental delay. Of these, 657 underwent a multi-disciplinary evaluation to rule out ASD. A total of 603 children were evaluated with ADOS Modules 1 - 3. Complete ADOS and final clinical diagnosis information was available for 584: Module 1 No words = 87; Module 1 some words = 90; Module 2 < 5 years = 107; Module 2 => 5 years = 91; Module 3 = 209. Final clinical diagnosis for all modules combined was Autism = 142 (24%); Non-autism ASD = 185 (32%) and Not spectrum = 257 (44%). Sensitivities for both old and new algorithms ranged from 76 to 99 across the modules. Specificities were low for both

old and new algorithms, but were consistently lower with the new algorithm. Specificity = 29% for Module 1 No words. The most common non-spectrum clinical diagnosis for children classified as ASD by the ADOS was global delay. For Module 3, specificity = 34% and the most common non-spectrum diagnosis for children classified as ASD by the ADOS was anxiety/ADHD.
Conclusions: The ADOS provides valuable observational information to the diagnostic team in the clinicalevaluation of a child for ASD. However, in this clinical setting where children with numerous kinds of developmental disorders are evaluated, the specificity of the instrument is low and the information must be assessed as part of the overall evaluation by the multi-disciplinary team. In settings such as schools or private practitioners' offices where the ADOS has become the primary determinant of diagnostic classification, ASD may be over diagnosed.

111.017 17 The Anatomic Severity Scale Correlates with Level of Impairment On Measurements of Autism and Intellectual Disability in Children with Smith-Lemli-Opitz Syndrome (SLOS). R. W. Y. Lee*[1], I. Bukelis[1], F. D. Porter[2], W. E. Kaufmann[1] and E. Tierney[1], (1)*Kennedy Krieger Institute*, (2)*National Institutes of Health/NICHD*

Background: SLOS is an autosomal recessive, multiple malformation syndrome caused by an inborn error of cholesterol biosynthesis (Tint, 1994). Mutations in the gene encoding 7-dehydrocholesterol reductase (DHCR7) impairs conversion of 7-dehydrocholesterol (7DHC) to cholesterol, resulting in low cholesterol and elevated concentrations of abnormal sterols in tissues and blood. A pilot study showed significant hypocholesterolemia in a subpopulation of children with autism (Tierney, 2006). Autism is commonly found in SLOS (Tierney, 2001). Studies demonstrate cholesterol has multiple biologic functions as a structural component of myelin and lipid rafts, synaptogenesis, formation of bile acids and neurosteroids, and hedgehog signaling (Fantini, 2009). A clinical scoring system that measures the involvement of multiple organ systems has been confirmed in SLOS cases (Kelley, 2000; Bailer, 1987). Further studies are required to elucidate the role of impaired cholesterol biosynthesis in autism. Objectives: This study hypothesizes that the anatomic severity scale correlates with severity of impairment on measurements of autism, IQ, adaptive function, and sterol levels. Methods: 23 subjects with SLOS between the ages of 4 years and 18 years received the ADI-R, ADOS, Vineland adaptive behavioral scales (VABS), Stanford-Binet-IV, and Mullen Scales. Plasma 7DHC and 8DHC levels were acquired by GC-MS. Anatomic severity scores were obtained by a blinded physician examiner. Simple and multiple regression analyses were used. Results: Significant correlations were found between severity score and ADI-R-social (p=0.02), ADI-R-verbal communication (p=0.02), ADI-R-non-verbal communication (p=<0.01), ADOS-play (p=0.02), VABS (p=<0.01), VABS-social (p=0.02), VABS-motor (p=0.01), VABS-daily living (p=0.01), full scale IQ (FSIQ) (p=<0.01), non-verbal IQ (p=<0.01), verbal IQ (p=0.01), plasma 7DHC (p=0.01), and plasma 8DHC (p=<0.01). Multiple regression showed FSIQ was the primary predictive factor in social but not communicative ADI-R. Conclusions: These findings suggest that higher anatomic severity scores correlate with increased scores on autism measures in children with SLOS, but this is likely mediated by intelligence. Higher severity scores correlate with sterol levels in children with SLOS. Further studies investigating the neurologic underpinnings of behavioral phenotypes and anatomic malformations within SLOS and other neurogenetic syndromes, may lead to new diagnostic and therapeutic strategies for autism and other neurodevelopmental disabilities.

111.018 18 Use of the Leiter International Performance Scale-Revised with Children with Autism Spectrum Disorders. S. N. Grondhuis*, J. A. Mulick and M. G. Aman, *The Ohio State University*

Background: Both the Leiter International Performance Scale-Revised (Leiter-R) and the Stanford-Binet 5th Edition (SB5) are standardized intelligence measures that can be used with a variety of specialty populations. The Leiter-R is a nonverbal assessment measure useful in evaluating clients with restricted language capabilities. Although the Leiter-R and more traditional SB5 are frequently used to assess intellectual ability in children with autism spectrum

disorders (ASD), data about the relationship between these measures are not available for the most recent editions of the tools. Objectives: To determine whether children with ASD appear to function differently when assessed using the nonverbal Leiter-R than the verbally-presented SB5, and to evaluate whether the magnitude of this relationship changes with the age of the child. Methods: A retrospective chart review of patient files from a major children's hospital was conducted, and data from 1,063 patients at risk for an intellectual or developmental disability were obtained. From that sample, analyses were conducted on 129 children who received both the Leiter-R and the SB5 and also an ASD diagnosis (Autistic Disorder: n=68, Pervasive Developmental Disorder Not Otherwise Specified: n=57, and Asperger's Disorder: n=4). In all, 83.7% were male (n = 108); mean age of the sample, in months, was 67.09 (SD = 34.06). Results: Preliminary results indicate that children with ASD performed significantly higher on the nonverbal Leiter-R (mean = 89.59, SD = 23.00) than the SB5 (mean = 70.04, SD = 19.09). This difference was both statistically [$t(128) = 15.92$, $p < .0001$, effect size = 1.40] and clinically significant. Planned analyses that will be available by the conference will examine whether the ages of the children or their levels of intelligence alter the relationship between the two measures, and if the severity of discrepancy is greater given a specific diagnosis (Autistic Disorder, PDD-NOS, or Asperger's Disorder). Conclusions: Clinicians use intelligence measures not only to aid in the diagnostic process, but also to make clinical recommendations regarding education and treatment options. The average 19.55 point discrepancy between mean scores of the two tests is substantial, and it may have important implications for clinical recommendations and decisions. Furthermore, it is important to realize that the mean difference between the two instruments was approximately 20 points, meaning that it was substantially larger in some children. In many cases, it will be important to obtain information with both a nonverbal test like the Leiter-R as well as a more general estimate of IQ (like the SB5), as this would give a better representation of the intelligence of the child than a single test alone, as well as areas of strength and relative deficit. Children with ASD have a unique set of impairments, and understanding the breadth of their abilities and the impact that a communication deficit has on a particular child can be both clinically and practically relevant.

111.019 19 Application of the ADOS Severity Metric in a Sample of Young Children. S. Shumway*, A. Thurm and D. L. Mead, *National Institute of Mental Health, National Institutes of Health*

Background: A severity metric for core features of autism was recently developed, which standardizes raw scores from the Autism Diagnostic Observation Schedule (ADOS) according to language level and age, to assess symptoms of autism independent of language ability (Gotham, Pickles, & Lord, 2009).

Objectives: This study used the recently published severity metric to: 1) examine the distribution of ADOS severity scores across diagnostic groups; 2) further investigate the relationship between severity and participant characteristics (IQ, adaptive functioning, verbal impairment); and 3) examine ADOS severity scores over time in a subset of the sample.

Methods: To date, 256 children completed diagnostic assessments, including administration of the ADOS (168 module 1, 88 module 2), measures of nonverbal and verbal IQ (Mullen Scales of Early Learning, Differential Ability Scales-II), and adaptive functioning (Vineland II). At the time of the assessment, 141 children were diagnosed with autism (mean age=54.0 months, SD=21.9), 30 with PDD-NOS (mean age=44.9 months, SD=12.5), 53 non-ASD developmental delays (mean age=47.1 months, SD=14.9), and 32 with typical development (mean age=33.0, SD=6.6). A subset of children with autism (n=64) had a second ADOS between 4 and 15 months (mean=10.3 months, SD=3.4) following the first assessment.

Results: Preliminary findings revealed a Time 1 mean ADOS severity score of 7.54 (SD=1.4) for children with autism, 5.80

(SD=1.7) for PDD-NOS, 2.45 (SD=1.61) for non-ASD developmental delays, and 1.25 (SD=.44) for TD, consistent with the original paper in which ADOS classification anchored scores of 6-10 for autism, 4-5 for PDD-NOS, and 1-3 for nonspectrum.

For children with ASD (autism n=141, PDD-NOS n=30) at Time1, ADOS *raw total scores* were highly correlated with developmental/cognitive scores: nonverbal (r=-.49) and verbal (r=-.67) IQ. These correlations were lower with ADOS *severity scores*: nonverbal (r=-.21) and verbal (r=-.28) IQ, and found to be significantly lower when statistically compared (verbal difference: z=4.77, p<.001; nonverbal difference: z=2.93, p=.003). In addition, ADOS *raw total scores* were significantly correlated with adaptive functioning (r=-.38), while ADOS *severity scores* were not (r=-.11) (correlation difference: z=2.62, p=.009). For children with autism with two ADOS time points (n=64), results of a one-way within subjects ANOVA revealed no significant difference between Time 1 (mean= 7.4) and Time2 (mean= 7.27) ADOS severity, F(1, 63)=.46, p=.50. The majority of scores at time 2 remained within 1 point of Time 1 scores.

Conclusions: Results from this study indicate that ADOS (module 1 or 2) severity scores in a sample of young children with autism, PDD-NOS, and nonspectrum are similar to the mean severity scores for these groups in the original standardization sample. ADOS severity scores also appear more independent from cognitive and adaptive functioning. In addition, severity scores remained relatively stable in this sample with varying treatments. Further analysis of larger samples that contain multiple predictor variables will be important in determining when and how severity scores change in individuals with ASD.

111.020 20 DOES Intensive TREATMENT Lead to BETTER RESULTS in Toddlers with AUTISM Spectrum Disorders (ASD). R. Choueiri*[1], S. Wagner[2] and E. Perrin[1], (1)*Floating Hospital for Children, Tufts Medical School*, (2)*Behavioral Development & Educational Services*

Background:

Little is known about the predictive factors for a positive response to intensive treatment in toddlers with ASD. Recommendations are from reports of clinical improvement after intensive 1:1 therapy. But in clinical practice, we sometimes see children receiving less therapy making progress while children receiving intensive therapy make little progress.

Objectives:

We sought to compare the developmental progress of toddlers with ASD receiving variable hours of treatment.

Methods:

Seventeen children referred to a developmental clinic for evaluation of a possible or known ASD, ages 26 and 32 months, are followed in this prospective pilot project. All received assessments with the Mullen Scales of Early Learning (MSEL), Autism Diagnostic Observation Schedules (ADOS), Vineland Adaptive Behavior Scales (VABS), the Pervasive Developmental Disorders Behavior Inventory (PDDBI) and play interactions developed for this project. Intensive treatment at 25 hours a week was recommended for all but was not always delivered. Children are evaluated every 6 months for 2 years.

Results:

Mean age of the 17 children was 28.8 months. All have completed at least one year follow-up, at an average of 14.6 months after the initial evaluation. Fourteen are boys and 3 are girls. We examined the relation between total hours of 1:1 treatment per week and change scores at the average months of follow-up for the: MSEL, PDDBI, VABS and the play measures. Eight children received > 10 hours of treatment a week and 9 received Vineland at follow-up, but children with >/= 10 hours/wk of treatments were rated as having less reduction. No significant change was reported in the Adaptive Behavior Composite in either group.

Conclusions:

These preliminary data in a small sample do not support the belief that greater intensity of treatment leads to more clinical improvement in toddlers with ASD. Other factors are important in the response to treatment. Play interactions developed for this project will need further validation but may offer a quick clinical measure for autism symptoms improvement.

111.021 21 Sleep Is Associated with Problem Behaviors in Children with Autism Spectrum Disorder. S. E. Goldman* and B. A. Malow, *Vanderbilt University*

Background: Sleep problems are common in children with Autism Spectrum Disorder (ASD) with rates estimated to range from 44 – 83%. Previous research has suggested that sleep problems are associated with challenging behaviors in children with ASD. However, these samples were small and did not use standardized definitions of ASD. Substantiation of these findings within a large cohort of individuals would support the development of treatments targeted at improving sleep disturbances as an avenue to improve behavior.

Objectives: The goal of this analysis was to identify the sleep factors associated with problematic daytime behavior.

Methods: The study population was 1056 children, ages 3 – 18, participating in the Autism Treatment Network (ATN). The ATN is a registry collecting data on children with ASD across 14 sites in the United States and Canada. All children have a clinical diagnosis of ASD confirmed by the Autism Diagnostic Observation Schedule (ADOS). Sleep behaviors were derived from the Children's Sleep Habits Questionnaire (CSHQ), a validated, parental questionnaire describing sleep behaviors in children, including overall sleep problems, sleep anxiety, sleep duration, and parasomnias. Daytime behaviors were obtained from the Child Behavior Checklist (CBCL), a validated, parentally completed questionnaire used to examine behaviors in children. Two separate forms spanning the age ranges 1_–5 years and 6–18 years are available. We analyzed T-scores from scales common to both age groups, as well as analyzing each age group individually.

Descriptive statistics were calculated for all major variables. Pearson product-moment correlation coefficients were calculated to identify associations between sleep and behavior. We chose a correlation coefficient value of ≥0.30 and p-value <0.05 to represent significance.

Results:

CSHQ surveys were completed by 1056 parents (564 ages 2-5 and 492 ages 6-18). Across all ages, the CSHQ total score was associated with the total CBCL score (r =0.47) and CBCL affective problems subscale (r = 0.55). The CSHQ total score and sleep anxiety domains were both associated with the CBCL anxiety subscale (r = 0.34 for both). The CSHQ sleep duration domain was associated with the CBCL affective problems scale (r = 0.46), and the parasomnia domain was associated with the total problem scale (r = 0.36). In the older children the CSHQ sleep total domain was associated with the CBCL total problem scale (r = 0.43) and the CBCL affective problems scale (r = 0.50).

Conclusions:

Our findings support the hypothesis that sleep factors are associated with problematic daytime behaviors in a large cohort of children with well-defined ASD. We showed that the behavioral domains of affective disorders and anxiety are associated with problematic sleep. The high rates of association call for longitudinal studies to demonstrate cause and effect as well as pharmacological and behavioral trials to define the effects of improving sleep on daytime behaviors.

SUPPORT: Grant support received from the Autism Treatment Network, Health Resources and Services Administration (UA3 MC11054).

111.022 22 Symptoms of Autism Spectrum Disorders (ASDs) in SMITH-MAGENIS Syndrome (SMS). P. Cavolina[1], L. Boccone[2], G. Putzolu[1], M. Carta[3], R. Fadda[4] and G. Doneddu*[5], (1)*A.O.B. (Azienda Ospedaliera Brotzu)*, (2)*Centre for Microcitemie*, (3)*A.O. Brotzu*, (4)*Department of Psychology*, (5)*Azienda Ospedaliera Brotzu*

Background:

Smith-Magenis syndrome (SMS) is characterized by distinctive facial features, developmental delay, cognitive impairment and behavioural abnormalities. The facial appearance shows midfacial hypoplasia, relative prognathism, and heavy brows with a "pugilistic" appearance (Greenberg et al. 1991; Potocki et al., 2003). The behavioural phenotype includes sleep disturbance, stereotypes, inattention, hyperactivity, maladaptive behaviours including frequent outbursts/temper tantrums, impulsivity, distractibility, aggression and self-injurious behaviours including self-hitting, self-biting, and/or skin picking, inserting foreign objects into body orifices (polyembolokoilamania), and yanking fingernails and/or toenails (onychotillomania) (De Leernsyder et al. 2001; Smith, Dykens & Greenberg, 1998a, 1998b). The diagnosis of Smith-Magenis syndrome is based on clinical findings and confirmed by detection of an interstitial deletion of 17p11.2 by G-banded cytogenetic analysis and/or by fluorescence in situ hybridization (FISH). Probes for FISH testing must include the RAI1 gene which is the only gene known to account for the majority of features in Smith-Magenis syndrome. Autism Spectrum Disorders (ASDs) type behaviours have been reported in many cases, but not been extensively studied with objective and standardized diagnostic tools.

Objectives: The first goal of this study is to describe ASDs behaviours in patients exhibiting the Smith- Magenis Syndrome, using reliable, objective assessment tools.

Methods: To achieve this aim we examined 5 participants with Smith- Magenis Syndrome (SMS), between the ages of 11 and 35 years (3 males and 2 females; av. chron. age 24.5 s.d. 9.5). Each subject was evaluated using the Autistim Diagnostic Observation Schedule (ADOS) and the Leiter-R scale. The parents completed the Autism Diagnostic Interview – Revised (ADI-R) and the Vineland Adaptive Behaviour Scales (VABS).

Results: All subjects were functioning considerably below average (I.Q. av. score 38.8 ; s.d. 11.6) with IQ scores ranging from 30 to 57. Based on VABS, subjects in our sample were functioning significantly below average in all domains of adaptive functioning: Communication (mean 9.8 s.d. 30), Socialization (mean 74.2 s.d. 42.6) and Daily Living Skills (mean 92.6 s.d. 22.8). Scores on Communication, Socialization, Daily Living Skills scales were not significantly related to IQ. On the ADI-R interview two subjects were above autism cut-off in two domains (Verbal Communication av. score 9.5 s.d. 2.1 and Non Verbal Communication av. score 7 s.d. 1.4; Social Reciprocal Interaction av. score 11.5 s.d. 7.7). On ADOS test the same subjects were above autism cut-off (Communication and Language av. score 3; Social Reciprocal Interaction av. score 10 s.d. 4.2).

Conclusions: This study provide a description of ASD symptoms in subjects with SMS based on objective, validated assessment techniques. Data from the current study indicate that 2 of the 5 subjects with Smith-Magenis Syndrome show symptoms of Autism Spectrum Disorder. These results might be used to drive more effective and individualised intervention in subjects with SMS.

111.023 23 The Measurement of Reduced and Oxidized Glutathione Levels in the Sera of Autistic Children in Oman.

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Background: Glutathione is the major intracellular antioxidant and it plays a crucial role in cellular defense against oxidative stress generated by free radicals. The ratio of reduced glutathione (GSH) to oxidized glutathione (GSSG) is an indicator for the cellular redox status. Recent studies have shown that autistic children have a low GSH/GSSG ratio as compared to controls group. There are no published reports about such studies in Oman.

Objectives: This study is aiming to measure the following biochemical parameters in the serum samples of autistic children that are recruited for this study:

1- Reduced glutathione (GSH) level.

2- Oxidized glutathione (GSSG) level.

Methods: A cross-sectional study that involves screening recently diagnosed autistic children in Oman, for GSH/GSSG ratio estimation using commercial assay kit, catalog #k264-100, Biovision *Inc, USA*.

Results: A low GSH/GSSG ratio indicates a cellular oxidative stress as evident by low level of reduced GSH as compared to oxidized GSH level.

Conclusions: Results of this study will emphasize the oxidative stress role in the pathogenesis of autism in Oman.

111.024 24 The Role of FMR1 in the Language Profile Associated with the Broad Autism Phenotype. J. Klusek* and M. Losh, *University of North Carolina at Chapel Hill*

Background: Fragile X syndrome (FXS) is the most common known cause of autism. The gene causing FXS (*FMR1)* is associated with significant genetic risk for autism, with 21-50% of individuals with FXS meeting criteria for autism (Moss & Howlin, 2009). While the genetic basis of autism is well established, detection of susceptibility loci has proven challenging. Studies of autism and the broad autism phenotype in genetically defined syndromes such as FXS provide the rare opportunity to examine potential gene-behavior associations in an etiologically homogeneous condition.
This study investigated the role *FMR1* in autism symptomatology through the study of 1st degree relatives who are at increased genetic liability (and in the case of FXS, who are *FMR1* premutation carriers). Specifically, we examined particular language phenotypes that may index genetic liability to autism, and which could be linked to *FMR1*. Language impairment is core to both autism and FXS, and is thought to be genetically mediated. Specifically, phonological processing and verbal fluency have been documented as weaknesses associated with autism. Phonological processing and verbal fluency skills seen in *FMR1* premutation carriers and mothers of children with autism may constitute genetically meaningful features related to autism, and may therefore help to illuminate a possible role of *FMR1* in the presentation of autism and the broad autism phenotype.
Objectives: This study characterized the language domains of phonological processing and verbal fluency in 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 associated with autism.

Methods: The rapid automatic naming (RAN) and non-word repetition (NWR) subtests of the Comprehensive Test of Phonological Processing (Wagner, Torgesen & Rashotte, 1999) were administered to mothers of individuals with FXS (n=52), autism (n=24), and typically-developing children (n=15) to assess verbal fluency and phonological working memory. RAN was scored live for completion time and number of errors. NWR was scored from video by a trained, blinded rater for total number of errors. Ten percent of NWR samples were randomly selected and scored for intra-rater reliability (95% agreement).

Results: Analyses indicated significantly longer RAN completion times for autism and FXS mothers in comparison to controls (p=.032, p=.005, respectively). No significant differences were detected between the FXS and autism parent groups (p= .900). No significant differences were found in RAN total number of errors (F(2,88)=.080, p= .923) or NWR total number of errors (F(2,57)=.698, p=.502).

Conclusions: Both mothers of children with FXS and mothers of individuals with autism presented with overlapping profiles in verbal fluency skills, relative to controls. Phonological processing skills were not found to be impaired in either group. These findings suggest that verbal fluency skills may be a component feature of the broad autism phenotype and that *FMR1* could play a role in this phenotype associated with genetic liability to autism.

111.025 25 The Serotonin-Melatonin Pathway in Autism Spectrum Disorders: An Extensive Biochemical Study. C. Pagan*[1], P. Chaste[2], E. Herbrecht[3], J. Callebert[4], E. Jacqz-Aigrain[5], M. F. Hurtaud[6], M. Leboyer[3], T. Bourgeron[7], J. M. Launay[4] and R.

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Background: Autism is known to be associated with hyperserotoninemia and, more recently, with decreased blood melatonin level. Melatonin is a neurohormone synthesized from serotonin and involved in circadian rhythms and sleep regulations. Thus, serotonin and melatonin are two ends of a biochemical pathway, and little is known concerning all the steps of this pathway in patients with Autism Spectrum Disorders. Moreover, the clinical relevance of these biochemical endophenotypes remains to be determined.
Objectives: Here we explore the serotonin-melatonin pathway in a large cohort of patients with ASD, in order to (i) better characterize the biochemical abnormalities of this pathway in ASD, (ii) determine the clinical correlates of these biochemical abnormalities, and (iii) assess the relevance of these biochemical parameters as biomarkers for ASD diagnosis.
Methods: The five parameters related to the serotonin-melatonin pathway, i.e. serotonin, arylalkylamine N-acetyltransferase (AA-NAT) enzyme activity, N-acetylserotonin, acetylserotonin methyltransferase (ASMT) enzyme activity, and melatonin, were measured in the blood of 203 patients with ASD, their unaffected relatives (291 parents and 92 sibs), and age- and sex-matched controls. Biochemical data were correlated with clinical data obtained from ADI-R for 117 patients.
Results: Patients with ASD display elevated blood serotonin and N-acetylserotonin levels ($p<0,001$) compared to controls and unaffected relatives, and decreased ASMT activity and melatonin levels ($p<0,001$) compared to controls. When confronted to clinical data, melatonin deficiency appears significantly associated with stereotyped behavior (ADI-R axis D, $p=0,003$). Finally, comparisons between ASD patients, controls and unaffected sibs on the one hand, and between autism and Asperger syndrome on the other hand, reveal that hyperserotoninemia is a relevant biomarker of autism, with good specificity and sensitivity.
Conclusions: This study confirms the previously reported major abnormalities of the serotonin-melatonin pathway in ASD. The typical biochemical profile of ASD patients suggests a deficit of the ASMT enzyme, consistent with our previous work. Serotonin and melatonin are both clinically relevant parameters, serotonin as a specific biomarker of autism, and melatonin for behavioral correlates. These results highlight the clinical interest of the serotonin –melatonin pathway in ASD, and its potential role as a susceptibility factor to autism.

111.026 26 Use of the Social Responsiveness Scale as a Screening Tool for Children Referred for Evaluation of Developmental Disabilities. E. M. Griffith*, S. E. O'Kelley, T. Perez, F. J. Biasini, K. Guest and K. J. Bailey, *University of Alabama at Birmingham*

Background: Clinicians conducting diagnostic assessments of children at risk for developmental disabilities face the challenge of obtaining both a broad overview of functioning, as well as specific information to aid in differential diagnosis. Moreover, often children are referred with general developmental concerns, but present to clinic as requiring more specialized assessment, such as for Autism Spectrum Disorders (ASD). Very few well-validated screening tools are available for identifying children, especially school-aged, in need of ASD-specific evaluations. Yet with increased awareness and recognition of the symptoms of ASD in the general population, evaluation requests are increasing.

Objectives: To evaluate the utility of the Social Responsiveness Scale (SRS) in an interdisciplinary tertiary care clinic serving school-aged children and to determine its utility for:

· identifying children referred to a general developmental clinic who were in need of more specific ASD evaluations,
· assisting clinicians in either ruling in or ruling out a diagnosis of ASD

Methods: The SRS was completed in both a general developmental interdisciplinary clinic (IDC) (as a screening tool) and an interdisciplinary Autism Clinic (AC) (as a supplement to the ADOS and ADI-R). Final diagnoses were determined by members of the interdisciplinary team based on all available data and clinical impressions.

Results: The SRS has been completed on 40 children across both clinics, with final diagnosis available on 23 children (mean age = 7 years) at present. Seven of the children received diagnoses of ASD, with other children receiving diagnoses of language disorders, intellectual disability, mixed developmental delays, learning disabilities, anxiety or mood disorders, and disruptive behavior disorders. Using a Total raw score cutoff of 85 (appropriate for clinical populations with increased likelihood of ASD), 11 children exceeded the cutoff for significant difficulties in reciprocal social behavior. Eight of these children were receiving ASD-specific evaluations, while the remaining 3 were undergoing general developmental evaluations. Positive predictive value of the SRS in the combined clinical sample was 36%, while negative predictive value was 75%. Notably, positive predictive value of the children evaluated through IDC was 0%, as none of the three children (despite their caregivers suspecting ASD) actually received this diagnosis. Evaluations and analyses are ongoing and will allow for further exploration of the use of the SRS in an anticipated clinical sample of at least 60 children.

Conclusions: Based on preliminary data, a number of children without ASD are being identified as exhibiting significant difficulties in reciprocal social behavior within this tertiary care setting, with nearly half of the sample screening positive for likely ASD, but only 30% receiving a clinical diagnosis of ASD. Further analyses will investigate factors that influence the predictive value of the SRS, including initial referral question, as well as cognitive and adaptive functioning.

111.027 27 Validating the Accuracy of a Rapid Phenotyping Paradigm Using Web-Based Parent Input. H. Lee*[1], A. R. Marvin[2], T. Watson[3], J. Piggot[1], S. S. Marvin[2], E. Yahudah[2], R. Friedman[2], S. Scheller[2], J. K. Law[2], P. Law[2], J. N. Constantino[3] and S. F. Nelson[1], (1)*University of California, Los Angeles*, (2)*Kennedy Krieger Institute*, (3)*Washington University School of Medicine*

Background: Autism is known to be substantially inherited but specific molecular genetic abnormalities have only been identified for a small minority of all cases, indicating that there may be a large number of distinct genetic risk factors, each with relatively small explanatory power, either in the form of many rare strong effect variants, or common variants of modest effect. In order to delineate the genetic component of autism and identify specific genetic variants, sample sizes much larger than those currently under study will be needed. Despite tremendous efforts, only 3-4000 European-descent autism families are currently available for genetic study even with 15-20 years of sample collection and phenotyping effort.

Objectives: The objective of this study is to demonstrate the accuracy of a rapid phenotyping paradigm consisting of brief parent- and teacher-report questionnaires, and medical record documentation of autism spectrum disorder (ASD) diagnosis, in order to minimize the costs and time of sample recruitment in the interest of more rapidly increasing the available sample size.

Methods: Families were invited to participate via the online Interactive Autism Network (IAN). The IAN registry, which grows at 300 individuals per month, currently has over 11,000 families registered with at least one autistic child: less than 5% have participated in genetic studies, but indicate willingness to participate. In order to assess the diagnostic specificity of the recruitment procedure, an email recruitment letter was sent to ASD-affected families in which the probands were: *verbal* (this is the case for 74% of the families in IAN); age 4-18 years; living near UCLA, Kennedy Krieger Institute or Washington University, St. Louis; had Social

Communication Questionnaire (SCQ-lifetime version) scores greater than or equal to 12 at the time of entry. These families were invited to one of the three clinics and assessed by ADI-r (Autism Diagnostic Interview-Revised), VABS (Vineland Adaptive Behavior Scale), an observational confirmation procedure (Autism Diagnostic Observation Schedule—ADOS—at 2 sites, expert-clinician observation at the third), followed by clinician best estimate diagnosis (BE).

Results: Interim analysis of the sample set was performed after 47 families were enrolled and assessed. 100% were ASD positive by BE and 100% were ASD positive by developmental history on the ADI-r. 91.5% were also positive by ADOS / clinical observation (this figure improved to 95% when excluding patients on the basis of sub clinical teacher-report Social Responsiveness Scale (SRS) score), suggesting that a few of the children with an established historical diagnosis may have substantially improved by the time of this study. There were no significant demographic or phenotypic differences between the enrolled probands and the larger population of verbal ASD subjects registered in IAN.

Conclusions: These data support the reliability of a rapid phenotyping paradigm for verbal subjects with ASD, and constitute a fundamental aspect of feasibility for large-scale efforts to advance—by an order of magnitude—the world collection of family-based biomaterials for autism genetic research.

111 Cognition

111.028 28 "Everyday Memory" Impairments in Autism Spectrum Disorders. C. R. G. Jones*[1], F. Happé[2], A. Pickles[3], A. J. S. Marsden[4], J. Tregay[4], G. Baird[5], E. Simonoff[6] and T. Charman[1], (1)*Institute of Education, University of London*, (2)*Institute of Psychiatry, KCL*, (3)*University of Manchester*, (4)*UCL Institute of Child Health*, (5)*Guy's Hospital*, (6)*Institute of Psychiatry*

Background: The term 'everyday memory' refers to the use of memory in day-to-day life. For example, remembering directions, remembering to carry out a chore at a particular time, or remembering to ask someone something. Despite anecdotal evidence suggesting that individuals with Autism Spectrum Disorders (ASD) have difficulty with everyday memory, this hypothesis has yet to be formally tested. Objectives: To test the everyday memory abilities of individuals with ASD. Methods: 94 adolescents with an ASD (mean age 15 years 6 months (SD 6 months); mean full scale IQ 85.4 (SD 17.7)) and 55 age- and IQ-matched adolescents without an ASD completed measures of everyday memory from the Rivermead Behavioural Memory Test (RBMT) and a standard word recall task (Children's Auditory Verbal Learning Test-2: CAVLT-2). Four subtests from the RBMT were selected: Route and Message, Appointment, First and Second Name, and Belonging. The subtests all measure the ability to remember within in an everyday context (e.g. remembering what to do when an alarm rings; remembering a route). Results: The group with ASD showed significant impairments on the RBMT, alongside impaired performance on the CAVLT-2. Social and communication ability was significantly associated with spontaneous remembering in an everyday memory context but not with the CAVLT-2. Conclusions: This is the first study to suggest that everyday memory is impaired in ASD. Further, we interpret the data as suggesting that poor social and communication skills in ASD impact upon everyday memory competence.

111.029 29 Absence of Lateralization of Visual Scanning to Varying Facial Affect in Toddlers with Autism. L. A. Edwards*[1], G. Ramsay[2], W. Jones[2] and A. Klin[1], (1)*Yale University School of Medicine*, (2)*Yale School of Medicine*

Background: The ability to derive socially relevant information from faces is fundamental to interpersonal communication and reciprocal social interaction. Studies in typically-developing individuals have demonstrated that emotional facial affect is expressed on the face in a laterally asymmetric manner: using chimeric faces, in which an image of the face is bisected vertically so that its left or right half is mirrored about the midline to create a new image, left side composites are rated as more emotionally intense than right side composites. These findings, however, have not been extended to the case of dynamic

facial stimuli, nor have they been extended to test the effect of this lateralization on the way that viewers look at faces. We hypothesized that visual scanning of faces exhibiting dynamic and varying facial affect would reflect these lateral asymmetries in expression, with the central tendency of fixation locations shifting toward the side of the face showing greatest emotional expression.

Objectives: This study examines lateralization of visual scanning in typically developing toddlers and toddlers with autism during viewing of dynamic faces displaying a range of naturally-occurring intensity and valence of affect.

Methods: Two-year-olds with autism spectrum disorders (age = 2.28 (0.58) years; gender = 11M, 4F; n = 15) and control children matched on age-, verbal-, and nonverbal function (age = 2.03 (0.68) years; gender = 24M, 12F; n = 36) watched video scenes of female actors playing the role of caregiver, while eye-tracking data were collected. Dynamic facial expressions in the caregiver videos were quantitatively ranked by adult observers, naïve to the aims of the study, for intensity and valence of affect using a modified analytic hierarchy process of paired comparisons. Then, using the ratings of affect as a regressor, we examined lateralization of visual fixation data in relation to varying degree of naturally-occurring facial affect.

Results: Preliminary results suggest that both emotional intensity and valence of dynamic faces alter visual fixation patterns and lateralization of gaze in two-year-old, typically-developing children. In examples of positive and high intensity social affect, typically-developing two-year-olds show increased visual scanning of the female actors' left hemifaces. In two-year-olds with autism, however, facial expressions have little impact on visual scanning, and no lateralization trends are apparent. Across varying social affect, toddlers with autism looked 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.

111.030 30 An Exploration of Mathematical Abilities in High Functioning Autism (HFA). C. Piatt*, C. Korenowski, J. Volden and J. Bisanz, *University of Alberta*

Background:

Asperger (1944) asserted that observing *how* individuals think is as important as establishing the level at which individuals think. In studies of cognitive development, assessing strategy use has been a productive avenue for understanding how children think (Pressley & Hilden, 2006; Siegler, 2005). Variability in generating and using strategies when solving math problems is associated with increased generalization (Alibali, 1999; Siegler, 2006). Therefore, investigating strategy generation and use is proposed as a way to describe how children with ASD think and eventually, as a way to investigate generalization – a difficult process for children with ASD (Klin et al., 2005).

Both Asperger (1944) and Kanner (1943) provided limited descriptions of how children with ASD solved math problems. Since the 1940s studies of math in ASD have been focused on standardized measures of math skills (reviewed by Chiang & Lin, 2007) or on savant skills such as calendar calculation (e.g., Thioux et al., 2007). There has been little, if any, work on *how* children with ASD learn about math or if they show the same kind of strategy generation, use, and variability observed in typically developing children.

Objectives:

To investigate the development of mathematical thinking in children with high functioning autism (HFA) by exploring their

performance, reasoning, and strategy use on tasks that are well-characterized in typical development such as equivalence problems (e.g., 6 + 3 + 7 = ___ + 7) (Alibali et al., 2009) and the principle of inversion where *a + b – b must* equal *a* (Bisanz et al., 2009; Siegler & Stern, 1998).

Methods:

Measures of mathematical thinking including counting, estimation, equivalence, and inversion were given during play-based sessions that were video-taped. Two boys (ages 6 and 9 years-old) with HFA, both recruited from the community and both in mainstream classrooms, have participated. Recruitment continues.

Results:

Both boys showed robust math abilities and used distinct strategies. For example, when solving two-digit arithmetic problems presented either numerically or in the context of word problems, W.K., age 6, used two strategies in combination, a counting-on strategy and keeping track of his counting by using parallel number lines (i.e., for 31 minus 12, counting "13, 1, 14, 2, 15, 3…" and so on until 31) instead of using another means, such as his fingers. In another example, R.A., age 9, was able to explain correct use of the shortcut inversion strategy (e.g., for 13 + 24 – 24 explaining that adding and subtracting the same thing leaves 13) when solving inversion problems presented both with Arabic numerals and arbitrary non-numeric symbols.

Conclusions:

This study is the first to explore the strategies children with HFA use as they solve math problems. As the study continues we will be able to document the range and effectiveness of strategies used by children with HFA. In addition, self-reports of the strategies used by both boys suggest that children with HFA may be able to reflect on and describe their problem-solving approach.

111.031 31 Beta-Adrenergic Modulation of Context Processing in Individuals with An Autism Spectrum Disorder. K. E. Bodner*[1], S. S. Saklayen[2], D. Q. Beversdorf[1] and S. E. Christ[1], (1)*University of Missouri*, (2)*The Ohio State University*

Background: Previous studies have shown improvements in cognitive flexibility and verbal problem solving following administration of a beta adrenergic antagonist to individuals with an autism spectrum disorder (ASD). The observed effect is presumed to be related to the adrenergic projections to the prefrontal cortex and related brain regions. It remains unclear, however, to what extent this benefit may extend to other prefrontally-mediated aspects of executive function.

Objectives: To evaluate the potential effect of propranolol, a beta-adrenergic antagonist, on additional aspects of executive function (i.e., working memory and inhibitory control) using a context processing task in individuals with and without an ASD.

Methods: An AX continuous performance test (AX-CPT) was used to assess context processing in 14 individuals with an ASD (mean age = 18.8 yrs; mean FSIQ = 103) and a demographically-matched comparison group of 13 typically developing individuals (mean age = 19.2 yrs; mean FSIQ = 108). In the AX-CPT, participants were shown a series of cue-probe letter pairs, with each cue letter being followed shortly by a probe letter. They were instructed to press a target button when the probe letter *X* followed the cue letter *A.* For all other cue-probe combinations, they were to press a non-target button. AX cue-probe stimuli were presented on 70% of the task trials. The remaining 30% of trials were split evenly across 3 additional conditions: (1) the AY condition in which the cue letter A was followed by a letter other than X, (2) the BX condition in which the cue was a letter other than A but the probe was still X, and (3) the BY condition in which neither the cue nor probe were A or X. Performance in the AY condition is taken as a measure of inhibitory control in that participants must inhibit the prepotent tendency to respond to a probe following the cue letter A. Also, good working memory can aid in performance in the BX condition. (Participants may press the target

button in response to a probe letter X if they cannot remember what preceded it.)

Results: Overall the groups performed comparably in the AY condition of the task, suggesting intact inhibitory control for the ASD group [Main effect of group: $F(1, 24)=1.64$, $p>.2$]. In contrast, individuals with ASD made more errors in the BX and BY conditions of the task, consistent with working memory difficulties [Main effect of group: Fs$(1, 24)>8.90$, $p<.05$]. Importantly, administration of propranolol was associated with improvements in working memory (i.e., decreased number of BX errors) for the ASD group but had no effect on performance in the control group [Group by Rx Interaction: $F(1, 24)=5.53$, $p<.05$]. Other aspects of task performance (e.g., inhibitory control as reflected by AY errors) were unaffected [$p>.05$ in all instances].

Conclusions: The present findings suggest that pharmacological treatment with propranolol may help individuals with ASD to overcome difficulties with executive control and context processing. Additional research, however, is needed to better understand the neurophysiological mechanisms underlying this observed effect.

111.032 32 Children with Autism Use Emotional but Not Referential Cues to Predict Others' Actions. G. Vivanti*[1], C. McCormick[2], G. S. Young[1], N. Hatt[3], F. Abucayan[1], A. Nadig[4], S. Ozonoff[5] and S. J. Rogers[5], (1)*UC Davis M.I.N.D. Institute*, (2)*M.I.N.D. Institute, University of California Davis*, (3)*University of California, Davis*, (4)*McGill University*, (5)*M.I.N.D. Institute, University of California at Davis*

Background:

Predicting others' actions is a crucial ability that underlies cognitive and social development. Typically developing children predict agents' actions relying on social cues such as the agent's head and gaze direction and her emotional expressions. In the current study, we investigated to what extent children with autism are able to identify and use such signals to predict an agent's behavior.

Objectives:

The aim of the study is to test 4 hypotheses:

(1) Children with autism will be able to predict an agent's action by relying on the most likely end-state of the action and the standard use of the materials

(2) Unlike typically developing children, children with autism will not be able to predict the agent's behavior relying on the agent's head and gaze direction

(3) Unlike typically developing children, children with autism will not be able to predict the agent's behavior by relying on the agent's emotional expressions

(4) Children with autism will fail to predict the agent's behavior as a consequence of diminished attention to changes in the agent's head direction and emotional expressions

Methods: 18 8- to 12-year old children with high functioning autism and typically developing subjects matched for IQ and age observed a series of videos showing a person performing an action. The videos stopped before the action was done and participants were asked to complete the observed action. There were three conditions. In condition 1 the agent's face was neutral and the action itself was sufficient to predict the agent's behavior. In condition 2 the agent's behavior could be predicted only by considering the agent's gaze direction. In condition 3 the agent's behavior could be predicted only by considering her emotional expressions. During the observation of the videos, participants' eye movements were recorded using an eye-tracking system.
Results:

As predicted, in condition 1 the two groups did not differ in the ability to predict the agent's behavior relying on the most likely end-state of the action. In condition 2, however, children with autism showed significant difficulties in predicting the agent's behavior on the basis of her gaze direction. Eye-tracking analysis revealed that that was a consequence of their diminished attention the agent's face. In condition 3, surprisingly, both groups were able to predict the agent's behavior based on her emotional expressions. Eye-tracking analyses revealed

that in this condition children were looking at the agent's face as much as participants in the control group.

Conclusions:

Difficulty in predicting others' actions is not a unitary phenomenon in autism. Children with autism might not be able to predict others' behavior because they do not detect referential cues such as an agent's gaze and head turning. However, when the agent displays emotional expressions, children with autism pay "normal" attention to her face and successfully predict her actions. Implications for treatment will be discussed.

111.033 33 Cognitive Flexibility in Autism Spectrum Disorders: Deficits On a Pure and Sensitive Card Sorting Task. L. Van Eylen*[1], J. Steyaert[2], J. Wagemans[1] and I. L. J. Noens[1], (1)*Katholieke Universiteit Leuven*, (2)*UPC-K.U.Leuven*

Background: The rigid and repetitive pattern of interests and activities seen in individuals with an autism spectrum disorder (ASD) has been related to deficits in cognitive flexibility. However, studies examining this cognitive flexibility deficit in ASD have yielded inconsistent findings, mainly due to differences is tasks used. There are two problems with these tasks. Firstly, some tasks are impure measures of cognitive flexibility, since task performance requires a broad range of cognitive processes. As a consequence it is questionable whether failure on these tasks is indeed due to cognitive flexibility deficits. Secondly, some tasks might not be sensitive enough to detect cognitive flexibility deficits.

Objectives: The aim of this research is to test whether or not children with an ASD have difficulties with cognitive flexibility on a more pure and sensitive task.

Methods: We modified a card sorting task previously used to investigate brain correlates of cognitive flexibility in healthy subjects (Watson, Azizan, & Squires, 2006). In this modified task subjects had to sort a target card according to colour or shape. After each response, feedback was given, indication which of the two possible sorting rules was correct. The sorting rule changed randomly after 7, 8 or 9 successive correct answers. Task performance was compare between 21 children with ASD (IQ > 80; aged between 8 and 14 years old) and 21 healthy controle subjects, matched for age, verbal IQ, performal IQ, full-scale IQ and gender.

Results: Compared to healthy control subjects, children with an ASD made significantly more perseveration errors and they anticipated a switch less frequently. Concerning the reaction times, both groups showed significant switch costs. In addition, these costs were higher for children with an ASD compared to healthy controls.

Conclusions: These results indicate that children with an ASD do have problems with cognitive flexibility, even when measured with a controlled experimental task. However, it remains to be investigated whether performance on this task correlates with day-to-day behavioural flexibility, and whether it can explain the pattern of rigid and repetitive interests and activities seen in children with an ASD.

111.034 34 Discriminant Validity of ToM Storybooks and TEC in An Italian Sample of PDD Children. P. F. M. Molina, D. Bulgarelli and E. Salomone*, *University of Turin*

Background: The "theory of mind" (ToM) deficit, the ability to attribute representational mental states, is one of the core deficits in Pervasive Developmental Disorders (PDDs). The difficulty in attributing mental states such as beliefs, intentions and desires to oneself and others is considered to be responsible for the major impairments in the social and communicative domains in autism. Emotional comprehension is another specific deficit in autism which can account for the peculiarities of the social communication in PDDs. A main line of research in the field concerns therefore the designing of tests and tasks to assess this abilities and their interrelationship in PDD subjects. The ToM Storybooks (Blijd-Hoogewys, et al., 2008) measures a full range of ToM components and it is not limited to the standard false belief task, differently from the classical research tasks. TEC (Test of Emotion Comprehension: Pons, Harris, 2000; Albanese, Molina, 2008) is meant to assess emotion comprehension as defined by

several components concerning the nature and causes of emotions, and the control of emotional expression. ToM Storybooks and TEC are promising tools for the evaluation of ToM and emotion comprehension respectively in PDDs. Both tests have been translated into Italian by the proponents and are currently being standardized on the Italian population. The standardization sample of the TEC includes 967 Italian children, stratified by gender, age (3-11 years) and region (North or Centre of Italy), while the ToM Storybooks Italian standardization study includes 204 normally developing children (from 3 to 8 years, equally distributed by gender and year of age). The overall correlation between the two tests is good, even controlling for age (N=60; rho=.77, p<.01; controlling for age: r=.37, P<.01).

Objectives:

The current study aims at verifying ToM Storybooks and TEC discriminant validity in a sample of PDD subjects and at confirming the correlation between the two instruments in atypically developing children.

Methods: The study includes 9 PDD children (all males, were diagnosed according to ICD-10; average chronological age=114 months) so far, and we expect to collect data on 20 more children in the next months. ToM Storybook and TEC were administered to all subjects. Leiter-R Scale and PPVT-R were used to control for non-verbal cognitive level and linguistic competence respectively.

Results:

All children show a delay in linguistic competence (PPVT-R standardized score: mean=80.67; SD=14.63), while the non verbal cognitive IQ is good (Leiter-R: mean=101; SD=15.47). Nevertheless, the most severe delay regards the social cognition: both TEC and ToM Storybooks performances are lower than 25° percentile for all the children but one (TEC standardized score: mean=-1,88, SD=1,66). The correlation between the tests is very good (r=.761, p<.05), even controlling for age (r=.813, p<.05), for IQ (r=.730, p<.05) and for language (r=.814, p<.05). A matching procedure (Jarrold, Brock, 2004) with a typically developing sample is ongoing and will be discussed at the congress.

Conclusions:

Our data seem promising in supporting discriminant validity of TEC and ToM Storybooks in respect of social cognition evaluation in PDD children, and confirm the relationship between the two tests.

111.035 35 Divided Auditory Attention in Children with Autism Spectrum Disorders. M. Wills*[1], B. Yerys[2], J. James[1], R. Oliveras-Rentas[1], G. L. Wallace[3], D. O. Black[3], K. F. Jankowski[1], A. M. Bollich[1] and L. Kenworthy[1], (1)*Children's National Medical Center*, (2)*Children's National Medical Center, George Washington University*, (3)*National Institute of Mental Health, National Institutes of Health*

Background: Auditory divided attention, or the ability to simultaneously complete two independent auditory tasks, is critical for completing complex multi-step tasks, which may be social (participating in a 'to and fro' conversation), or non-social (getting dressed). Although multi-step tasks are particularly difficult for children with autism spectrum disorders (ASD), auditory divided attention has not, to our knowledge, been previously been investigated in ASD.
Objectives: To examine auditory divided attention in children with high-functioning ASD, and to ascertain its relevance to social and executive functioning.
Methods: In Study 1, a clinic-referred sample of 89 children with high-functioning ASD (diagnosed using DSM-IV criteria, ADI and ADOS) received a comprehensive multidisciplinary evaluation. Data collected from the Score-DT subtest of The Test of Everyday Attention for Children (TEA-Ch) was used to assess auditory divided attention. Regressions between composite ADI/ADOS domain scores, Score-DT performance, other executive tasks and nuisance variables were conducted to measure the relationship between auditory divided attention and ASD symptoms.
In Study 2, 28 children with high-functioning ASD and 18 typically developing children were matched on age, IQ, sex-ratio, and socioeconomic status. To measure auditory divided attention, a child-friendly version of the Consonant Trigrams Test (CTT) was

administered to both groups. As an alternative measure of ASD symptoms, the Social Responsiveness Scale (SRS) was implemented. Total scores on the CTT and the SRS were correlated to determine the relationship between auditory divided attention and ASD symptoms. Parental reports were collected with the ADHD Rating Scale and the Behavior Rating Inventory of Executive Function (BRIEF) to better assess the attention and working memory components of the CTT.
Results: Within the ASD sample, multiple regression revealed that performance on the Score-DT task predicted autism social domain scores (t =-2.77, p< .02), even after accounting for age and other executive abilities.
In the 2nd study, scores on the CTT were significantly higher for typically developing children than their matched ASD's, t(44)=3.15, p≤.001. However, when ADHD symptom ratings were included as a covariate, group differences were no longer significant, F(1,37)=1.79, p=.18. Despite the elimination of group differences, the inclusion of ADHD symptoms as a covariate strengthened the relationship between CTT performance and the working memory subscale of the BRIEF, r(22)=-.43, p<.05.
Finally, the correlation between total SRS score and performance on the CTT, although non-significant, was of moderate effect size, r(28)=-.27, p=.17.
Conclusions: Children with high-functioning ASD demonstrate a diminished ability to divide attention between auditory stimuli compared to matched controls. Furthermore, divided attention capacities relate to the severity of social impairment in ASD. Divided attention in ASD is moderated, however, by ADHD symptoms, an important finding that should be further explored. Taking the two studies together, the ability to divide attention during auditory tasks relates to greater social and executive impairments and may constitute an intervention target to improve academic and social functioning.
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111.036 36 Executive Function and Symptom Expression Among High Functioning Children with ASD. S. Faja*[1], G. Dawson[2] and J. Tiwana[3], (1)*The Children's Hospital of Philadelphia*, (2)*UNC Chapel Hill*, (3)*University of Washington*

Background: It has been hypothesized that some symptoms of autism may be related to prefrontal dysfunction. Yet ASD symptom severity has not been consistently correlated with executive function (EF) ability (e.g., Landa & Goldberg, 2005; Ozonoff & McEvoy, 1994; Ozonoff et al., 2004). A relation between social communication skills and tasks related to executive function was found in preschoolers with autism and controls (McEvoy et al., 1993). However, Stahl & Pry (2002) presented evidence for a relation between shifting and joint attention only in typical controls, but not a group with ASD.

Objectives: To test whether young, high-functioning children with ASD exhibit impairments in an EF task requiring set-shifting and flexibility, the Dimensional Change Card Sort Task (DCCS; Carlson, 2005; Frye et al., 1995). And, to test whether performance on this measure relates with symptom expression.

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 and additional assessment of symptom severity included the Social Skills Rating System (SSRS) and Repetitive Behavior Scale-Revised (RBS-R). All children in both groups had cognitive ability in the average to above average range. The DCCS was administered to assess EF. Children were first presented with a sorting dimension, and then the sorting dimension was switched. Finally, both dimensions were combined and an extra-dimensional symbol indicated the dimension by which to sort.

Results: Groups did not differ in the number of items correct during the post switch phase, $t(17) = -1.37$, $p = .19$, or the proportion of passes during the extra-dimensional phase, $\_^2$ (1, N = 38) = 2.62, $p = .11$. Yet, the number of correct sorts during the extra-dimensional phase made by each group approached significance, $t(36) = -1.926$, p =

.06. With groups combined, the SSRS standard score related with the number of correctly sorted cards in the extra-dimensional phase, $r(39) = .505$, $p = .001$. Among children with ASD only, the score for extra-dimensional sorting related to the SSRS standard score, $r(19) = .558$, $p = .009$, and the Responsibility subscale, $r(19) = .543$, $p = .011$. A significant inverse relation between the total number correct during the extra-dimensional phase and the ADOS Social Affect score, $r(19) = -.48$, $p = .03$ was also detected. Children with greater symptom scores in the Social Affect ADOS domain had lower accuracy in extra-dimensional sorting during the DCCS. The DCCS did not relate with the RBS-R.

Conclusions: Groups did not significantly differ on the DCCS and children with ASD were not universally impaired on this task. Yet, this measure of basic EF directly related with observed ADOS Social Affect symptoms and overall social function measured by parent report on the SSRS. This suggests that by early school age, EF ability is related to social communication functioning in non-cognitively impaired children with ASD. These findings have implications for understanding the neural substrates of social impairment in ASD.

111.037 37 Greater Face-Gender Effects On Emotional Face Preferences in Infant Siblings of Children with Autism Spectrum Disorders (ASD). L. J. Carver*[1], V. Sampath[2] and K. R. Dobkins[3], (1)*UC San Diego*, (2)*University of California San Diego*, (3)*University of California, San Diego*

Background:

Previous studies have documented atypicalities in processing facial expressions of emotion in children and adults with autism spectrum disorders (ASD). 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 looking preferences to facial expressions of emotion 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).

Methods: Data from 38 Low-Risk (15F, 23M) and 16 High-Risk (5F, 11M) infants contributed to this study. Forced-Choice Preferential Looking was used to measure infants' preferences to black and white pictures of "Disgust", "Happy" and "Neutral" faces (obtained from www.macbrain.org). Each infant was tested with three different pairings: 1) Disgust vs. Neutral, 2) Happy vs. Neutral, and 3) Happy vs. Disgust. On each trial, one of the three pairings was presented, with one emotion presented on the left, and one on the right, side of the video monitor. The left/right position and the emotional pairing were randomized across trials. After each trial, the experimenter (blind to the monitor) judged which side (left or right) the infant preferred to look at. Six different faces were employed, with the gender of the face (Face-Gender) being split (3 Female, 3 Male). Within a condition, values greater than 50% indicate a preference for one emotion over another. Two-factor ANOVAs (Subject Group x Face-Gender) allowed us to look for overall group differences, effects of Face-Gender of emotional preferences, and the interaction between the two.

Results: For Disgust vs. Neutral, both groups showed a preference for Disgust (Low-Risk: 56.1%, $p = 0.0001$, High-Risk: 59.3%, $p = 0.001$), but there was no group difference. There was, however, a significant interaction between Subject Group x Face-Gender ($p = 0.04$), which was driven by a significant Face-Gender effect in High-Risk infants ($p = 0.01$), but not in Low-Risk infants. Specifically, for High-Risk infants, the Disgust preference was significantly greater for Female faces (66.4%) than Male faces, (52.2%). And, for Female faces, the Disgust preference was significantly greater in High-Risk than Low-Risk infants ($p = 0.01$). Interestingly, for Happy vs. Neutral, both groups showed a preference for Happy, but only for Male faces (Low-Risk: 54.0%, $p = 0.05$, High-Risk: 59.4%, $p = 0.03$). Neither group showed significant preferences for Disgust vs. Happy, presumably because the two emotions are equally salient.

Conclusions:

These preliminary behavioral data suggest larger Face-Gender effects on emotional face processing in High-Risk infants. Specifically, for Female faces, High-Risk infants exhibit an exaggerated preference for Disgust. This could arise either from fundamental differences in emotional processing (e.g., greater amygdala responses to negative emotions) or atypical experience with disgusted faces (e.g., perhaps disgusted female faces are more novel in their environment). Either way, such differences could provide a potential endophenotypic marker associated with ASD.

111.038 38 HOW Magic Changes Our Expectations about AUTISM. S. R. Leekam*[1], G. Kuhn[2] and A. Kourkoulou[1], (1)*Cardiff University*, (2)*Brunel University*

Background: Individuals with Autism Spectrum Disorder (ASD) are less sensitive to social cues and have superior perception for non-social details,

Objectives: We therefore predicted that they should be less susceptible to magic tricks, such as the ball illusion, in which the magician's social cues of head movement and eye gaze play a crucial role in misdirecting people's attention and expectations.

Methods: Participants were 15 high functioning ASD young adults 17-22 years and 16 age and IQ-matched comparison individuals. A magician demonstrated the trick in a videotaped presentation. Participants indicate where they had last seen the ball. Eyemovements were recorded. Results: Surprisingly, individuals with ASD were more susceptible to the illusion than the comparison group. Eye-tracking data indicated that subtle temporal delays in allocating attention might explain their heightened susceptibility. Additionally, although ASD individuals showed typical patterns of looking to the magician's face and eyes, they were slower to launch their first saccade to the face, and had difficulty in fixating the fast moving observable ball when it was thrown for real.

Conclusions: Considered together, the results indicate difficulties in the rapid allocation of attention towards both people and moving objects.

111.039 39 The Abstraction of Prototypes by Infants at Low and High Risk for Autism. M. S. Strauss*, H. Z. Gastgeb, K. W. Chua, S. Green, S. F. Hannigen and D. Wilkinson, *University of Pittsburgh*

Background: Prototype formation is a critical skill in forming categories. Prototypes are central representations of the average of variations within a category. Forming a prototype decreases memory load allowing individuals to store a single representation of experienced items. Within the first year, typical infants can form prototypes of faces [Rubenstein, Kalakanis,& Langlois, 1999; Strauss, 1979], objects [Younger, 1990], and dot patterns [Younger & Gotlieb, 1988]. Research on prototype formation in individuals with autism suggests that they may be unable to abstract prototypes. Klinger found that both children and adults with autism were unable to abstract a prototype of animal-like categories [Klinger, et al, 2006; Klinger & Dawson, 2001. Similarly, a recently published study (Gastgeb, et al., 2009) found that adults with autism were unable to abstract prototypes of faces.
Objectives: Given evidence that individuals with autism have difficulty abstracting prototypes, the current research was interested in studying whether infants who are at risk for developing autism as a result of having an older sibling with autism would also demonstrate difficulties abstracting prototypes. Given the extensive research literature (e.g., Rakison & Oakes, 2003) indicating that typical developing infants both form categories and abstract prototypes well before twelve months of age, and given the importance of these abilities for both learning about the world and developing language, deficits in these abilities by infants at-risk for autism would have a significant impact on their cognitive and social development. Thus, this research looked at the ability of high and low risk siblings to abstract prototype patterns. Methods: The study was designed after Younger & Gotleib (1988). Infants were tested at 6- and 11 months of

ages. The infants were either at high risk (HR) of developing autism because they had an older sibling(s) already diagnosed for the disorder, or at low risk (LR) for developing autism because they had older sibling(s) without autism. Infants were familiarized with category instances that varied around a prototypical dot pattern such as a "Z" made up of 9 dots. Category instances were constructed by randomly distorting the individual dots of the prototypical pattern. After familiarization, infants received pairings of the unseen prototype pattern next to a novel dot pattern. It was expected that, if the infants were abstracting the prototypical pattern, they would spend more time fixating the novel stimulus pattern. Infants looking times were determined objectively with eye-tracking technology.
Results: It was found that, LR infants at both ages were able to abstract the prototypical dot pattern ($t(27)= 2.41$, $p= .02$). In contrast, there was no evidence that the HR infants had abstracted the prototype ($t(22) = .40$, $p=.69$).

Conclusions: Similar to children and adults with autism, infants at risk for autism also have difficultly abstracting prototypes. Since the stimuli were dot patterns, this may have been the result of their inability to scan the pattern sufficiently to abstract an overall pattern. Eye-tracking data is being analyzed to determine if this was true. Importantly, the study demonstrates early core cognitive deficits in infants at risk for autism

111.040 40 The Development of Theory-of-Mind and the Theory-of-Mind Storybooks. E. M. A. Blijd-Hoogewys*[1], P. L. C. van Geert[2], M. Serra[3] and R. B. Minderaa[3], (1)*Lentis*, (2)*University of Groningen*, (3)*University Medical Center Groningen*

Background: Theory-of-Mind (ToM) is a social cognitive ability which typically developing (TD) children develop roughly between their third and sixth birthday. A well-known group of children with severe ToM problems is children with an autistic disorder. Less is known about the ToM functioning of children with lesser variants of autism, like children with PDD-NOS.

Objectives: The goal of this research was to get insight in the development of ToM abilities in children with PDD-NOS. This requires repeated measurements as well as a ToM instrument that can be applied in such a design. Because a new test was developed, the psychometric qualities of this test had to be dealt with and norm scores needed to be calculated. In order to compare developmental trajectory differences in children with PDD-NOS, also the ToM ability in typically developing children was researched more into detail.

Methods: A new test, the ToM Storybooks was developed. This is a comprehensive test measuring a variety of early ToM components and associated aspects children develop between their third and fifth year. Both TD children (N=324, 3-12 years) and children with PDD-NOS (N=30, 3-8 years) were administered the ToM Storybooks and language comprehension tests. The children with PDD-NOS were diagnosed as having PDD-NOS according to DSM-IV-TR criteria. Before being included in the research, they received an intelligence test and tests that could validate their diagnosis, namely the Vineland Adaptive Behavior Scales and the Children's Social Behavior Questionnaire. The children were tested every 4 months over a period of 20 months.

Results: The ToM Storybooks were found to have good psychometric qualities: the internal consistency, test-retest reliability, inter-rater reliability, discriminate validity, divergent and convergent validity was good. The ToM development in TD children was found to differ between boys and girls. Therefore, norms for both sexes were computed separately: ToM quotients and an age equivalents can be calculated. A three-step developmental model was obvious, with the greatest increase between 3.5 and 4.7 years of age. Next to that, two statistically significant discontinuities were found: at 56 and 72-78 months. These discontinuities, which took the form of temporal decreases, were accompanied by decreases in variability, suggesting a developmental shift in ToM understanding. Similar results could be established in children with PDD-NOS. Despite their obvious ToM problems, they also displayed a spontaneous ToM development. At the first measurement, they had

significant lower ToM scores than their TD peers. But, at the last measurement, they had caught up with their ToM delay. The same developmental sequence was followed, but at a slower pace. Also the temporal decrease in ToM score as known from the TD group was delayed in this group (at 85-90 months).

Conclusions: The ToM Storybooks have good psychometric properties. They can be used in both research and clinical settings. In contrast with existing models, we found evidence of a non-linear pattern of growth in both groups, comprising temporary regressions in ToM scores. The ToM development in children with PDD-NOS was delayed, not deviant.

111.041 41 Using Virtual Reality to Provide Controlled Ecologically Valid Social Interaction Paradigms for Studying Cognitive Control of Initiating Joint Attention. W. L. Jarrold*[1], M. Solomon[2], J. Bailenson[3], M. Gwaltney[1], S. Ozonoff[4] and P. C. Mundy[1], (1)*U.C. Davis*, (2)*MIND Institute, Imaging Research Center*, (3)*Stanford*, (4)*M.I.N.D. Institute, University of California at Davis*

Background: The inability to initiate joint attention to share experience spontaneously with others is a cardinal symptom of autism (Mundy, 2003; Mundy & Sigman, 1989). This joint attention disturbance reflects social information processing/cognitive control disturbances including difficulty in self-monitoring visual attention; diminished tendency to attend to others' gaze and affect; and failure to flexibly integrate this self/other information. It has been suggested that these three functions are supported by a distributed cortical network involving components of the dorsal medial frontal, orbito-frontal, parietal (precuneous) and temporal cortices (Mundy et al. 2000; Mundy & Newell, 2007). These same systems appear to be engaged when virtual reality (VR) agents make eye contact with a participant, or when a participant follows the gaze of a VR agent (Schilbach et al. 2006).
Objectives: To develop and validate VR paradigms for the assessment and examination of social attention in higher functioning children with autism. In particular , to capitalize on the features of VR to provided controlled measures of spontaneous initiation of social attention in children with autism.
Methods: Ten individuals with HFA and ten with typical development all aged 8-17 will be recruited via the MIND Institute subject tracking system. Participants will be presented with VR tasks in a 10 X 14 foot laboratory room, using a VR system produced by WorldViz (http://www.worldviz.com). The paradigm is based on methods used to improve the use of social gaze in teaching situations (Bailenson et al. 2008). In the no fade condition of our paradigm, participants are told to do their best to make eye contact with each of 9 virtual peers when telling a story. In the fade condition, ignored agents fade -- this prompts better attention distribution because an agent's opacity is not restored until the participant's head "looks" at that agent's face. For subjects in which fade precedes no fade conditions, we investigate whether "training" from the first condition improves shared attention during the second condition when the agent-fading prompt is removed.
Results: We have implemented Bailenson's paradigm with several small changes. First, agents' eyes blink to maximize realism. Second, agents' head motion, obtained while measuring actual human head motions watching lectures, now also includes head nods. Third, agents can respond interactively to the attention of the subject such as nodding, raising eyebrows or re-engaging attention (e.g. if the virtual agent's attention starts to wander). Videos of the virtual environment will be shown. Data collected to date indicate that individual differences in the deployment of social attention are detectable and that attention prompts [i.e. fading] do measurably increase the distribution of attention.
Conclusions: VR provides a potentially highly beneficial experimental platform for the study of the cognitive control processes involved with joint social attention. Stimuli can interact in complex socially meaningful and ecologically valid ways with minimal error variance compared to studies using human confederates. Extensive fine-grained behavioral measurements (e.g. head orientation over time, mean looking times, patterns of looking at individual agents) can

be collected and analyzed using multivariate methods and machine learning algorithms.

111.042 42 What's in a Voice? Mindreading and Prosody in Autism Spectrum Disorders. C. Chevallier*, *Institute of Psychiatry, King's College London*

Background: Recent tests of Theory of Mind (ToM) demonstrate that individuals with an Autism Spectrum Disorder (ASD) struggle to recognise mental or emotional states conveyed in the voice (see e.g., Golan, et al., 2007; Rutherford, et al., 2002) but the exact relationship between ToM and vocal cue recognition requires further investigation. In particular, studies often mix various emotions types hence making it difficult to identify a *selective* impairment in processing vocal cues linked to ToM.

Objectives: This study aims to tackle this issue by drawing on psychological research and pragmatic theories in order to distinguish five vocal-cue categories based on the amount of mindreading they require: manners of speech (e.g. singing), physical states (e.g. being tired), basic emotions (e.g. happiness), social emotions (e.g. embarrassment), and speaker's attitudes (e.g. irony). We argue that only the former two require ToM and predict that they will be especially challenging for ASD individuals.

Methods: Teenagers with a high functioning ASD and Typically Developing (TD) controls matched on chronological age, verbal mental age and basic auditory skills were included. In Experiment 1 (ASD: n=17, Mean CA=14;2, TD n=17, Mean CA=13;8), sentences with a neutral content and a marked prosodic contour were presented to the participant, who then had to pick the foil which best described the speaker's state. For example, the item "Jane's Mum wonders why Jane is not with Ben. Ben says: *I told her to walk home from school!*" was followed by two foils: "Ben is proud. He thinks he had a great idea!" and "Ben is sorry. He forgot he was supposed to pick her up!". Each item could be uttered with two distinct intonation contours (appearing in different lists) so that content effects were overridden. In order to identify compensatory strategies, Experiment 2 (ASD: n=20, Mean CA=13;10, TD n=20, Mean CA=13;8) used the same material in the context of a dual task (detecting a sound in the target utterance). Finally, in Experiment 3 (ASD: n=16, Mean CA=13;10, TD n=16, Mean CA=13;11), the complexity of the dual task is increased (detecting the number of 'Ts' in the target utterance).

Results: Contrary to our predictions, ASD participants were not *specifically* impaired in conditions requiring higher order mindreading skills. In Experiment 1, ASD and TD participants had similar accuracy rates and reaction times across all conditions. This was confirmed in Experiment 2 despite the increased demands imposed by the dual task. Finally, in Experiment 3, ASD participants showed no ToM-specific impairment in a highly demanding dual task. On the contrary, we observed that they were slower than TD participants in all conditions, which suggests that, when placed under high cognitive load, they struggle to identify vocal cues in general, independently of underlying mindreading requirements.

Conclusions: Our study confirms that people with autism have difficulties dealing with emotional cues in challenging contexts. Yet, our results - together with past empirical findings - show a combination of competences and impairments that is inconsistent with the idea that atypical recognition of vocal cues is caused by impaired ToM.

111.043 43 Audiovisual Synchrony Predicts Level of Visual Fixation On Mouth and Eyes in 2-Year-Olds with Autism. J. Xu*[1], G. Ramsay[1], A. Klin[2] and W. Jones[1], (1)*Yale School of Medicine*, (2)*Yale University School of Medicine*

Background: Previous studies 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 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 primary goal 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 an imbalance in preferential attention to social versus physical contingencies. Secondarily, if this relationship exists, this study aims to elucidate its developmental progression.

Methods: Physical contingencies were identified by quantifying AVS in naturalistic, child-directed caregiver videos. AVS was defined as simultaneous change in motion and change in sound amplitude, measured within localized regions of interest (ROIs) comprising eyes, mouth, body, and object areas. Our hypothesis was that for toddlers with ASD, but not for typically-developing children, visual fixation to each ROI would be positively correlated with level of AVS.

Results: We found that, in toddlers with ASD, visual fixation to faces is strongly correlated with level of AVS. In the ASD group, level of fixation on the mouth across different movie clips was positively predicted by level of AVS ($r^2 = 0.40$, $p < 0.01$). Surprisingly, we found that fixation on the eye region in children with ASD was also highly correlated with AVS ($r^2 = 0.47$, $p < 0.01$). Visual fixation in typically-developing children was not significantly correlated with AVS in either facial region ($p > 0.05$). In response to our secondary aim, preliminary results suggest that sensitivity to AVS also varies developmentally, with a peak in sensitivity at 24 months.

Conclusions: These results suggest that toddlers with ASD look at different locations of the face as a function of the physical contingencies embedded therein: they vary their attention to eyes and mouth in direct relation to synchronous change in motion and sound. In contrast, typically-developing toddlers do not appear to vary their fixation patterns on the basis of these physical contingencies; instead, other studies (Edwards et al, IMFAR 2009) suggest that TD toddlers vary their fixation patterns in relation to social cues, such as the level of intensity of facial affect. This contrast implies that children with autism take a markedly different avenue for learning about the actions of others than their typically-developing peers, and may be a target for new diagnostic and therapeutic approaches in the future.

111.044 44 Autism and the Conjunction Fallacy. K. Morsanyi*, S. J. Handley and J. S. B. T. Evans, *University of Plymouth*

Background: The conjunction fallacy violates a fundamental rule of probability, that the likelihood of two independent events occurring at the same time (in "conjunction") should always be less than, or equal to the probability of either one occurring alone ($P(A) \geq P(A \& B)$). People who commit the conjunction fallacy assign a higher probability to a conjunction than to one or the other of its constituents. In the most famous demonstration in the literature (Tversky & Kahneman, 1983) people read a description of Linda, a 31-year-old, smart, outspoken woman who was a philosophy major, concerned with discrimination and social justice, and a participant in antinuclear demonstrations. When asked to judge a number of statements about Linda according to how likely they are, people usually rank the statement "Linda is a bank teller and is active in the feminist movement" above the statement "Linda is a bank teller", thus committing the fallacy. The conjunction fallacy has been cited as a classic example of the tendency towards the automatic contextualisation of problems (i.e., the fundamental computational bias). This sort of automatic contextualisation, however, is not universal. According to an influential cognitive account of autism, the Weak Central Coherence theory (Frith & Happé, 1994; Happé, 1999), typically developing individuals tend to create global representations, and they process information in context, whereas autistic individuals engage in more detailed, local or piecemeal processing.

Objectives: To date there is virtually no research which has examined the use of reasoning heuristics in autistic individuals. Thus, the aim of the present study is to determine whether the fundamental computational bias, the tendency to automatically contextualise any given input, operates as powerfully amongst autistic individuals as in typical populations. In light of the Weak Central Coherence account, and considering the findings regarding contextual processing of complex verbal materials (e.g., López & Leekam, 2003), we expected autistic participants to be less susceptible to the conjunction fallacy than non-autistic participants.

Methods: In two experiments we compared the performance of a group of high functioning adolescents with autism and a group of typically developing adolescents (between the age of 11 and 16) on a set of conjunction fallacy tasks. The samples were matched on cognitive ability (as measured by the WISC, and the Raven Progressive Matrices) and executive functions (working memory, inhibition and set-shifting).

Results: Experiment 1 showed significantly fewer conjunction errors amongst the autistic sample. Experiment 2 extended these findings to a new set of problems, demonstrating that the difference between the groups did not result from increased sensitivity to the conjunction rule, or from impaired processing of social materials amongst the autistic participants.

Conclusions: Although adolescents with autism showed less bias in their reasoning, they were not more logical than the control group in a normative sense. The fact that autistic participants display less sensitivity to contextual cues than typically developing individuals when they evaluate choice options can have profound consequences to their everyday lives. The compatibility of our findings with the Weak Central Coherence account will also be discussed.

111.045 45 Bottle or No Bottle: Effects of Breastfeeding in the ASD Population. S. M. Munger*, N. Adams, E. H. Sheridan, M. W. Gower, J. Barstein, T. Perez and E. M. Griffith, *University of Alabama at Birmingham*

Background: No research is available in examining the impact of breastfeeding on the intellectual quotient (IQ) of children with Autism Spectrum Disorders (ASD). However, previous research shows significantly higher IQ scores in typically developing children that were breastfed during infancy than those who were not. This suggests that breastfeeding may have a protective effect on children. A potentially protective effect in ASD is especially interesting due to both the numbers of children with both ASD and Intellectual Disability and hypotheses regarding the role of immune disorders in the development of ASD.
Objectives: The current study is being done to determine if there is any relation between breastfeeding, IQ, and the severity of symptoms exhibited by individuals with ASD.
Methods: Individuals who were evaluated and diagnosed with ASD were chosen from an archival database. The current study utilized scores from the Autism Diagnostic Observation Scale (ADOS) to determine symptom severity and the Wechsler Individual Scale-IV (WISC-IV) to ascertain IQ. Additionally, medical background records were used to determine if individuals were breastfed, bottle fed, or both. Data entry is ongoing, and at the time of this poster presentation, approximately 100 individuals will have the required data.
Results: One-way Analysis of Variance will be used to assess the potential impact of breastfeeding versus bottle feeding versus both methods of feeding on IQ scores and symptom severity. We predict that ASD severity level will be lower in individuals who were breastfed during infancy. In addition, we hypothesize that IQ levels will be higher in those who were breastfed during infancy.
Conclusions: Previous research shows that little has been done with the autism population compared to the typically developing population around factors that could serve a protective function to later development. Given the strong correlations between better outcome in those without autism and breastfeeding, it is anticipated that this could be an area of good impact. Thus, recommending breastfeeding to all expectant mothers could possibly increase the positive effects on their children's health and quality of life.

111.046 46 Change-Blindness: Lack of Typical Salience for Social Information in Autism Spectrum Conditions. C. Ashwin*[1], A. Woolgar[2] and S. Baron-Cohen[3], (1)*University of Bath*, (2)*Medical Research Council: Cognition and Brain Sciences Unit*, (3)*University of Cambridge*

Background: Autism spectrum conditions (ASC) are characterized by social and communicative difficulties alongside repetitive and restricted behavior. Some have proposed that social information is less salient than in typical controls. In line with this, people with ASC look less at faces and are less likely to use social information for inferring mental states about others. However, there has been a lack of experimental testing of whether social information captures the attention of people with ASC or not. One experimental method for investigating the focus of people's attention is the change blindness paradigm, where people have to spot a single change that is present between two otherwise identical displays. A visual disruption occurs each time the scenes alternate, making it very difficult to spot the change unless attention is focused on the location of the change within the display. By including social and non-social information within displays, change blindness paradigms can be used to investigate whether social information is particularly salient to typical control participants, and is less salient to those with ASC.

Objectives: To use two different social change blindness paradigms to test whether there are differences in the allocation of attention to social and mechanical items in people with ASC compared to controls.

Methods: We tested 20 adult males with ASC, along with 20 age, IQ, and sex matched control males and 20 matched control females on two different social change blindness paradigms. One of the tasks used scenes of everyday life with changes to either social or mechanical items within the scenes. The other task used individual pictures arranged in a matrix, to test attention to social and mechanical items with a more featural type of processing which may be easier for those with ASC.

Results: Overall, participants detected changes to social items faster than mechanical items. However, people with ASC were slower than controls to detect changes to social items, an effect that was found across both social change blindness tasks. No differences were found between the ASC and control groups in time to detect changes in the mechanical items. These findings were not due to a general difficulty by the ASC group in doing the tasks, as no significant main effects of group were found for either task.

Conclusions: Social information is normally very salient and tends to capture attention. However, social information is less salient to those with ASC, and so is less likely to be within the focus of their attention. These findings have implications for the development of social cognition in ASC.

111.047 47 Cognitive Flexibility as a Window Into Restricted, Repetitive, Behaviors and Interests: From Behavior to Brain. B. Yerys*[1], L. Kenworthy[2], K. F. Jankowski[2], E. Wing[2], J. James[2], W. D. Gaillard[2], C. J. Vaidya[3] and G. L. Wallace[4], (1)*Children's National Medical Center, George Washington University*, (2)*Children's National Medical Center*, (3)*Georgetown University*, (4)*National Institute of Mental Health, National Institutes of Health*

Background: Recent evidence in adults and children with autism spectrum disorders (ASD) has documented a relationship between restricted, repetitive behaviors and interests (RRBI) and standard neuropsychological measures of cognitive flexibility (Kenworthy, Black, Harrison, della Rosa, & Wallace, 2009; Lopez, Lincoln, Ozononff, & Lai, 2005; South, Ozonoff, & MacMahon, 2007). Furthermore, recent functional neuroimaging (fMRI) studies have shown a relationship between RRBI symptoms and brain regions active during cognitive flexibility tasks (Shafritz, Dichter, Baranek, & Belger, 2008). However, there is limited evidence of this relationship at the behavioral or brain level of analysis in children with ASD.
Conclusions: This collection of studies suggests that neuropsychological and cognitive neuroscientific measures of cognitive flexibility may provide an endophenotype into an understudied, core symptom cluster of ASDs: RRBI.

Furthermore, additional studies in functional neuroimaging can be conducted with a high degree of success, and continuing this work will allow us to leverage both behavior and neural information in the parsing of heterogeneity that is characteristic of ASD.
Objectives: Examine the relationship between RRBI and cognitive flexibility at the behavioral and neural level of analysis in children with ASD.
Methods: Two studies will be presented: i) a neuropsychological study of 126 children (42 ASD; 84 Typically Developing controls (controls)) completing the Intradimensional/Extradimensional Shift task from the CANTAB; ii) preliminary data from an fMRI study of the simplest levels of set-shifting using a 3T Siemens Trio scanner with the Total Imaging Matrix (Tim) upgrade. Both studies recruited high-functioning children with and without ASD (FSIQ>70).
Results: Study i: The ASD group completed as many stages as controls but made significantly more errors in the Extradimensional reversal stage (Stage 9) than controls. In the ASD group, Stage 9 errors correlated significantly with RRBI symptoms from the ADI, rho(78)=0.44, $p<0.05$ Study ii: Preliminary data suggests that both groups activate expected frontal-parietal networks while completing a simple motor shifting task; qualitatively, controls have more numerous and bilateral clusters of activation in frontal regions relative to the ASD group.
Conclusions: This collection of studies suggests that neuropsychological and cognitive neuroscientific measures of cognitive flexibility may provide an endophenotype into an understudied, core symptom cluster of ASDs: RRBI.
Furthermore, additional studies in functional neuroimaging can be conducted with a high degree of success, and continuing this work will allow us to leverage both behavior and neural information in the parsing of heterogeneity that is characteristic of ASD.

111.048 48 Exploring the Emotional Audio-Visual Integration Ability in Autism-Using a Paradigm of Voice to Facial Expression Interference. Z. H. Xiao and L. X. Wang*, *Beijing Normal University*

Background: Previous studies suggested that the audio-visual integration ability in autism preserved well in the non-social contingencies, but was deficit in the advanced social cognitive processing, such as emotion and language (Williams et al.2004; James et al.2006; van der Smagt et al.2007_GSmith et al.2007; Mongillo et al.2008_GMagnee et al.2008a_GMagnee et al.2008b). The mechanism of audio-visual integration deficit in social cognitive processing in autism is still in debate.

Objectives: According to the audio-visual integration model (Belin, 2007), we used the paradigm of voice to facial expression interference to explore the mechanism of emotional audio-visual integration in autism.

Methods: Sixteen pairs of teenagers with and without autism (MA=13:3 years), which were matched on Chinese norms of RSPM score, CA, gender and manual laterality, participated in the study. In Experiment 1, emotional face and voice were presented simultaneously, the participants were asked to discriminate the facial expressions (sadness or happiness) by pressing different keys. In Experiment 2, faces and voice with neutral emotion were presented simultaneously, the participants were asked to discriminate the gender of the face (male or female) by pressing different keys.

Results: Results of Experiment 1 showed a significant main effect of consistency of emotional face and emotional voice, and a significant interaction effect of group and consistency. This interaction effect disappeared when emotional voice effect was controlled. Results of Experiment 2 showed a significant main effect of consistency, but no significant interaction effect of group and consistency, and no that of modal (unimodal vs. bimodal) and group.

Conclusions: According to the audio-visual integration model, results of the present study suggested that the adolescents with autism preserved well emotional audio-visual integration ability at structure analysis stage, but abnormal emotional audio-visual integration at effect analysis stage. We further found that the cause of abnormal

emotional audio-visual integration was from the difficult of emotional voice recognition which was result of voice processing deficit at voice effect analysis stage.

111.049 49 High Risk Infants' Visual Scanning and Attention Disengagement in Response to Emotional Faces. J. B. Wagner*[1], R. Luyster[1], H. Tager-Flusberg[2] and C. A. Nelson[3], (1)*Children's Hospital Boston/Harvard Medical School*, (2)*Boston University*, (3)*Children's Hospital Boston*

Background: Autism spectrum disorder (ASD) is typified by social and communicative impairments. With so much social information gleaned through faces, a growing body of research has asked whether atypical face processing might contribute to these social-communicative difficulties.

Longitudinal work has begun to prospectively follow infant siblings of children with ASD, who are themselves at elevated risk for the disorder, in order to ask whether the abnormal patterns of face processing seen in older individuals with ASD might be present early on in development.

Objectives: Prior work studying infants at-risk for ASD has pointed to general deficits in attention disengagement and work with older ASD individuals has showed deficits in emotion recognition. In order to follow up on these findings, the present study asks whether infants at-risk for ASD will a) show attention disengagement to faces that is modulated by emotional expression; and b) whether disengagement is influenced by scanning patterns to core facial features.

Methods: Using a Tobii eye-tracker, eye movements were recorded in 9-month-old infants at-risk for ASD (by virtue of having at least one older sibling with ASD) during both a looking time task and an overlap task. During the looking time task, infants were presented with images of fear, happy, and neutral faces. Eye-tracking data captured duration of looking to each face, as well as duration of looking to core features of the face (i.e., eyes and mouth). During the overlap task, infants were presented with a centrally-located face displaying a fear, happy, or neutral expression, and this stimulus remained present while a peripheral target appeared on the right or left side of the screen. Eye-tracking data examined latency to disengage from the face as a function of emotional expression. These preliminary findings are based on 12 9-month-old infants at-risk for ASD.

Results: Contrary to prior work with typically-developing infants that finds an attentional bias for fear faces, the facial expression of the central stimulus had no significant effect on attention disengagement latencies in at-risk infants, $F(2, 22) = 0.77$, $p = .48$. It took equally long for infants to disengage attention from fear faces (M = 549 ms) as compared to happy, M = 514 ms, $t(11) = 1.024$, $p = 0.33$, and neutral faces, M = 557, $t(11) = -0.19$, $p = 0.85$. Individual variability in the fear bias was then assessed as a function of visual scanning patterns to fear, happy, and neutral faces during the looking time task. Results indicate that infants who spend a greater proportion of time looking to the eyes and mouth when viewing fear faces show longer disengagement latencies to fear faces as compared to happy and neutral ($r = .64$, $p = .046$).

Conclusions: The present work highlights the importance of examining individual differences in these at-risk samples in order to better characterize the heterogeneity of ASD. This approach provides a window into the mechanisms by which early visual attention could influence lower level attentional biases.

111.050 50 Increasing Facial Recognition Skills in Children with Autism. M. W. Gower*, T. Perez, N. Adams and E. H. Sheridan, *University of Alabama at Birmingham*

Background: Children with autism consistently demonstrate deficits in facial processing compared to their typically developing peers. They also demonstrate difficulties with global processing of both facial and non-facial stimuli. Research has shown that children with autism spectrum disorders tend to focus more on the mouth area, rather than the eyes, when looking at faces. Facial recognition skills have been shown to be highly positively correlated with improved social skills, which are correlated to such desirable outcomes as better emotion recognition abilities and increased prosocial behaviors (Denham et al., 2003, Eisenberg et

al., 1996).
Thus far, studies investigating attempts to increase facial recognition skills in populations of children with autism have not found significant improvements (Faja et al., 2008). However, recent research utilizing avatars in the computer-based social skills intervention FaceSay™ has shown it to significantly increase facial recognition skills in a population of adolescents with autism spectrum disorders (Hopkins, 2007) and socially at-risk children in Head Start (Perez, 2008).

Objectives: The current study sought to replicate previous findings of studies using the FaceSay™ intervention in a population of three- to six-year-old children with autism spectrum disorders and typically developing children.

Methods: The games in FaceSay™ utilize avatars, which are virtual people that are capable of interacting with humans, and each game in the intervention is targeted at training children pay attention to all the components of the face, promoting appropriate facial recognition skills. The children played the game for 15-30 minutes, depending on their ability to attend to the games, twice per week. The intervention lasted 12 weeks, and the children in this study were tested on the Benton Facial Recognition Task prior to and after participating in the intervention.
Results: A factorial analysis of covariance (ANCOVA) was completed to assess the effect of game assignment (Face Say™, Tux Paint) and diagnosis (with or without an Autism Spectrum Disorder), as well as the interaction between the two factors on post-intervention facial recognition skills. The pre-intervention scores on the Benton Facial Recognition test and age served as the covariates. After adjustment by the covariate, there were no significant main effects or interaction effects. However, when diagnosis was removed from the model and FaceSay™ was compared to Tux Paint, a significant difference was found, $F(1,22) = 4.715$, $p = .041$, $\_^2 = 0.18$.
Conclusions: After looking at the means of the groups before and after taking part in the intervention, it became apparent that the children with autism were performing at the same level as their typically developing peers on the Benton Facial Recognition Task after the intervention. The lack of significant overall findings in the first analysis was likely due to issues related to power and the fact that the typically developing children were likely performing at near ceiling levels prior to the intervention. Our findings suggest that this is a useful intervention to increase the facial recognition abilities of young children with autism.

111.051 51 Parent and Teacher Report of Behaviors in Children with Autism Spectrum Disorders: The Effects of Parent Stress and Teacher Burnout. J. C. Landoll*[1], P. S. Schoultz[1], D. C. Coman[1], A. Gutierrez[1], M. Alessandri[1], K. Hume[2], L. Sperry[3], B. Boyd[4] and S. Odom[4], (1)*University of Miami*, (2)*Frank Porter Graham Child Development Institute, University of North Carolina, Chapel Hill*, (3)*University of Colorado Denver*, (4)*University of North Carolina*

Background:

Many early childhood behavioral assessments rely on parent and teacher reports of behavior. Historically, agreement between parent report and teacher report on ratings of child behaviors and psychopathology has been low to moderate (Achenbach, McConaughy, & Howell, 1987). However, research has demonstrated increased agreement between parent and teacher reports among younger children, including preschoolers (Vitaro, Gagnon, & Tremblay, 1991). For children with developmental delays, teachers can be a valuable resource for assessing behaviors and psychopathology, but it is important to understand the differences between parent and teacher reports. Low inter-rater agreement is often attributed to situational factors in home and school environments that produce different behaviors; however, there may be informant characteristics (i.e., maternal stress) that affect agreement (Winsler & Wallace, 2002). While research has shown that maternal stress accounts for increased reporting of problem behaviors in young children with autism spectrum disorders (Szatmari, Archer, Fisman, & Streiner, 1994), much less is known about the effect teacher burnout has on teacher reports of problem behaviors (Lecavalier, Leone, & Wiltz, 2006).

Objectives:

The purpose of this study is to assess the agreement between parent and teacher reports of behaviors on the Social Responsiveness Scale (SRS) and the Repetitive Behavior Scale-Revised (RBS-R). The SRS has been shown to be an effective gauge of autistic behaviors in both parent and teacher reports (Constantino, LaVesser, Zhang, Abbacchi, Gray, & Todd, 2007), thus high agreement is predicted. For the RBS-R, it is expected that associations between parent and teacher reports will fall in the low to moderate range. However, the RBS-R has not previously been given to teachers, so this study will provide a chance to explore the similarities and differences in responding. It is expected that maternal stress and teacher burnout will act as moderators in the relationship between parent and teacher report for both measures.

Methods:

Data were collected as part of a larger multi-site study comparing preschool treatment models. The current study uses one site's data, and preliminary analyses were conducted on data from one year. Parents and teachers of twenty preschoolers with autism spectrum disorders completed the SRS and the RBS-R. Parental stress was measured on the Parenting Stress Index and teacher burnout was measured on the Maslach Burnout Inventory.

Results:

Preliminary results found non-significant correlations between parent and teacher reports on the SRS. However, when examining the raw score differences between parent and teacher reports, highly stressed parents reported significantly lower scores on the SRS than teachers, compared to low stress parents, t (19) = 3.65, $p < .01$. Additionally, teachers who showed elevated levels of burnout had higher agreement with parent reports, _ = 2.48, $p < .05$, compared to those with low burnout, _ = -.76, $p = .25$. No associations were found between parent and teacher reports on the RBS-R.

Conclusions: Findings support study hypotheses suggesting maternal stress and teacher burnout may moderate the agreement between raters. Future research exploring issues such as parent-teacher communication, as well as agreement on additional early childhood measures is needed.

111.052 52 Response Variability in a Low-Functioning Individual with Autism: Practical and Theoretical Implications. E. J. Pickett*, N. M. Billings, L. V. Van Droof and B. Gordon, *Johns Hopkins Medical Institutions*

Background: In addition to difficulty with initial learning, it is also widely recognized that low-functioning individuals with autism exhibit considerable variability in demonstrating what they presumably have learned. Such variability has many practical consequences, such as the difficulty obtaining valid assessments. But it also may have a more profound theoretical significance, because it may arise, in whole or in part, from an intrinsic weakness and/or variability in the underlying neural representations of knowledge in such individuals.
Objectives: To establish the magnitude of response variability for well-known stimuli, in a simple response paradigm, in familiar and unchanging circumstances, in one extensively studied low-functioning individual autism. We reasoned that variability found under these circumstances would have a greater chance of being due to intrinsic variability, rather than extraneous factors.
Methods: DL (not his real initials) is a nonverbal, low-functioning male with autism, 18 years old at the time of testing. Stimuli were selected that were purportedly well known to DL, based upon parental report and experimental observation. DL, prior to the study described here, had been tested in his home over a period of 6.5 months by the same team of investigators using similar methods. The two experiments reported here used a two-alternative forced-choice picture-to-picture matching task. In each trial, DL was asked to choose one of two color photographs presented on a computer screen that matched a hard-copy stimulus photo that the experimenter held above the screen. Four conditions were presented to compare DL's performance with the 24 known items to

his performance with unfamiliar items. Condition 1: both the target and distracter photos were Known items. Condition 2: targets and distracters were Unfamiliar. Condition 3: targets were Unfamiliar, distracters were Known. Condition 4: targets were Known, distracters were Unfamiliar. Each condition was presented in ten blocks over five sessions in consecutive order, with Experiment 1 completed prior to Experiment 2. The experiments were identical with feedback for accurate responses only in Experiment 2. All sessions were videotaped. **Results:** In Experiment 1, DL achieved 100% accuracy on 30% of the blocks. However, performance varied between 44% and 100%, averaging 96% in Condition 1, 92% in Condition 2, 95% in Condition 3, and 60% in Condition 4. Performance decreased in Experiment 2 despite the feedback. Accuracy ranged from 27% to 94%, averaging 70% in Condition 1, 67% in Condition 2, 56% in Condition 3, and 46% in Condition 4. **Conclusions:** Although DL demonstrated competency with the matching task, his performance was quite variable even with highly familiar stimuli on a simple, familiar task, in familiar circumstances. Our data do not yet let us determine the cause of this pronounced variability. Fluctuating motivation and attention are the obvious possible culprits, but not necessarily evident from the videotaped record. Evaluations of such individuals may have to be sensitive to the possibility that the neural processes required for such tasks may be functioning with much less signal strength, and/or with much greater intrinsic noise, than may be the case in other subject populations.

111.053 53 Subcortical Visual Network for Face Processing: Implications for Autism. V. Troiani*, E. T. Hunyadi, M. Riley, J. D. Herrington and R. T. Schultz, *Children's Hospital of Philadelphia*

Background: Autism Spectrum Disorder (ASD) is associated with difficulties in face processing, with amygdala hypoactivation frequently reported in face discrimination tasks. The amygdala is proposed to be a component of a subcortical superior colliculus-thalamic-amygdalar visual processing pathway, thought to strongly influence perceptual learning during infancy. Thus, understanding the network of regions active in this subcortical pathway is critical in fully understanding the face processing deficits in ASD. Pasley and colleagues (2004) showed that this subcortical pathway was more strongly activated for perception of faces than objects. The current study utilized a more sophisticated binocular rivalry task, including whole brain EPI coverage and an improved conscious task, in order to isolate the network of regions involved in subliminal face processing in neuro-typical individuals.

Objectives: To examine the subliminal face processing pathway in neuro-typical young adults, using a binocular rivalry task and fMRI.

Methods: During fMRI data collection, 12 young adult participants performed a consonant/vowel identification task of the first letter of consciously perceived words, while alternating blocks of subliminal faces or houses were presented through the non-dominant eye.

Results: : In a whole brain, random-effects analysis, participants exhibited significantly greater activation for subliminally suppressed faces than suppressed houses in the precuneus and left inferior parietal cortices– areas not evaluated by Pasley due to a narrow EPI data collection window. A priori ROI analysis of bilateral amygdalae revealed significantly greater left amygdala response for subliminal faces compared to houses. Psycho-physiological interaction (PPI) analysis was used to test for regional specific connections to the amygdala, using individually defined ROIs. Results demonstrated task dependent correlations between the left amygdala and bilateral pulvinar, as well as early visual cortices.

Conclusions: The current results present a more complete subliminal face processing pathway, in addition to replicating previous findings. The pulvinar nucleus is implicated in orienting towards salient stimuli. The precuneus has bidirectional connections to the pulvinar nucleus as well as cortico-cortical projections to parietal cortex, a region critical for spatial attention. One interpretation is that a subcortical pulvinar response to a potentially salient stimulus is followed by an increase in amygdala activity and an

allocation of spatial resources in parietal cortex, directed by the precuneus. This research builds on previous work identifying a subcortical visual processing pathway, which may aid in revealing more specific deficits underlying the origin of face processing difficulties in ASD.

111.054 54 The Challenge Task: The Development of a Group Observational Measure for Flexibility in Children with High-Functioning Autism Spectrum Disorders. J. L. Sokoloff*[1], L. Kenworthy[1], A. Pierce[2], K. Kane[1], J. F. Strang[1], M. Adler[2] and L. G. Anthony[3], (1)*Children's National Medical Center*, (2)*Ivymount School*, (3)*Children's National Medical Center, George Washington University Medical School*

Background: Parents, teachers and clinicians of children with high-functioning autism spectrum disorders (ASD) have observed cognitive and behavioral flexibility deficits that inhibit the child's ability to socialize and complete every day tasks in various settings. A recent review of the literature revealed that it is very difficult to capture these observed deficits in laboratory measures (Geurts, Corbett, & Solomon, 2009). To date, a group observational measure that is sensitive to core flexibility difficulties and capable of tracking improvements in children with high-functioning ASD has not been developed. Objectives: Design and pilot test an ecologically-valid observational measure that captures difficulties, strengths and change in flexibility in children with high-functioning ASD. Methods: Eighteen school-aged children with high-functioning ASD participated in the Flexibility Challenge Task at a summer camp program designed to improve social and executive functioning. Subjects participated in two tasks (pre- and post- camp). Each task takes place in a group format of 4-5 children and takes approximately 45-60 minutes to complete. The Flexibility Challenge Task consists of several socially-relevant activities which include games that require shifting an activity or accommodating another person's actions, such as working together to: complete a jigsaw puzzle, draw specified scenes, play charade-like games, and make clay sculptures collaboratively. These activities are designed to elicit difficulties and strengths in cognitive and behavioral flexibility. Activities specifically target initiation, shifting, coping, social reciprocity, generativity, inhibition, and global flexibility. Videos of the Challenge Tasks were coded by an observer who was blind to whether it was a pre- or post- camp task. Reliability observations were then completed with a second coder for 25% of the videotapes. Results: Preliminary analyses of 12 of the 18 subjects revealed significant differences in children's pre- and post- camp scores on paired sample T-tests. Children improved on the following task items: number of guesses in charades (generativity) $t(12)=-2.43$, $p=.039$; perseveration (shifting) $t(12)=2.53$, $p=.03$; stereotypical behaviors (ASD symptoms) $t(12)=2.83$, $p=.02$; negative emotions (affect) $t(12)=2.94$, $p=.01$; and global flexibility $t(12)=-2.83$, $p=.02$. Inter-rater reliability between video coders was 90%. Final analyses on additional children will be presented. Conclusions: Our preliminary findings suggest that this group observational measure is sensitive to difficulties, strengths and change in flexibility and can be coded reliably. Ultimately, the Flexibility Challenge Task can assist researchers to accurately measure change in core flexibility deficits over time in an ecologically-valid measure. References: Geurts, H.M., Corbett, B., & Solomon, M. (2009),The paradox of cognitive flexibility in autism. Trends in Cognitive Sciences 13(2), 74-82

111.055 55 The Role of Maternal Education and Stress On Developmental Rates for Preschool Children with Autism Spectrum Disorders. P. S. Schoultz*[1], J. C. Landoll[1], D. C. Coman[1], A. Gutierrez[1], M. Alessandri[1], K. Hume[2], L. Sperry[3], B. Boyd[4] and S. Odom[4], (1)*University of Miami*, (2)*Frank Porter Graham Child Development Institute, University of North Carolina, Chapel Hill*, (3)*University of Colorado Denver*, (4)*University of North Carolina*

Background:

Previous research supports a link between maternal factors (e.g., maternal stress, maternal education) and developmental outcomes in children with autism spectrum disorders (ASD) (Harris, 1984; Osborne, McHugh, Saunders, & Reed, 2007). For example, higher levels of parental stress have been shown to relate to poor treatment outcomes in children with ASD (Osborne, McHugh, Saunders, & Reed, 2007). Other research has shown that lower levels of

maternal education have a variety of negative outcomes for children (Thornberry, Krohn, Lizotte, Smith, & Tobin, 2003; Pogarsky, Thornberry, & Lizotte, 2006), while higher levels of maternal education have been associated with a variety of positive outcomes. Studies have shown a positive correlation between maternal education and language development (Dollaghan et al., 1999) as well as literacy (Reese, 1995) in typically developing children. Research also suggests that children of highly educated mothers are less at risk for mental retardation (Chapman, Scott, & Mason, 2002). However, there is little research that examines the link between maternal education and rate of child development in children with ASD.

Objectives:

The current study examines the link between maternal education and developmental rate in preschool children with ASD, and the effect of maternal stress on these relationships. Phenotypic variability (including developmental rate) in ASD could potentially be attributed to a wide variety of modifying processes, including family factors such as maternal education and maternal stress. These modifying processes on their own do not necessarily convey risk for autism but instead influence the behavioral phenotypic expression of this disorder (Mundy, Henderson, Inge, & Coman, 2007). Despite the lack of research examining ASD and maternal education, researchers believe maternal education will show similar effects on developmental outcomes for children with ASD.

Methods:

Data were collected as part of a larger multi-site study comparing preschool treatment models for students with ASD. Pre- and post-test month scores on the Mullen Scales of Early Learning (MSEL) and the Preschool Language Scale-IV (PLS4) were used to calculate related developmental rates during intervention. Maternal stress was measured using the Parenting Stress Index (PSI). Preliminary analyses will be presented on first year data from one site participating in the larger study. It is hypothesized that higher levels of maternal education will be positively correlated with developmental rates during treatment on both the MSEL and PLS4, and that this relationship will be moderated by maternal stress.

Results:

Preliminary results did not find any significant correlations between maternal education and developmental rate. However, when examining the moderating effects of maternal stress, results showed that for parents with high levels of stress, maternal education was a predictor of developmental rate on one subscale of the MSEL, _ = -1.27, p = .01.

Conclusions:

The results support the hypothesis that stress moderates the relationship between maternal education and developmental rate. These results suggest that intervention targeted at the families with elevated levels of maternal stress may be beneficial to the overall development of children with ASD.

111.056 56 Theory of Mind Evaluated by Tom Storybooks in Children with Autistic Spectrum Disorders: a Longitudinal Study. B. Cartier-Nelles*[1], E. Thommen[2], A. Guidoux[1], S. Wiesendanger[1] and E. M. A. Blijd-Hoogewys[3], (1)*University of Applied Sciences Western Switzerland of Lausanne*, (2)*University of Fribourg and University of Applied Sciences Western Switzerland of Lausanne (EESP), Switzerland*, (3)*Lentis*

Background: Theory of mind in autism has been extensively investigated during the last thirty years. Children with autism are generally less good than control groups in theory of mind tasks (Yirmiya et al., 1998; Peterson, et al., 2005). Few studies have tried to examine the actual development of such understanding in autistic children and even less so longitudinally. Teaching social skills and comprehension of mental states are one of the privileged educational interventions in children with autism. Though, how to assess these interventions is still in debate.
Objectives: The aim of our research is to follow longitudinally the evolution of theory of mind comprehension in children with autism.

Therefore, an instrument sensible enough to detect an eventual evolution in this comprehension was needed.
Methods: The testing was carried on in two sessions, separated by one year. Twenty eight children with autism (5- to 15-years old, M =10.6) participated in the study, all were evaluated with the Wechsler Nonverbal Scale, the E.CO.S.SE (the French equivalent of the TROG) and diagnosed with the DSM-IV-TR. The assessment on theory of mind was based on the French version of the ToM Storybooks (Blijd-Hoogewys et al., 2003). A control group of 14 children - paired on age and verbal ability - is tested for comparison.
Results: The first test reveals that children with autism are able to attribute simple mental state to story characters. They generally understand what a belief is as well as belief changing, but they are specially impaired in false belief tasks. The testing with the control group and the second test session is ongoing and will be discussed at the congress.

Conclusions: Implications from this research are multiple. First, the sensibility of the ToM Storybooks to evaluate the evolution in children's theory of mind will be important for testing progress. Second, the evaluation of the developmental course of theory of mind understanding in children with autism is useful for those who try to understand this process and teach children in these abilities. Third, the comparison with control groups will confirm the specific difficulties of theory of mind comprehension in persons with an autism spectrum disorder. The results of our research will be useful for professionals and researchers.

111.057 57 Academic Functioning in Children with ASDs Who Have Achieved Optimal Outcomes. E. Troyb*[1], K. E. Tyson[1], M. Rosenthal[1], L. E. Herlihy[1], M. Helt[1], A. Orinstein[1], I. M. Eigsti[1], L. Naigles[1], M. L. Barton[1], E. A. Kelley[2], M. C. Stevens[3], R. T. Schultz[4] and D. A. Fein[1], (1)*University of Connecticut*, (2)*Queen's University*, (3)*Institute of Living, Hartford Hospital / Yale University*, (4)*Children's Hospital of Philadelphia and the University of Pennsylvania*

Background: A study is currently following children who have a history of autism spectrum disorder (ASD), but who no longer meet diagnostic criteria for such a disorder. These children have achieved social and language skills within the average range for their ages and receive little or no school support. Several recent studies suggest that this small subset of children, once diagnosed with ASD, achieve an "optimal outcome" (Sutera et al., 2007, Kelley et al., 2006, and Helt et al., 2008).

Objectives: This study examines the academic abilities of children who achieved "optimal outcomes" (OO).

Methods: Performance of 26 children who achieved OO (M(age) =13.0), 20 high functioning children with a current ASD diagnosis (HFA, M(age) = 13.1), and 22 typically-developing peers (TD, M(age) = 13.4) were compared on the Passage Comprehension, Applied Problems and Word Attack subtests of the Woodcock-Johnson, III (WJ-III). Additionally, 21 children with OO were compared to 14 children with HFA and 20 TD peers on their performance on the Contextual Conventions, Contextual Language and Story Construction subtests measuring the spontaneous writing sample of the Test of Written Language, Third Edition (TOWL-3). The groups were matched on age and sex. Although groups were not significantly different on verbal IQ (M(VIQ)=105.6, 113.7, 114.1, for HFA, OO and TD, respectively), the HFA group scored 8.3 points lower than the other groups.

Results: Children in all three groups scored in the average range on the subtests of the WJ-III. Performance on the Applied Problems and Word Attack subtests did not differ significantly between the three groups. On the Passage Comprehension subtest, children in the OO and TD groups performed similarly and exhibited less difficulty than did children with HFA (M(TD)=113.1, M(OO)=110.6, M(HFA)=102.6, $p<.05$). Children across groups performed in the average range on the subtests of the TOWL-3. Scores measuring the mechanics of written language were comparable for the OO and TD groups, while children with HFA had significantly more difficulty with these skills than did the children who achieved OO (M(TD)=10.5, M(OO)=12.3, M(HFA)=9.3, $p=<.05$). Children in the OO group performed similarly to their TD peers on the subtest

measuring the use of grammar, sentence structure and vocabulary, and both groups had higher scores than the HFA group on this subtest (M(TD)=12.6, M(OO)=12.6, M(HFA)=9.9, p<.05). A comparison of scores on a measure of story construction indicated that children in the OO and TD groups received similar scores and exhibited less difficulty relative to children in the HFA group (M(TD)=11.4, M(OO)=10.9, M(HFA)=8.7, p<.05).

Conclusions: The results of this study suggest that the decoding, reading comprehension, writing and arithmetic abilities of children who achieve OO are similar to those of their TD peers. Although children with HFA performed in the average range on all measures, they showed greater difficulty with reading comprehension, mechanical aspects of written language, structure of written language and story construction than did children who achieved OO. Preliminary evidence suggests that children who achieve OO exhibit stronger academic skills than are displayed by children who have retained their ASD diagnosis.

111.058 58 Adaptive Functioning and Cognitive Development in Young Children with Autism. G. Mathai*[1], L. 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. Although approximately 25-75% of individuals with autism have below-average IQ (< 70), autism can occur with equal severity in individuals of average and above-average IQ (Chakrabarti & Fombonne 2001). Findings are mixed regarding the relationship between social behaviors and intelligence. Severe maladaptive social behavior despite an IQ within normal range has been described (Volkmar, et al. 1987). On the other hand Freeman et al. (1999) found an association between WISC-R full scale IQ and the composite score of the Vineland Adaptive Behavior Scales (VABS) indicating an interdependency of the constructs.
Objectives: The purpose of this study is to examine how adaptive behaviors in the communication and social domains impact cognitive development in young children with autism. The information thus obtained may be critical for targeting 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 5.0 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 lower preschool level is usually for ages 2:6 to 3:5, but complete norms are available up to age 4:11, which allows for lower-ability 5-year-olds to be tested at a more appropriate developmental level. The 4 core subtests are comprised of Block Building (visual-perceptual matching), Naming Vocabulary (expressive vocabulary), Verbal Comprehension (receptive language) and Picture Similarities (non verbal reasoning). Adaptive functioning in the communication and social domains was assessed using the VABS (Sparrow, et. al. 2005). The communication domain includes adaptive functioning in receptive, expressive and writing abilities, while the social domain includes adaptive functioning in interpersonal relationships, play and leisure and coping skills. Multiple regression analysis was used to determine, from two predictor variables (standard scores on the communication and social domains as assessed by the VABS) 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.
Results: Correlations showed that VABS communication standard scores were significantly ($p < .05$) related to DAS block building developmental T scores, DAS verbal comprehension developmental T score and DAS picture similarities developmental T score. VABS communication and socialization standard scores were significantly ($p < .05$) related to DAS Naming developmental T scores.

Conclusions: Results clearly demonstrate that adaptive functioning, particularly in the area of communication 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.

111.059 59 Adults with Autism's Understanding of Emotion in Context. S. A. Cassidy*, P. Mitchell, D. Ropar and P. Chapman, *University of Nottingham*

Background: Previous research into emotion recognition skills in autism has proved highly contradictory. High functioning adults with autism have been shown to pass some emotion recognition tasks using posed static expressions (e.g. Spezio et al. (2007); Neuman et al. (2006)), whereas more naturalistic tasks have revealed more pronounced emotion recognition impairment (e.g. Baron-Cohen et al. 1995; 2001). No previous research has addressed emotion recognition skills in real life social interchanges, where individuals with autism most likely experience emotion recognition difficulties. Objectives: The current study investigated adults with autism's ability to recognize emotions in context, using spontaneous expressions elicited during a social interaction. Methods: 19 Adults with autism and 19 age and IQ matched controls watched video clips of spontaneous expressions, then judged what situation the person reacted to and the emotion of the person. Results: Participants with autism were impaired relative to controls in correctly inferring what situation elicited the emotion response. This impairment was due to impairment in correctly inferring emotion. However the participants with autism gave situation responses congruent with emotion to the same extent as typically developing controls. Conclusions: Results suggest that although adults with autism are impaired at inferring emotion and context from spontaneous dynamic expressions, understanding of what behaviors are appropriate to different social contexts is relatively unimpaired. These results stress the importance of using tasks more representative of social interaction in everyday life in order to better understand the impaired and unimpaired aspects of emotion understanding in autism.

111.060 60 Are Siblings Important Agents of Cognitive Development? Examining the Effect of Siblings On the Cognitive Skills of Children with Autism. K. A. O'Brien* and V. P. Slaughter, *University of Queensland*

Background:

Due to the nature of autism, the social deficits exhibited often limit the quality and amount of social interaction these children experience. Family members therefore tend to be the people they interact with most frequently. Parents in one study were found to over-compensate for their children with autism, feeling the need to fill in for their developmentally delayed child, which may be doing more harm than good. Siblings did not compensate thus providing the child with autism more opportunities to initiate social interactions (El-Ghoroury & Romanczyk, 1999). Two areas where children with autism appear to have deficits are theory of mind and executive functioning. McAlister and Peterson (2006) conducted a study to assess the extent that theory of mind and executive functioning abilities in typically developing children are affected by the presence of having or not having a child aged sibling at home to play with and talk to. Their findings indicated that the social influence of a child aged sibling is beneficial to both executive function and theory of mind in typically developing children during the preschool period (McAlister & Peterson, 2006).

Objectives:

To replicate and extend McAlister and Peterson (2006) on interrelations between number of child siblings (1 to 12 years) and theory of mind and executive function development, to look at families where one of the children has autism.

Methods:

Theory of mind (ToM) and executive functioning abilities (EF) of 38 children with a diagnosis of autism (1 female, 37 males) aged between 3 years 11 months and 13 years 0 months (M=7.38, SD=2.75) were assessed using a battery of theory of mind tasks including tests of appearance reality,

false belief, change in location and pretend representation, and a battery of executive functioning tasks. Their verbal mental age (VMA) was assessed using the PPVT-III and their autism diagnosis was confirmed using the autism diagnostic observation schedule (ADOS). Number of siblings and sibling order was noted. Only child aged (12 months to 12 years) were included. (Assessment is continuing with 60 children planned to be completed by May 2010).

Results:

Preliminary results suggest a significant relationship between number of younger child aged siblings and both VMA, r=.532, p<.01 and EF r=.406, p<.05. ToM has a non-significant positive relationship with number of younger siblings. There were non-significant negative correlations between number of older siblings and ToM, EF and VMA. ToM composite scores were significantly correlated with age, r=.467, p<.01, EF composite scores r=.545, p<.01 and VMA r=.497, p<.01.Preliminary analyses of the presence of siblings found no significant effects for ToM or EF but a significant effect for

Conclusions: Having younger siblings seem to have positive effects on the VMA and EF of children with autism. As yet effects for ToM have not been found. Preliminary analyses have not found any significant effects for having older siblings, but possible negative effects may be due to an over-compensatory effect which parents of children

111.061 61 Characterizing Theory of Mind in Autism Spectrum Disorders: The Importance of Siblings. N. Basehore*[1], A. Lukowski[1], M. M. Abdullah[1], A. R. Ly[1], K. Thorsen[2], K. Osann[1] and W. A. Goldberg[1], (1)*University of California, Irvine*, (2)*UCI School of Social Ecology*

Background: A deficit in theory of mind (ToM) has been implicated as a primary characteristic of Autism Spectrum Disorders (ASD; Baron-Cohen et al., 1985); however, some research indicates that this deficit is not universal in all children with ASD (Ozonoff et al., 1991). Previous findings suggest that some variability could be attributed to language or cognitive delays (Tager-Flusberg & Joseph, 2005); however, little is known about contextual influences. Whereas previous literature indicates that the presence of siblings is associated with enhanced ToM ability in typically developing children (Perner et al., 1994), this contextual factor has not been examined in children with ASD.

Objectives: The present research aims to examine whether number of siblings is associated with ToM performance in children with ASD.

Methods: Participants were 24 children with ASD from a larger national study. Parents were mostly Caucasian, middle-class, and well-educated. ASD diagnoses were made when the national study was initiated. At about age nine, children were administered a battery of four ToM tasks: verbal and non-verbal appearance-reality tasks and two first-order false-belief tasks. Each task was administered twice, separated by approximately two weeks. For each set of ToM tasks, a score of zero was assigned for not passing both assessments, a score of one for passing one of the assessments, and a score of two for passing both assessments. Scores were obtained for each task and a composite score was calculated. Sibling information was gathered by telephone or mail and was coded as no siblings, one sibling, or two or more siblings.

Results: ANCOVA was used to determine whether children with two or more siblings performed differently from those with one sibling, with receptive language ability (PPVT) serving as a covariate. Results indicated that children who had more than two siblings performed better on the verbal appearance-reality tasks (M = 1.09, SE = .22) relative to children who had one sibling (M = 0.46, SE = .22; $F(1, 22) = 4.40$, p = .05); the remaining task scores and the composite score did not differ between groups. All analyses were also conducted with child age serving as a covariate and the results were comparable.

Conclusions: The findings suggest that a greater number of siblings may facilitate performance on some aspects of ToM, particularly the appearance-reality distinction. Results support research that posits social benefits for children with siblings (McAlister & Peterson, 2006). This work contributes to the

literature on cognitive differences in children with ASD by indicating that variability in ToM performance exists in relation to the family context. It is believed that sibling interaction provides a more developmentally appropriate model for an emerging ToM than that provided by adult interaction. These findings bear importance for the development of appropriate intervention strategies for children with ASD.

111.062 62 Cognitive Control in ASD: Methods to Explain Inconsistencies in Earlier Findings. H. M. Geurts*, *University of Amsterdam*

Background: Both researchers and clinicians acknowledge that individuals with ASD often encounter difficulties in adapting their behavior to a changing environment. These challenges are hard to assess and understand with our current neuropsychological toolkit, and findings in ASD often are inconsistent. Therefore, it was recently argued that (1) more mechanistic tasks (i.e. tasks that are known to involve specific brain regions and neural circuits) should be applied; and (2) both top down and bottom up processes should be taken into account when assessing cognitive control.
Objectives: To give examples of how mechanistic tasks can explain inconsistencies in former research by determining when and why individuals with ASD struggle with cognitive control.
Methods: We will present a literature overview of recent studies focusing on mechanistic cognitive flexibility and inhibitory control tasks. We will then focus on our own study of the intersection between emotion and cognitive control. In this specific study we focused on how emotion (bottom up) and cognitive control (top down) interact. We used a Go/NoGo paradigm, with socially relevant stimuli and varying presentation rates (fast and slow), with 18 children with ASD and 22 TD children (aged 8 to 13 years).
Results: There were no overall inhibition deficits in children with ASD; however, when processing emotional stimuli, children with ASD performed worse than TD children in the slow presentation rate condition. These results suggest that rather than possessing a core deficit in inhibitory control, children with ASD may exhibit low arousal levels in response to social stimuli.
Conclusions: By focusing on specific cognitive control mechanisms such as cognitive flexibility and inhibitory control, we can disentangle which processes are deficient and which are intact. This approach may be more fruitful than just focusing on a general construct such as executive functioning. Furthermore, an additional bottom up factor --arousal level --was revealed as important.

111.063 63 Cognitive Control Mechanisms Underlying Impaired Learning in Adults with Autism Spectrum Disorders. M. Solomon*[1], M. J. Frank[2], A. Smith[3], D. Badre[2], A. Kayser[4] and C. S. Carter[1], (1)*MIND Institute, Imaging Research Center*, (2)*Brown University*, (3)*U.C. Davis*, (4)*Unviersity of California, San Francisco*

Background: Many classic symptoms of inflexible behaviors found in ASDs can be explained as learning deficits involving impairments in the ability to extract subtle patterns of reinforcement-related signals from the current environment to direct behavior, and/or problems in "generalizing" learning in one context to another.

Objectives: To explain flexibility deficits by studying probabilistic reinforcement, transitive interference, and hierarchical learning, based on computational models of interactions between the basal ganglia, hippocampus and the prefrontal cortex (PFC), which is believed to represent progressively more abstract action rules within a gradient of progressively more rostral PFC regions

Methods: Age, IQ, and gender matched young adults with ASD (n=28) and typical development (TYP; n=31) participated in Studies (i) and (ii). In Study (i) they completed a probabilistic selection (PS) task with three stimulus pairs, AB, CD, and EF. They learned to choose one of two stimuli based on probabilistic feedback valid 80%, 70%, and 60% of the time. PS performance is thought to involve the inter-workings of the basal ganglia and the orbito-frontal cortex (OFC). In Study (ii) participants completed a transitive inference (TI) task. They 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, novel combinations BD and AE were tested. This task relies on the hippocampus, basal

ganglia, parietal cortex, OFC, and rostrolateral PFC. In Study (iii), 12 participants with ASDs and 15 TYP completed a hierarchical learning task. They learned stimulus-response mappings under two conditions: "flat" (appropriate mappings could not be described by more general rules, and thus had to be learned individually) and "hierarchical" (learning could be greatly facilitated by uncovering more abstract rules to guide responding). This task involves intact functioning of the basal ganglia, hippocampus, and pre-PMD. Data analysis for all tasks used both univariate methods and Bayesian state-space models.

Results: In Study (i), ASDs acquired the simplest AB (80%) pair at rates equivalent to TYP, but exhibited slower learning for the more difficult CD (70%) pair. They out-performed TYP on the EF stimulus pair for which valid feedback only was provided 60% of the time. This suggests ASDs exhibit OFC deficits. In Study (ii), ASDs learned simple stimulus response associations comparably to TYP, but showed reduced interference from intervening training trials. At test, they showed no significant differences on the novel BD pair, although their performance on the AE pair was worse. Again, findings suggest PFC impairments. In Study (iii), ASD performed comparably to the TYP group in the flat condition, but showed deficits on the hierarchical task, suggesting an inability to uncover the more abstract rules, which is consistent with an impairment in PFC function.

Conclusions: This pattern suggests that ASDs have cognitive control related learning deficits. They rely on rote learning-based strategies (related to intact basal ganglia and hippocampal function) rather than using more flexible PFC-based strategies reliant on abstracting subtle patterns of reward-related information; on rapidly updating reward contingencies; and on integrating task information in the service of goal directed behavior.

111.064 64 Comparing Face and Object Recall with Clinical Instruments for Individuals with Autism Spectrum Disorders.

L. Guy*[1], D. Glass[2], T. Cermak[2], J. Campbell[3], O. Ousley[4], K. Rockers[5] and A. Pakula[1], (1)*Marcus Autism Center, Emory University School of Medicine*, (2)*Marcus Autism Center*, (3)*University of Georgia*, (4)*Emory University*, (5)*Emory University School of Medicine*

Background:

Deficits in social cognition constitute core difficulties for individuals with autism spectrum disorders (ASD). One important domain of social cognition involves appropriate encoding, discrimination, recognition, and recall of faces. Specific impairments in processing faces versus objects have been described in the literature for ASD with evidence that memory for faces may be impaired despite intact memory for objects. Selectively impaired processing of faces may impact social communication as failure to appropriately encode, discriminate, recognize, and recall faces may affect reciprocal social interactions and lead to interpersonal difficulties.

Objectives:

The purposes of this study are: (a) to examine the ability of individuals with ASD to recall faces using the Memory for Faces (MF) and Memory for Faces Delayed (MFD) subtests of the NEPSY-II, a neuropsychological measure with limited data reported for individuals with ASD, (b) to compare face versus object recall for individuals with ASD using the NEPSY-II MF and MFD subtests and the Differential Ability Scales – Second Edition (DAS) Recall of Objects-Immediate (ROI) and Recall of Objects-Delayed (ROD) subtests, and (c) to examine if facial memory uniquely predicts ASD symptomatology as rated by clinicians, parents, and teachers.

Methods:

Participants are 59 children ages 5.3 – 16.75 years who participated in the Simons Simplex Collection (SSC), a multiple site, university-based research study, which collects genetic and phenotypic information from families that have one child with ASD. The SSC battery includes 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 study, additional measures were collected: (a) the MF and MFD subtests from the NEPSY-II, and (b) the ROI and ROD subtests from the DAS-II. The MF task is designed to assess encoding, discrimination, and recognition of faces. The MFD task assesses long-term memory for faces. The ROI and ROD subtests assess immediate and short-term recall of objects.

Results:

Descriptive data analysis will be used to examine participants' NEPSY-II and DAS-II subtest performance. Dependent samples *t* tests will be utilized to examine if individuals show better object versus face processing for immediate (i.e., MF-ROI contrast) and long-term recognition (i.e., MFD-ROD contrasts). Hierarchical regression analysis will be used to determine if NEPSY-II task performance predicts social communication impairments as measured by various clinical instruments, such as ADOS, parents' ratings of ASD symptomatology (i.e., SRS Parent scores), and teachers' ratings of ASD symptomatology (i.e., SRS Teacher scores). The unique contribution of NEPSY-II test performance will be examined in hierarchical fashion with chronological age and cognitive functioning entered prior to NEPSY-II test scores.

Conclusions:

Findings will provide additional information regarding the phenotypic expression of ASD and the clinical utility of NEPSY-II social perception tasks. In particular, findings will add to our understanding of the uniqueness of impairments for face versus object processing and recognition for a well-defined group of children with ASD. Further, findings will contribute knowledge regarding the potential utility of the NEPSY-II to identify social perception deficits with individuals with ASD.

111.065 65 Dissociation of Cognitive and Emotional Empathy: the Multifaceted Empathy Test for Children and Adolescents: MET-J. L. Poustka*[1], A. Rehm[1], S. Steiner[1], M. Bock[1], B. Rothermel[1], M. Holtmann[1] and I. Dziobek[2], (1)*Central Institute of Mental Health*, (2)*Freie Universität Berlin*

Background: Empathy, generally defined as the ability to understand and share another peronßs emotional state, is a multidimensional construct, consisting of cognitive (inferring mental states) and emotional (observer's emotional response to another person's emotional state) components. Both autism spectrum disorders (ASD) and conduct disorders (CD) have been described as disorders with empathy impairment. While most instruments assessing empathy focused rather on one component of empathy, the Multifaceted Empathy Test (MET) was designed to measure cognitive and emotional empathy simultaneously and independently using a series of photorealistic stimuli (Dziobek et al., 2008).

Objectives: To test a modified and age adapted version of the MET for adolescents from 10 to 17 years (MET-J) to differentiate empathy components in adolescents with ASD and CD.

Methods: We examined 15 adolescents with ASD (diagnoses were confirmed with ADI and ADOS), (mean age 13,6, SD=1,14 mean VIQ=107; SD=12,72) 15 adolescents with CD (mean age 14,4; SD=1,29; mean VIQ=101; SD=8,0) and 15 typically developing controls matched for age, sex and verbal IQ (mean age 13,6; SD=1,13; mean VIQ=110, SD=7,80). The age adapted version of the Multifaceted Empathy Test for adolescent (MET-J) was administered to all subjects; results were compared to results of well-validated self-report questionnaires assessing empathy (IRI, EQ).

Results: Groups differed significantly on both components of empathy, assessed with the MET-J. Adolescent with ASD showed impairments in cognitive empathy, but did not differ from healthy controls in emotional empathy. Adolescent with CD showed a inverted pattern of dissociation of empathy components, compared to adolescents with ASD .

Conclusions: As our results suggest, the Multifaceted Empathy Test for Children and Adolecents (MET-J) is an appropriate and feasible instrument to measure empathy in this age group. According to our findings, adolescent with ASD are impaired in their capacity to take the perspective of another

person and infer the correct mental state; however they do not differ in their ability to respond with adequate concern to the distress of others. Adolescents with CD show an inverse pattern of empathy compared to adolescents with ASD (unimpaired cognitive empathy vs. impaired emotional empathy). The double dissociation of cognitive and emotional empathy observed in ASD and CD could provide a more precise characterization of the behavioral phenotype of individuals affected by empathy impairments. A common classification of ASD and disorders with disruptive behaviors or psychopathic traits as "empathy disorders" should be regarded with caution.

111.066 66 Iconic Memory: Examining the Visual Information Processing Abilities in Children with Autism Spectrum Disorder. C. A. McMorris*, J. M. Bebko and L. N. Hancock, *York University*

Background: Iconic memory is an individuals' ability to accurately remember a number of items after a brief (e.g., 100 msec.) visual exposure. Previous research indicates that when a large amount of information initially enters the visual system, it remains in raw visual form, or as an 'icon'. During this time, information is coded and transferred to a more permanent store where it can be rehearsed and maintained in memory for longer periods of time (Sperling, 1960). Information processing capabilities such as these have been shown to be influenced by a variety of developmental and intellectual abilities. In particular, Baumeister and colleagues (1984) examined not only the memory capacity of individuals with an intellectual disability but also the rate of decay (i.e., how long the information stayed in short term visual storage). Results indicated that compared to typically developing adults, individuals with an intellectual disability recalled less information, and had a faster rate of decay. These authors suggest that quantitative and structural differences in iconic memory and information processing exist between typical and atypical individuals. Objectives: To date, previous research has primarily focused on the iconic memory capabilities of typically developing children and adults, as well as individuals with intellectual disabilities; however limited research has observed these abilities in children with Autism Spectrum Disorder (ASD). Thus, the current research is intended to examine children with ASD's iconic memory abilities and rate of information decay, as well as how other individual variables, such as level of cognitive functioning, influence children's visual memory. Methods: Twenty-nine typically developing (TD) children and children diagnosed with an ASD were briefly presented with a circular array of eight letters and asked to: 1) recall as many letters as they could (whole-report); or 2) recall the letter that was cued for recall (partial-report). Results: ASD and TD groups did not differ in the number of items accurately recalled on the whole- and partial-report trials nor the rate that information decayed from the iconic store. Additionally, results provided further evidence that information processing capabilities are influenced by a number of individual variables including, chronological age, language abilitiy, and stage of cognitive development. Conclusions: The present findings suggest that iconic memory may be an intact cognitive process in children with ASD. More specifically, compared to typically developing children, individuals with ASD: 1) are able to intake comparable quantities of briefly presented information; 2) have similar rates of information decay; and 3) require equivalent time to process information. The current research findings not only provide insight into the iconic memory capabilities of children with ASD, but also help to clarify the stage at which information processing may begin to deterioriate in individuals with ASD. The present study also contributes to identification of the intact and impaired facets of memory, which can potentially aid in developing both educational and treatment programs for children with ASD.

111.067 67 Joint Attention as a Predictor of Developmental Change in Preschool-Aged Children with Autism Spectrum Disorders. S. Novotny*[1], D. C. Coman[1], P. S. Schoultz[1], A. Gutierrez[1], M. Alessandri[1], K. Hume[2], L. Sperry[3], B. Boyd[4] and S. Odom[4], (1)*University of Miami*, (2)*Frank Porter Graham Child Development Institute, University of North Carolina, Chapel Hill*, (3)*University of Colorado Denver*, (4)*University of North Carolina*

Background: One of the hallmark impairments in social-communication in children with Autism Spectrum Disorders (ASD) is a deficit in joint attention. Joint attention (JA) refers to a set of behaviors, such as showing or pointing, used to include a social partner into an experience involving an object or event. Prior research suggests that JA is an integral part of language development because it facilitates the process of word-object mapping (Morales, Mundy, Delgado, Yale, Messinger, Neal, & Schwartz 2000). Due to their low levels of JA, children with ASD develop at slower rates than their typically developing peers. In order to increase their developmental rates of learning to the level of their typically developing peers, these rates need to be improved through intervention-based programs. Alessandri, Bomba, Holmes, Van Driesen, and Holmes (2002) found that early intervention through structured behaviorally based learning programs can significantly increase a child's cognitive, social, language/communication, and motor developmental rates of learning.

Objectives: The goal of the current study was to assess the association between joint attention skills, language development rates, and autism severity. Specifically, this study investigated two levels of JA, both initiating joint attention and responding to joint attention, as predictors of developmental rates during treatment and autism severity.

Methods: Participants included 22 preschool-aged (*M* = 46.59 months, *SD* = 6.56) children with a confirmed diagnosis of ASD. Joint attention skills were measured at the beginning of the school year with the Early Social Communication Scales (ESCS; Mundy, Hogan & Doehring, 1986). The Mullen Scales of Early Learning (MSEL; Mullen, 1995) and the Preschool Language Scale, 4th edition (PLS-4; Zimmerman, Steiner & Pond, 2002) measures were administered at the beginning and the end of the school year to assess functioning across several developmental domains. Developmental rate was calculated by dividing the difference in MSEL and PLS age equivalent scores (from the beginning of the year and the end of the year) by the difference in chronological age from pre to post-treatment. Autism severity was measured by the Autism Diagnostic Observation Schedule (ADOS; Lord, Rutter, DiLavore, & Risi, 1999).

Results: Results of a Pearson R correlation showed that RJA was positively correlated with Total Language Score developmental rate on the PLS (r = .504, p = .017). RJA was also negatively correlated with autism severity (r = -.611, p = .001).

Conclusions:

Results indicated significant associations between JA skills, language developmental rates, and autism severity. Though directionality cannot be determined, these results suggest that higher abilities in responding to JA may increase rates of language development during treatment and children may also appear less symptomatic. Further research should examine a possible causal relationship between autism severity, joint attention and developmental change during treatment. Determining which factors influence a child's development during treatment may be important to creating programs that target the developmental gap between children with ASD and their typically developing peers.

111.068 68 NEPSY-II Social Cognition Profiles for Children with Autism Spectrum Disorders and Their Siblings: Preliminary Results. B. E. Deerrose*[1], J. M. Phillips[1], K. J. Parker[1] and A. Y. Hardan[2], (1)*Stanford University*, (2)*Stanford University School of Medicine/Lucile Packard Children's Hospital*

Background:

Recent research has focused on the prevalence rates of autistic symptomatology in the siblings of individuals with an autism spectrum disorder (ASD). This interest is related to the evidence linking genetic risk factors to the development of autism. It has led to the development of a body of literature supporting the existence of social and language deficits, although not severe, in siblings of individuals with autism.

Objectives:

This investigation used the NEPSY-II Social Perception scales – Theory of Mind and Affect Recognition – to investigate social deficits in

children with an ASD and their siblings compared to an age- and gender-matched control group. The NEPSY-II has been shown to be both reliable and valid as an instrument and is one of the few established neuropsychological assessments to include a theory of mind subscale.

Methods:

Participants included children with autism, their siblings, and neurotypical controls between the ages of 3 and 12 years. Subjects were recruited to participate in a larger study examining the relationships between oxytocin biology and social deficits as measured by the NEPSY-II's Theory of Mind and Affect Recognition tasks. Autism diagnosis was based on the Autism Diagnostic Observation Schedule (ADOS), Autism Diagnostic Interview Revised (ADI-R), and expert clinical opinion.

Results:

To date 105 participants (62 boys and 43 girls) have completed the study procedures including 28 children with an ASD, 29 siblings, and 48 controls. There were no significant age or gender differences between groups. As expected, children with an ASD performed significantly worse on both tasks compared to the control sample [Affect Recognition: $F(1, 71) = 20.933$, $p = 0.000$, Theory of Mind: $F(1, 71) = 29.407$, $p = 0.000$]. Interestingly, the siblings group performed better than the affected probands on both Theory of Mind [$F(1, 52) = 15.830$, $p = 0.000$] and Affect Recognition [$F(1, 53) = 7.153$, $p = 0.010$] tests, with no differences between siblings and controls. Additionally, no significant gender differences were observed, either overall or within groups.

Conclusions:

Findings from this preliminary investigation indicate that the siblings of children with an ASD have minimal deficits in theory of mind tasks and affect recognition, as measured by the NEPSY-II. Future studies with larger sample sizes are needed to further examine these observations, especially in light of the mounting evidence suggesting that siblings exhibit some levels of social deficits.

111.069 69 Prototype Learning in Preschoolers with Autism Spectrum Disorders. S. McCurry*, H. Noble, L. G. Klinger and M. R. Klinger, *University of Alabama*

Background: Infants and young children typically learn about their world by forming summary representations (i.e., prototypes) of different categories of objects and events. By 78 hours after birth, infants with typical development (TD) show this ability (Walton & Bower, 1993). However, Klinger and colleagues (Klinger & Dawson, 2001; Klinger, Klinger, & Pohlig, 2005) reported that individuals with ASD have impaired prototype categorization abilities. They suggested that this may be an early developing cognitive impairment that may lead to the development of ASD symptoms. However, no research has examined prototype categorization in young children with ASD.

Objectives: The present study examined prototype learning in preschoolers with ASD and TD using a non-matching to sample task. We hypothesized that preschoolers with ASD would show decreased prototype category learning compared to preschoolers with TD. Further, we predicted that impaired prototype category learning would be related to autism symptoms, nonverbal reasoning, and language ability in preschoolers with ASD, but not preschoolers with TD.

Methods: In this ongoing study, six children with TD (mean age of 41 months) and five children with ASD (mean age of 57 months) matched on receptive language ability have completed the prototype learning task to date. Participants learned categories of novel animals whose features varied along several dimensions. Categorization skills were assessed using a non-matching to sample paradigm in which children were taught to chose the novel animal. Rewards were attached to the back of each card, such that choice of the novel animal resulted in a small toy or treat. Using this method, each child was familiarized to a category of animal (i.e., the MIP family). During test trials, children were shown two novel exemplars of the same animal family, one of which was the mathematical average of all previously seen animals (i.e., the prototype) and the other which was a non-averaged exemplar. A

preference for the non-prototype animal was taken as evidence that children viewed the prototype as familiar rather than novel and suggested that children learned the animal category prototype.

Results: Performance was compared to chance (i.e., 50%). Children with ASD chose the novel animal 54% of the time which did not differ from chance, $t(5)=.31$, $p=.77$. Thus, there is no evidence that children with ASD showed prototype learning. However, children with TD chose the novel animal 75% of the time, suggesting that they viewed the prototype as familiar, $t(4)=3.16$, $p=.03$. Thus, children with TD showed strong evidence of prototype learning. Groups were significantly different from each other, $t(9)=2.66$, $p=.06$.

Conclusions: Preliminary results suggest significant group differences between preschoolers with ASD and TD on the prototype learning task. Children with TD showed a prototype learning rate that was significantly different from chance while children with ASD did not demonstrate prototype learning above chance levels. Taken together, these findings suggest that young children with ASD are not showing evidence of prototype learning even with simple task demands and a completely nonverbal task. Further research examining the relation between prototype formation, autism symptoms, and developmental level is ongoing.

111.070 70 Sensitivity and Response to Direct and Averted Gaze in Toddlers with Autism Spectrum Disorders. K. A. Rice*[1], W. Jones[2] and A. Klin[1], (1)*Yale University School of Medicine*, (2)*Yale School of Medicine*

Background: Individuals use direct and averted gaze for a variety of social and communicative purposes, including conveying emotion and directing attention. Research has repeatedly found altered gaze monitoring in individuals with autism spectrum disorders (ASD). Atypicalities include diminished sensitivity to direct eye contact and a lack of differential response to attentional cues originating from eye gaze rather than from non-social cues. Much of the research has either relied on general observational measures (e.g., parent or clinician ratings of how a child responds to gaze cues) or has used fine-grained measures at the expense of naturalistic presentation (e.g., relying on static or otherwise simplified experimental paradigms), thus reducing ecological validity. It is unclear how this work translates into sustained naturalistic interaction, which requires an ongoing and fine-scaled temporal sensitivity to direct and averted gaze. Examining these processes in young children will help illuminate the developmental path of gaze monitoring in individuals with ASD. To that end, the present study investigates the reactions of toddlers to gaze shifts while watching naturalistic video of an actress.

Objectives: This study uses eye-tracking technology to measure the sensitivity and response of toddlers with ASD to direct and averted gaze during a natural viewing task.

Methods: Two-year-olds with ASD and typically developing (TD) two-year-olds, matched on age and nonverbal functioning, watched a three-minute video of an actress interacting with hand puppets. Throughout the video, the actress shifted her gaze back and forth from the viewer to the puppets. Her gaze shifts were spontaneous and contingent upon her social actions, resulting in variable durations of averted and direct gaze. Each toddler's visual scanning patterns were examined within a fixed temporal window following each gaze shift to measure temporal sensitivity and response to change in gaze. Two aggregated variables were also analyzed for each child, one of which combined responses for all instances of direct gaze, and the other which collapsed across instances of averted, puppet-directed gaze. All measures were then evaluated at the group level, comparing toddlers with ASD to TD toddlers.

Results: Preliminary analyses indicate that TD toddlers and toddlers with ASD respond differently to gaze shifts by the actress. TD toddlers appear more sensitive to instances of direct gaze, as they were quicker to look at the actress's face when she re-established eye contact. A similar bias toward the face was found during averted, puppet-directed

gaze. In these situations, TD children were slower to shift attention away from her face to the referenced object.

Conclusions: Toddlers with ASD differ from their TD peers both in their sensitivity to re-establishment of direct gaze and in their response to gaze shifts directed to a particular object. This early divergence from the typical response to natural gaze has implications for both social and communicative development.

136.013 13 The Difference Between High-Functioning Autistic Disorder and the Other Pervasive Developmental Disorders in Mind-Reading Ability. M. Kuroda*[1], A. Wakabayashi[2], T. Uchiyama[3], Y. Yoshida[3], T. Koyama[1] and Y. Kamio[4], (1)*National Center of Neurology and Psychiatry*, (2)*Chiba University*, (3)*Yokohama Psycho-Developmental Clinic*, (4)*National Center of Neurology and Psychiatry, Japan, National Institute of Mental Health*

Background: Many studies investigated the difference among the subgroups of Pervasive Developmental Disorders (PDD), defined by the Diagnostic and Statistical Manual, Forth Edition (DSM-IV) (APA, 1994), Text Revision (DSM-IV-TR) (APA, 2000) in the mind-reading ability, especially between high-functioning autistic disorder(HFA) and Asperge's disorder (AS). But the results have been inconsistent (Dahlgren et al. 1996, Kaland et al. 2002, Ozonoff et al. 1991ab, 2000, Royers et al. 2001, Spek et al, 2009). Regarding the predominant modality for the individual with AS in mind-reading, Golan et al. (2006) found that the male with AS had more difficulties recognizing emotions from faces than from voices.

Objectives: We aimed to examine the difference in the mind-reading ability between HFA and the other PDD which consist of AS and Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS) in both the visual and the auditory mind-reading tasks.

Methods: The participants consisted of 28 male adolescents and adults with PDD (mean age =24.5yrs, SD=7.7, range=16yrs-45yrs). They were divided into two groups: HFA group(n=17, FIQ=103.2, VIQ=103.9, PIQ=100.3, AQ33.3) and the other PDD group(n=11, FIQ=108.2, VIQ=109.4, PIQ=106.5, AQ34.3). The control group consisted of 50 male students recruited from Chiba University (mean age 21.2 yrs). The advanced mind-reading tasks that were consisted of 41 video clips (3 seconds~11seconds in length) from the TV drama "Shiroi Kyotou", a story about malpractice in a famous Japanese medical school. The tasks were designed to assess the mind-reading ability from either only the visual information (facial expression, gesture, posture) or only the auditory information (non-verbal aspects of speech: pitch/intonation/tone). One visual task and one auditor task were made for each corresponding clip. A word or a phrase which expressed the 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: In order to compare the correct response rates of the visual task and the auditory task among the HFA, the other PDD and the control groups, an ANOVA was performed with the correct response rates as depend variables, group (HFA/other PDD/control) and task(visual/auditory)as independent variables. Although there were significant differences between HFA (Visual=62.4%, Auditory=54.9%) and the other PDD (Visual=71.3%, Auditory=64.9%) in both the Visual and Auditory tasks, there are no differences between the other PDD and the control group (Visual=72.1%, Auditory=66.6%) in both.

Conclusions: The adequate difficult mind-reading tasks can distinguish the HFA from the other PDD. Clinically, the individuals with HFA may have severer social problems than the individuals with AS or PDD-NOS.

111 Developmental Stages

111.071 71 Associated Psychiatric Conditions, Problem Behavior, and Adaptive Functioning in Adolescents with ASD. C. M. Brock*[1], A. M. Estes[1], L. Sterling[2], J. Munson[1], B. King[3] and G. Dawson[4], (1)*University of Washington*, (2)*University of California, Los Angeles*, (3)*University of Washington and Children's Hospital and Regional Medical Center*, (4)*UNC Chapel Hill*

Background: In addition to the core social, communication and behavioral features of ASD, up to 80% of adolescents with ASD may suffer from additional psychiatric conditions and problem behaviors, which can further impair functioning. Researchers have reported exacerbation of associated symptoms and behavioral deterioration in one third to one half of children with ASD around the time of puberty and early adolescence. Because ASDs alone can be quite debilitating, associated symptoms are often not the primary focus of diagnosis or treatment. However, such symptoms can exacerbate impairments in individuals with ASD and may be treatable with behavioral and pharmacological interventions.

Objectives: Investigate whether 13-15 year olds with ASD have higher levels of psychiatric conditions and lower adaptive functioning compared with adolescents with typical development. Describe the relationship between level of cognitive functioning and associated conditions in this sample. Explore the relationship between pubertal onset and levels of associated conditions in adolescents with ASD.

Methods: 27 adolescents with ASD and 26 adolescents with typical development between 13-15 years of age were assessed for psychiatric conditions, problem behavior and adaptive functioning. Parent report of associated psychiatric conditions was obtained using the Child Behavior Checklist, problem behavior using the Aberrant Behavior Checklist and adaptive functioning using the Vineland Adaptive Behavior Scales. The Differential Ability Scales II was used to directly assess cognitive ability in both groups. Pubertal development was assessed using the Tanner Scale of Sexual Maturity.

Results: Parent report of psychiatric conditions indicates that adolescents with ASD have increased internalizing and externalizing symptoms, increased problem behavior and decreased adaptive functioning compared with typically developing adolescents. In addition, the relationship between level of cognitive function and associated psychiatric conditions, problem behavior and adaptive functioning will be investigated. The role of pubertal development will be discussed.

Conclusions: Research on associated conditions and adaptive functioning in adolescents is needed to increase awareness of the range of psychiatric conditions and adaptive functioning challenges facing adolescents with ASD. This awareness should be used to guide clinical assessment procedures in this age group and provide more effective intervention to adolescents with ASD.

111.072 72 Attention During Face-to-Face Interaction: When Do Infants at-Risk for Autism Shift Gaze?. N. Ekas*, L. Ibanez, W. Mattson and D. S. Messinger, *University of Miami*

Background: The developing ability to disengage from an arousing stimulus has salient implications for infant socio-emotional functioning. Infant siblings of children with autism spectrum disorder (ASD-sibs) are at an increased risk for the development of autistic disorders and subclinical deficits that impair socio-emotional functioning. Compared to the infant siblings of typically-developing children (COMP-sibs), young ASD-sibs spend similar amounts of time gazing at their parent's face; however, they shift their gaze to and from the parent's face less frequently than COMP-sibs. Research suggests that any group differences in emotional expressions during infancy are subtle. To date, there has been no research examining when infants at risk for ASD shift their attention. That is, are these infants more likely to shift their attention when emotionally aroused or when in a neutral state?

Objectives: The purpose of the current study was to examine whether 6-month-old ASD-sibs and COMP-sibs differ in the rate of shifting attention when exhibiting various emotional expressions.

Methods: ASD-sibs (n = 27) and COMP-sibs (n = 19) participated in the face-to-face/still-face (FFSF) at 6 months of age. The FFSF consists of three episodes: a 3 minute face-to-face (FF) episode, a 2 minute still-face (SF) episode, and a 3 minute reunion (RE) episode. FACS certified coders rated infant facial expressions (smile, cry-face, neutral

[neither smile nor cry-face]). The onsets and offsets of infant gazes at and away from the parent's face were also reliably coded.

Results: No significant group differences for infant emotional expressions were found. When compared to COMP-sibs, ASD-sibs spent significantly more time gazing away from the parent's face during the SF episode. Both groups of infants shifted attention more frequently during the FF and RE episodes than during the SF episode. As previously reported, ASD-sibs shifted their attention less frequently than COMP-sibs during the FF and SF episodes (Ibanez et al., 2008). No significant differences for attention shifting during infant negative or positive expressions emerged. ASD-sibs, however, were less likely than COMP-sibs to shift attention when exhibiting a neutral expression during the FF and SF episodes.

Conclusions: Although there are previously documented deficits in the flexibility of attention allocation among ASD-sibs, studies have not examined the emotion state that was the context for attention shifts. The present study specifies when ASD-sibs exhibit developing deficits in gaze shifting. Infants spent the majority of their time in a neutral state. This state appeared to represent a 'risk condition' for sticky attention for ASD-sibs as their attention shifts were slower during neutral expressions. It is possible that ASD-sibs are only motivated to shift attention under conditions of heightened arousal, suggesting a possible avenue for early efforts aimed at prevention and intervention. In sum, the results of the present study highlight the importance of considering the coordination of various modalities, as opposed to examining each one in isolation. Further analyses will be presented incorporating sequential analyses to micro-analytically investigate how infant gaze and emotional expression are temporally coordinated.

111.073 73 Comparison of Adaptive Behavior Trajectories in Childhood Disintegrative Disorder Versus Autistic Disorder. A. Westphal*[1], A. Ristow[1] and F. R. Volkmar[2], (1)*Yale University*, (2)*Yale School of Medicine*

Background:

Childhood Disintegrative Disorder (CDD) is a rare and poorly understood Autism Spectrum Disorder (ASD) characterized by a dramatic regression of adaptive skills after > two years of normal development. Previous studies have found that, subsequent to regression, children with CDD have worse outcomes than their counterparts with Autistic Disorder (AD) in terms of the number of functional domains impacted and the degree to which each domain is impacted. However it is unclear whether these differences are sustained over time. It has also been established that children with CDD have, on average, greater intellectual disability than those with AD. However, to date, children with CDD have not been compared to an IQ matched group with AD. Thus it is unclear whether intellectual function mediates the differences in adaptive outcome, or whether some more fundamental difference in the neuropathology of the disorders is responsible.

Objectives:

To compare adaptive behavior capacities and adaptive trajectories of children with CDD to a cognitively similar group with AD. To examine the adaptive behavior profiles associated with CDD to determine whether the disorder has differential impact on specific domains.

Methods:

In comparison 1, the domain and subdomain scores on the Vineland Adaptive Behavioral Scales of 11 children with CDD were compared to the scores of an age, IQ and gender matched group with AD usinga two-tailed paired t-test of dependent means. Effect sizes were calculated by dividing the average difference between groups divided by the standard deviation of the difference between groups, and were ranked according to standards developed by Cohen. In comparison 2, the trajectory of progress for

each CDD subject was calculated for the Vineland domains and subdomains in units of change in age-equivalent score per chronological year. A t-test of dependent means was used to compare the rates of change between categories. Due to the impossibility of matching subjects on the basis of age, IQ, gender, as well as the interval between testing periods, in comparison 3, the average progress of the CDD group in each domain and subdomain was compared to the rate of change of a line fit to the single time point scores of age, IQ and gender matched subjects with AD. All results were adjusted using the Bonferroni method.

Results:

In comparison 1, the differences in composite adaptive behavior, communication scores and receptive language sub-scores reached significance at $p<0.05$, however were not significant once adjusted. In comparison 2, rates of expressive language change were higher than other subdomain scores, however a comparison between rates of change in general Vineland categories did not reach significance. In comparison 3, adaptive trajectories did not distinguish the CDD subjects from the AD group.

Conclusions:

CDD and AD can be distinguished by pattern of onset and level of cognitive impairment. However once IQ is factored in, children with CDD have similar adaptive levels and trajectories to their counterparts with AD. Furthermore, children with CDD demonstrate no significant differences in the degree to which individual adaptive domains are impacted, experiencing a generalized skill loss.

111.074 74 Early Gesture Use in Infants with Autism Spectrum Disorders with and without Regression. K. P. Wilson*, J. Dykstra, L. Watson, G. T. Baranek and E. Crais, *University of North Carolina at Chapel Hill*

Background: Twenty to forty percent of parents report regression, or loss of early communication and/or motor skills, in their children with autism spectrum disorders (ASD). Recent studies investigating the existence and nature of a regressive phenotype in ASD have validated this phenomenon (Wiggins et al., 2009) and underscored important differences in gesture use prior to regression (Luyster et al., 2005). Werner & Dawson (2005) found similarities in joint attention behaviors in 12 month-old infants with ASD and regression and those with typical development; however, a more complete picture of gesture use in the first year of life has not been outlined. The relationship between early regression in communication and later symptom severity (Baird et al., 2008) highlights the clinical importance of this line of inquiry.

Objectives: To test the hypotheses that: (1) Infants later diagnosed with ASD whose parents reported regression use gestures with the same frequency at 9-12 months as typically developing (TD) infants; and (2) both of these groups use more gestures than infants with later ASD diagnoses without reported regression.

Methods: The study utilized retrospective video analysis, examining home video footage recorded prior to diagnosis. Videos recorded during infancy were obtained from parents of 41 children with ASD and 31 TD children. Researchers collected information from parents about occurrence and age of regression using a questionnaire. For the regression group, data were excluded for children whose parents reported regression prior to or during the 9-12 months period of recording.
Five-minute samples of randomly selected scenes from 9-12 months footage were compiled for coding of gesture use. Using a checklist, independent coders made three judgments regarding children's behaviors: (1) Was the behavior among those listed as potential gestures on the checklist? (2) Was there evidence that the child was directing the behavior to another person? (3) Did the behavior serve a communicative function of behavior regulation, joint attention, or social interaction? A consensus procedure was used

for disagreements to ensure optimal data integrity.

Results: Analyses included descriptive statistics and analysis of variance with appropriate follow-up tests. Screening of data revealed that of the 41 children later diagnosed with ASD, 21 had parent-reported regression, and 20 had parents who reported no regression. The group means for total gesture use in video samples from 9-12 months were: TD = 2.95, ASD with regression = 1.50, ASD without regression = 1.05. The ANOVA showed significant group differences in total gesture use. Follow-up tests showed significant difference between the non-regression and TD groups (p=.03). Total gesture use of the regression group was not significantly different from either the non-regression group or the TD group.

Conclusions: Total gesture use by children with ASD with parent-reported regression was at an intermediate level that did not significantly differ from either the TD group or the non-regression group at 9-12 months of age. The non-regression group was significantly different from the TD group, as hypothesized. Future directions and clinical implications will be discussed.

111.075 75 Examining Temperament in a Longitudinal Study of High-Risk Infants for ASD. K. M. Burner*[1], K. M. Venema[1], E. J. H. Jones[1], A. M. Estes[1], B. King[2] and S. J. Webb[1], (1)*University of Washington*, (2)*University of Washington and Children's Hospital and Regional Medical Center*

Background: Infant siblings of children with ASD experience a 2 to 50-fold increase in risk for developing autism. In the first year of life, high-risk infants who later go on to develop ASD may exhibit subtle disruptions in temperament that occur prior to the onset of clinical symptoms. A prospective study of infant siblings of children with ASD found that infants who were later diagnosed with ASD displayed higher levels of passivity and decreased activity at 6 months, atypical reactivity at 12 months of age (Zwaigenbaum et al., 2005), early irritability and proneness to distress and difficulty controlling attention and behavior at 24 months (Bryson et al., 2007; Garon et al., 2009). The present study represents one of the ongoing efforts to explore how temperament may influence the trajectory for high-risk infants.

Objectives: To examine temperament in high-risk and low-risk infants at 6 and 12 months of age. It is expected that by 12 months, the high-risk group will have lower positive affect, higher negative affect, and more difficulty regulating behavior on a parent report of temperament. The stability of temperament, as assessed via parent report, will be examined from 6 to 12 months as well as the relationship between temperament and early ASD risk symptoms at 12 months.

Methods: Participants included infant siblings of children with ASD (high-risk infants) and infant siblings of children without ASD (low-risk infants). Measures were administered at 6 and 12 months of age including a parent report of temperament, the Infant Behavior Questionnaire Revised (IBQ-R), a behavior observation of autism risk markers (the Autism Observation Scale for Infants (AOSI)), and a measure of cognition (the Mullen Scales of Early Learning).

Results: Preliminary results indicate no significant group differences on each factor of the IBQ-R at 6 or 12 months. Future analysis will include a larger sample and will examine the relationship between temperament domains on the IBQ-R and ASD risk symptoms at 12 months. Additional analyses will examine change scores from 6 to 12 months of age to look at the stability of parent report of temperament.

Conclusions: Preliminary results found no group differences of temperament at 6 months which is consistent with previous high-risk studies using parent report of temperament. The lack of group differences at 12 months may be due to the small sample size in the preliminary analysis. A larger sample is currently being obtained in which we expect that the high-risk group will reportedly have lower positive affect, higher negative affect, and more difficulty regulating behavior on the IBQ-R and that this temperament profile will be associated with symptom severity at 12 months as measured by the AOSI. The study of temperament in high-risk infants may help inform efforts

aimed at the earlier identification and intervention of ASD.

111.076 76 Hope and Worry in Mothers of Children with Autism and Down Syndrome. P. Ogston*[1], B. Myers[1] and V. H. Mackintosh[2], (1)*Virginia Commonwealth University*, (2)*University of Mary Washington*

Background: Mothers of children with ASD's report greater stress when compared to parents of typically developing children or children with Down syndrome. However, there is a paucity of research that has examined hope or worry in these parents.
Objectives: Mothers' perceptions of their child's disability, as well as their own characteristics, seem to better predict adjustment than measures of diagnosis or degree of impairment. The present study examined both parent and child characteristics in relation to mothers' hope and worry.
Methods: Two hundred-fifty nine mothers and step-mothers of children with autism spectrum disorders (n = 199) and Down syndrome (n = 60) participated in this study. Participants were recruited via advertisements placed in newsletters and on websites of organizations associated with autism spectrum disorders and Down syndrome. Data was collected via an online survey. Mothers provided demographic information pertaining to themselves as well as their child. They also completed The State Hope Scale, The Penn State Worry Questionnaire and The Maternal Worry Scale for Children with Chronic Illness.
Results: A hierarchical linear regression was used to predict dispositional (Penn State) worry. The independent variables were entered in 3 steps: (i) diagnosis, (ii) impairment, (iii) hope (State Hope Scale). Results indicate that the overall model predicts dispositional worry, where F (5, 253) = 13.78, p = .00.
A hierarchical linear regression was performed where future related (Maternal Chronic Illness) worry was the dependent variable. The independent variables were entered in 3 steps: (i) diagnosis, (ii) child's impairment (ATEC), (iii) child's age. Results indicate that the overall model predicts future related worry, where F (5, 253) = 10.64, p = .00.
A hierarchical linear regression was performed to predict hope (State Hope Scale). The independent variables were entered in 3 steps: (i) diagnosis, (ii) child's impairment (ATEC) (iii) Mother's Education (years). Results indicate that the overall model is a significant predictor of hope, where F (5, 252) = 15.16, p = .00.
It was found that mothers' level of maternal (future) worry differed depending on child's diagnosis where F (3, 255) = 3.01, p = .031. Mothers of children with autism reported more future related worry than mothers of children with Down syndrome, where p = .042. Mothers' level of hope varied by diagnosis, where F (3, 255) = 7.07, p = .00. Mothers of children with autism reported less hope than mothers of children with Down syndrome, where p = .00.
Conclusions: Mothers with higher hope reported lower dispositional worry. Children's level of impairment was significantly associated with dispositional and maternal (future) worry, where more severe impairment correlated with higher levels of worry. Child's level of impairment was also associated with hope, where mothers of children with less severe impairment reported higher levels of hope. Mothers' level of education was associated with hope, where mothers with more years of education reported higher levels of hope. These findings further inform our understanding of the experience of raising a child with an autism spectrum disorder or Down syndrome.

111.078 78 Medical Residents Knolwedge of and Comfort Assessing for Autism Spectrum Disorders: A Model for Training. A. Kinsman and N. R. Powers*, *Greenville Hospital System Children's Hospital*

Background: Primary medical care provides are often the first professionals to identify potential autism spectrum disorders (ASDs). The American Academy of Pediatrics (AAP) has established guidelines for the screening of and referring for evaluation of ASDs. However, many barriers exist to training residents in screening for, identifying and referring for evaluation of ASDs, including limited exposure to children with ASDs, volume of other training activities, and limited presence of specialty training in primary care training clinics. Such factors may

result in delays in identification of suspected ASDs and referral for evaluation.

Objectives: The objective in this study was to examine residents' (1) knowledge of ASDs and (2) perceived comfort in screening, identifying, and referring for evaluation of ASDs before and subsequent to specialty training in ASDs during their Developmental-Behavioral Pediatrics Rotation.

Methods: Prior to beginning their Developmental-Behavioral Pediatrics rotation, residents completed a pre-test designed to assess knowledge of ASDs and a survey regarding their uses of screen tools and comfort in identifying and discussing ASDs with their patients' families. Residents then participated in structured training activities including educational materials, participating in autism-specific intake interviews, administering screening measures, and active observation of diagnostic evaluations. Following completion of the rotation, the residents completed post-test measures assessing knowledge of and comfort with ASDs.

Results: Residents' knowledge of ASDs pre and post intervention will be examined. Differences in perceived comfort in screening for, identifying, and discussing ASDs with families will be determined. Frequency of the use of screening tools for ASDs will also be analyzed.

Conclusions: The impact of structured training on residents' knowledge of and comfort in screening for and discussing ASDs will be discussed. Implications of how training is provided to residents on occurrence of and timing of referral will also be discussed. Recommendations for training residents implementing AAP screening guidelines will be offered.

111.079 79 The Prevalence of Stunting, Underweight and Wasting Among Autistic Children in the Sultanate of Oman. Y. Al-Farsi*[1], M. Waly[2], M. Al-Shafaee[3] and M. Al-Sharbati[1], (1)*College of Medicine and Health Sciences, Sultan Qaboos University*, (2)*Sultan Qaboos University, College of Agricultural and Marine Sciences*, (3)*Sultan Qaboos University*

Background: Anthropometric measures are used to evaluate the nutritional status of infants and children. Z-scores (number of standard deviations (SD) above or below the mean) are valuable in monitoring the prevalence of stunting (height for age), underweight (weight for age) and wasting (weight for height) among preschool children.

Objectives: to assess the prevalence of stunting, underweight and wasting among autistic children in the Sultanate of Oman.

Methods: This is a cross-sectional study in which the autistic child's weight and height are expressed in standard scores of the median of the international references, National Centre for Health Statistics (NCHS), as relevant to their age and gender.
Results: Moderate stunting is indicated by height for age below -2 SD, moderate underweight is indicated by weight for age below -2 SD and moderate wasting is indicated by weight for height below -2 SD. Below -3 SD indicates a severe condition.
Conclusions: Stunting and underweight prevalence among autistic children represent long term, chronic, undernutrition and needs time to develop and recover, whereas wasting is due to short term, acute, malnutrition and can be improved rapidly. Improving the nutritional status of autistic children is crucial for improving these anthropometric indices.

111.080 80 The Social Communication Questionnaire in the General Population. M. Hornig[1], S. Schølberg[2], M. Bresnahan*[1], P. Surén[2] and A. BC Study Group[1], (1)*Columbia University*, (2)*Norwegian Institute of Public Health*

Background: Autism screening tools, including the Social Communication Questionnaire (SCQ), have been widely investigated in school-age referred populations; less is known about their utility in general populations, particularly at the preschool age

Objectives: Examine the distribution of total SCQ, SCQ domain and individual item scores in a general population birth cohort.
Methods: : Children in this analysis were drawn from the Autism Birth Cohort (ABC), a subset of a prospective birth cohort in Norway (the MoBa). Children whose parents

completed a questionnaire including the 40-item SCQ at child age 36-39 months were included (n=29,093). SCQ total scores(SCQ39-M) and social impairment, repetitive/ritualistic behaviors, and communication impairment domain scores were derived per manual guidelines (SCQ39-M). The association of child and parent characteristics, including sex, birth order (first- vs later-born), maternal age (< 25, 25-34, ≥ 35 years), maternal education (< 12 years, 12 years, 13-16 years, 17+ years), and referral status (questionnaire item regarding referral for educational/habilitation/psychiatric evaluation) with SCQ profiles were examined.

Results: The sample was comprised of 50.9% boys; nearly half were first-born. The mean age of mothers was 30.16 ± 4.4 years. 2.8% of children had been referred for community clinical/educational assessments. The mean of SCQ39-M scores was 6.31 ± 3.31. Only 1.2% received a total of 0 (i.e., no reported symptoms); 1.5 % had scores ≥ 15. Thirteen SCQ items were endorsed in >20% of children, and 9 of these were reported in >33% (echolalia, inappropriate questions, pronoun reversal, verbal rituals, compulsions and rituals, use of others boy, repetitive use of objects, complex mannerisms, friends). Boys had higher total SCQ39-M scores than girls (6.75 v 5.85). This pattern was reversed among nonverbal children, where total scores were greater among girls than boys (9.67 v 8.86). First-borns had higher SCQ39-M scores than later-born children (6.83 v 5.89), largely reflecting greater number of repetitive/ritualistic behaviors. Consistent with this finding, advancing maternal age was associated with decreasing total symptom reports. Furthermore, low maternal education was associated with higher SCQ39-M total scores. Children referred for services (education, habilitation, psychiatry) reported more symptoms than non-referred children

Conclusions:

SCQ patterns are associated with sex, birth order, maternal age, maternal education and referral history. Expanded awareness of factors influencing reporting, and factors regulating behaviors commonly endorsed for preschool children will help refine autism screening tools such as the SCQ and enhance generalizability of these instruments for detection of autism risk very young children.

111.081 81 Traits Contributing to the Autistic Spectrum. C. D. Steer*[1], P. Bolton[2], S. Roulstone[3], A. M. Emond[1] and J. Golding[1], (1)*University of Bristol*, (2)*Institute of Psychiatry, King's College London*, (3)*University of the West of England*

Background: ASD may represent a 'compound' phenotype that may be fractionated into different components each having separate as well as shared genetic and environmental causes. To date, the evidence to support this hypothesis is conflicting.

Objectives: To investigate the traits characterising ASD.

Methods: Using the large population-based Avon Longitudinal Study of Parents and Children cohort, 90 traits relating to social, communication and repetitive behaviours were identified between the ages of 6 months and 9 years. Data were available for 13,137 children after missing value imputation. Factor analysis was used to generate a set of derived traits from the total sample. As a consequence, these factors were blind to the ASD diagnosis. Varimax rotation was used to simplify the factor structure. Factor and individual traits were compared in their predictive power of ASD and in their associations with other co-morbid conditions including learning difficulties, SLI, SEN and DAWBA diagnoses relating to ADHD, ODD/CD and anxiety problems.

Results: In all, 79 children (0.60%) were diagnosed with ASD in this sample. The factor analysis suggested 7 factors explaining 43% of the variance. These were described as: verbal ability, language acquisition, semantic-pragmatic deficits, social understanding, repetitive behaviour, articulation and social inhibition. All factors were independently related to ASD ($p<0.001$). Comparison with other co-morbid conditions suggested that four of these had the strongest association with ASD while language acquisition, semantic-pragmatic deficits and articulation were more strongly related to other conditions. Of the individual

traits, four were identified via a compromise of parsimony, power in predicting ASD and adherence to the diagnostic triad. These were: Children's Communication Checklist at 9y (coherence subscale), Social and Communication Disorders Checklist at 91m, EAS temperament at 38m (sociability subscale) and a measure of repetitive behaviour at 69m derived from 3 questions. All 4 traits were independently related to ASD ($p<0.008$) and had the strongest associations with ASD compared to other co-morbid conditions. Comparison of these individual and factor traits suggested that both contained information not present in the other set of traits.

Conclusions: This study supports the compound phenotype hypothesis. The standard diagnostic triad may be an over-simplification of a more complex structure with in particular social elements being split into social understanding and social inhibition. Other aspects of the ASD phenotype were identified but these may be attributed to other co-morbid conditions rather than traits core to the diagnosis of ASD. The derivation of the factors from a population-based sample and dimensional aspects of both the factor and individual traits suggest that these traits measure a broader phenotype with impairments extending below the clinical threshold. The factor trait model was not superior to an individual trait model suggesting the theoretical advantages in combining information from a number of measures to identify latent traits were offset by the dilution effect of combining traits with varying degrees of association with ASD.

111.082 82 Unfolding of Social Communication and Repetitive Movements Over the Second and Third Years of Life in Children with Autism Spectrum Disorder. W. Guthrie*[1], L. Morgan[1], A. B. Barber[2], C. Schatschneider[3], C. Lord[4] and A. M. Wetherby[3], (1)*FSU Autism Institute, Florida State University*, (2)*University of Alabama*, (3)*Florida State University*, (4)*University of Michigan*

Background: Research is now emerging from low- and high-risk samples on patterns of change in toddlers with autism spectrum disorder (ASD). However, findings are inconsistent, which may be due to small samples and limited time points studied. Further research is needed on interrelationships of core domains to better understand the unfolding of early symptoms.

Objectives: To examine the emergence of and relationship between social communication and repetitive movements in children with ASD identified prospectively between 12 and 36 months. To determine if early symptom domains predict cognitive level and autism symptoms at 3 years.

Methods: Participants were recruited from two sources: 1) general pediatric sample screened by the FIRST WORDS Project (low-risk) and 2) children referred for suspected ASD or status as an infant sibling (high-risk). CSBS Behavior Samples were administered periodically between 12 and 36 months and coded for social communication (n=599) and repetitive movements (n=242). Measures of social communication on the CSBS included Social, Speech and Symbolic composites and measures of repetitive movements included Body and Objects composites. Autism symptoms were measured at age 3 with the Autism Diagnostic Observation Schedule (ADOS) and cognitive level with the Mullen Scales of Early Learning. A best estimate diagnosis of ASD (n=229) or developmental delay where ASD was ruled out (DD; n=91) was made for 320 children.

Results: The ASD group showed very slow rates of change on the CSBS Social composite over the second and third year, in contrast to the DD group which showed significant growth. Within the Social composite, the ASD group showed no change in Social Referencing, slow improvement in Communication, and significant improvement in Gestures. In contrast, both diagnostic groups showed significant growth in Speech and Symbolic. Further, both groups showed early emergence of and stability in Repetitive Movements with Body and Objects across the second and third years. Social communication was not significantly related to repetitive movements with objects early in the second year, however, moderate correlations were observed later. This finding was not observed in Repetitive Movements with Body. Social communication early in the second year

significantly predicted nonverbal and verbal cognitive level at age 3 (R=.53, p<.001) and this predictive relationship strengthened late in the second year (R= .69, p<.001). Repetitive movements throughout the second year did not significantly predict cognitive level. Social communication in the second year significantly predicted ADOS total algorithm scores with more variance explained later in the second year(R=.36, p=.004 early; R=.57, p<.001 late) and Repetitive Movements with Objects added significantly to this model (R=.45, p=.014 early; R=.68, p<.001 late).

Conclusions: These results suggest a deceleration of growth of some social skills in the second year compared to significant growth in speech and symbolic skills in children with ASD. Social communication and repetitive movements predicted autism symptoms by early in the second year but only social communication predicted cognitive level, and these relationships strengthen as the symptoms unfold over the second year. The significant role of repetitive movements in this unfolding appears to be limited to movements with objects.

111.083 83 Asperger Syndrome in Marriage and Parenthood. W. Y. P. Lau* and C. C. Peterson, *The University of Queensland*

Background: Despite the socio-emotional challenges Asperger Syndrome (AS) may present, many adults with AS do develop long-term relationships. To date, there is a dearth of systematic research evidence on couple relationship or parenthood where AS is in effect.
Objectives: The purposes of this study are two-fold: 1) to examine the dynamics of marital quality in relationships where one spouse has AS; 2) to explore the impact of parental diagnosis of AS on parental alliance among parents with children with AS.
Methods: Approximately 100 participants completed measures on Quality of Marriage Index (Norton, 1983) and Parental Alliance Index (Abidin, 1988). Parents were divided into four groups according to diagnoses of AS in the family: self has AS and child has AS (Group 1), spouse has AS and child has AS (Group 2), only child has AS (Group 3) and, no parent or child has AS (Control). Each group was similar in number and male to female ratio.
Results: Results indicated statistically significant differences between the four groups in all seven key indicators: *marital satisfaction* and *divorce cognition*, *parental investment*, *valuing spouse's parenting involvement*, *respecting spouse's judgment*, *desiring communication with spouse*. Post-hoc comparisons found that only Group 2 reported significantly lower *marital satisfaction* than Control. Both Group 1 and 2's scores on *divorce cognition* were significantly higher than Control. On the Parental Alliance Inventory, a similar pattern was found in *parental investment, valuing spouse's parenting involvement*, *respecting spouse's judgment* and *desiring communication with spouse*. Whilst Group 1 and 2 reported significantly lower scores than Control in all four indicators, Group 3 equalled Control. In other words, parents who themselves had AS as well as those with an AS spouse reported poorer parental alliance feelings than other groups.
Conclusions: These results suggested a number of things. Marital satisfaction seems more affected by parental diagnosis in addition to the child's diagnosis than if only the child has AS. Similarly, diagnosis of AS in child alone has less effect on parental alliance in the couple dyads than both generations having AS. These results bring in a new perspective to understanding the dynamic of families with children with AS. It is expected that this perspective will impact on theory and research on couples affected by AS and, clinical assessment and intervention for families with children with AS. Recommendations for further research are discussed.

111.084 84 Circumscribed Attention and Social Salience in Infants at Risk for Developing ASD. A. Nair*[1], N. Sasson[2], S. Paterson[3], J. Letzen[1] and R. T. Schultz[1], (1)*Children's Hospital of Philadelphia*, (2)*University of Texas at Dallas*, (3)*University of Pennsylvania and Children's Hosptial of Philadelphia*

Background: Individuals with autism spectrum disorders (ASD) orient and respond to social stimuli abnormally, which may be indicative of important differences in the distribution and prioritization of attentional resources. Previous work has shown that school-aged children with ASD exhibit

restrictive and perseverative patterns of attention when presented with complex visual arrays matched for social and nonsocial content (Sasson et al, 2008), though this pattern is driven primarily by disproportionate attention to objects related to circumscribed interests (CI; e.g., trains). Attention to social stimuli (i.e., faces) is reduced in the presence of CI objects, but appears normal in the presence of other object types, suggesting that heightened salience of CI objects in ASD may result in attentional prioritization that reduces attention to social information. Whether this pattern extends to very young children with ASD is of significant clinical relevance, as early emerging biases toward nonsocial information may affect the development of neural specialization (Johnson, 2000), including neural circuitry supporting abilities related to social information processing (Sasson, 2006; Schultz, 2005).

Objectives: To determine whether infants at risk for developing ASD exhibit reduced social attention in the presence of CI objects relative to non-CI objects.

Methods: Twenty-six infants between the ages of six and twenty-four months at risk for developing ASD (i.e., siblings of children with an ASD diagnosis) were recruited through the Infant Brain Imaging Study. Each infant was eye-tracked while passively viewing the Social vs. Object task, a novel free-viewing visual preference task consisting of twenty slides of paired face and object images. The twenty pairs included ten object images found to be common targets of CI for individuals with ASD (South, et al., 2005) that disproportionately capture attention in school-aged children with ASD (Sasson, et al., 2008), and ten objects not typically related to CI.

Results: An analysis of fixation time on stimulus categories revealed a three-way interaction between age (6 vs. 12 vs. 24 months), stimulus type (face vs. object) and object type (CI vs. non-CI) ($F(2, 26) = 5.61$, $p < .01$). Post-hoc Tukey analyses indicated that this interaction was driven by an increase with age in fixations to CI objects, resulting in an age-related decrease in fixations on concurrently paired social stimuli. In contrast, fixations to faces remained stable with age when non-CI objects were paired with faces. Several non-significant mean differences also emerged with age, suggesting that older children may be more likely to orient to CI objects relative to-non CI objects in the context of social stimuli, a trend that will be followed up with a larger sample prior to the meeting.

Conclusions: Findings suggest that between six and twenty four months, infants at risk for developing ASD become increasingly attentive to CI, but not non-CI, objects, a pattern that results in a decrease in social attention when these CI objects are present. Data collection is ongoing with a typically-developing comparative sample of infants to determine whether this pattern is specific to at-risk infants. These data should be available in time for the conference.

111.085 85 Detection of Autism in Infants with Fragile X Syndrome. J. Roberts*, L. McDonald and B. Kelleher, *Barnwell College, University of South Carolina*

Background: Fragile X syndrome (FXS) is the leading known heritable cause of intellectual disability affecting approximately 1: 3,600 individuals. Autism is one of the most prevalent and severe behavioral abnormalities associated with FXS with up to 90% of males with FXS exhibiting one or more features of autism, and 25% to 50% meeting DSM IV based diagnostic criteria for autism. In the field of idiopathic autism (non-FXS), an increased focus on the emergence of autistic behavior in the first year of life has revealed a number of behaviors that appear to be early indicators of autism. These behaviors include atypicalities such as prolonged latency to disengage visual attention and a pattern of early temperament characterized by passivity and decreased activity at 6 months followed by intense distress reactions and decreased positive affect in the second year of life (Zwaigenbaum et al., 2005). Given the high co-morbidity of autism in FXS and its debilitating effects, we are investigating early emerging behavioral indicators of autism and possible underlying physiological markers in infants with FXS. In preliminary work, we

found that 12-month-old infants with FXS (n=11) displayed longer look durations and longer latencies to disengage visual attention than typically developing controls (n=9). There was a moderate relationship between increased look duration to both increased severity of autistic behavior and elevated heart rate during decelerative phases (reflected cognitive processing) in the infants with FXS. The current work extends these findings.

Objectives: To identify early emerging behavioral features and potential underlying physiological mechanisms associated with the emergence of autism in FXS.

Methods: Using a prospective longitudinal design integrating behavioral and physiological methods, we will examine the relationship among maternal ratings and experimental laboratory based measures of temperament and heart activity to autistic behavior in a cohort of 12 infants with FXS assessed at 9, 12, 18 and 36 months of age. Additionally, we will conduct a cross-sectional analysis with a sample of 23 infants with FXS (aged 9 to 36 months). Our analyses are only partially complete at this time; however, all the data are collected, entered, and edited. We anticipate running the full model analyses in the next month.

Results: Analyses are limited to descriptive data at this time. These preliminary data suggest that the temperament profile of infants with FXS does increase in intensity over time with elevations in anger and lessened soothability and decreased attention observed across time on maternal ratings. Heart activity reflects elevated arousal and decreased variability as reported for older-aged children with FXS.

Conclusions: Infants with FXS are at very high risk for autism. Thus, understanding the early behavioral indicators of autism and possible underlying physiological mechanisms in the first years of life is critical to guiding diagnostic and treatment efforts in this high-risk population.

111.086 86 Development of Early Social Communicative Abilities in Toddlers with Autism Spectrum Disorder (ASD). S. Van der Paelt*, M. Dereu, M. Meirsschaut, R. Raymaekers, I. Schietecatte, P. Warreyn and H. Roeyers, *Ghent University*

Background: Impairments in the early social communicative abilities imitation, joint attention and pretend play are rigorously documented in children with ASD. Previous research shows that these impairments are not absolute. Little is known however about how these abilities develop.

Objectives: The aim of the present prospective study was to assess the development of imitation, joint attention and pretend play in toddlers with ASD compared to toddlers with other developmental difficulties. Objectives:

Objectives:

Methods: Data were collected from 9 children with ASD (confirmed by ADOS and ADI; ASD cases) and 9 children with (initial) language or developmental delay (non-ASD cases). The children were between 24 and 45 months old (M= 34) at initial assessment and between 47 and 52 months old (M= 49) at last assessment. Each participant was tested multiple times (2 to 5 times depending on age at first assessment) with approximately 6 months between consecutive assessments. Imitation, joint attention and pretend play were measured using respectively the PIPS, ESCS and TOPP.

Results: *Initiating joint attention (IJA):* The average number of IJA behaviors seems to remain stable, apart from a slight increase in the ASD cases after 42 months. At all ages non-ASD cases show almost twice as much IJA behaviors than ASD cases. There is great variability in developmental trajectories, especially in ASD cases. More than half of these children show a decrease in IJA behaviors between 30 and 42 months, whereas most non-ASD cases show an increase in IJA behaviors in that period. *Imitation:* On average the imitation skills of all children improve between 30 and 48 months. Whereas at 30 months non-ASD cases obtain a higher score on imitation skills than ASD cases, this difference seems to get smaller between 42 and 48 months. Looking at the individual trajectories, there seem to be two subgroups in both groups. Half of the

ASD cases show a rapid increase in imitation skills between 36 and 48 months, and have an age appropriate score by 48 months, making up for an initial delay. The other half makes less or no progress and remains to have a substantial delay at 48 months. Non-ASD cases can be divided in similar groups, but the progress in the children that attain an age appropriate score at 48 months seems to begin earlier, at the age of 30 months. *Pretend play:* On average the pretend play skills of all children improve between 30 and 48 months. At all ages ASD cases perform worse than non-ASD cases. Individual trajectories show great variability among ASD cases: most children improve as they get older, but not at the same rate.

Conclusions: Early social communicative abilities continue to develop between 30 and 48 months. At all ages ASD cases perform worse than non-ASD cases. Imitation and symbolic play skills improve in most children with ASD, whereas initiating joint attention remains rather stable on average. There is however great variability in individual developmental trajectories, especially in children with ASD.

111.087 87 Differences Between English- and Spanish-Speaking Mothers' Report On Toddlers' Profiles in the Modified Checklist for Autism in Toddlers (M-CHAT). N. M. Reyes*[1], M. A. Patriquin[1], A. Scarpa[1], V. Desai[2] and K. Kerkering[3], (1)*Virginia Tech*, (2)*Carilion Pediatric Clinic*, (3)*Pediatric Neurodevelopmental Clinic*

Background:

Previous research has found that children with Autistic Disorder, who are identified and treated before 5 years old, appear to benefit more from intensive treatment than those children treated after age 5 (Fenske, Zalenski, Krantz, & McClannahan, 1985). Although children with Autistic Disorder show deficits in pointing, showing objects, looking at others, and orienting to name early in their development (Osterling & Dawson, 1994), they are generally diagnosed between 3 (Kabot, Masi, & Segal, 2003) to 5 years old (Rhoades, Scarpa, & Salley, 2007) when their expressive and receptive language are notably delayed. In an attempt to decrease the age of diagnoses, the M-CHAT, a screening tool, has been used to screen toddlers with Autism Spectrum Disorders (Robins, Fein, Barton, & Green, 2001). However, to the authors' knowledge, no research has been conducted with Spanish-speaking populations and the utility of the M-CHAT.

Objectives:

To examine differences in response patterns on English and Spanish M-CHATs administered to English- and Spanish-speaking mothers of toddlers from an at risk population.

Methods:

Data were collected from 431 toddlers between 17 and 30 months of age (105 Spanish, 326 English). Because no previous research has been done with the Spanish M-CHAT, no hypotheses are made regarding response patterns between the English-speaking and Spanish-speaking populations.

Results:

Preliminary Pearson Chi-Square analyses showed that English-speaking and Spanish-speaking mothers demonstrated significantly different response patterns in 5 of the 23 items of the M-CHAT. Chi-Square analyses revealed that Spanish-speaking mothers were more likely to report higher levels of symptomatology on M-CHAT number 1, $c^2(1, N = 460) = 7.28$, $p > .01$, number 11, $c^2(1, N = 460) = 54.658$, $p > .01$, and number 18, $c^2(1, N = 460) = 24.56$, $p > .01$ than English-speaking mothers. However, English-speaking mothers were more likely to report higher level of symptomatology than Spanish-speaking mothers on item number 13, $c^2(1, N = 460) = 3.61$, $p = .058$, and number 22, $c^2(1, N = 460) = 5.15$, $p > .05$.

Conclusions:

This study found differences in response patterns between English-speaking and Spanish-speaking mothers of toddlers on five items of the M-CHAT, including a critical item (number 13). Spanish-speaking mothers reported higher levels of symptomatology on three items while English-speaking mothers reported higher levels of symptomatology on

two items from the 23-item M-CHAT. Our findings suggest differences in screening information provided between English- and Spanish-speaking populations. As a result, Spanish and English M-CHATs might be confounded by language differences; therefore, potentially producing erroneous conclusions about the presence or absence of a child's symptoms. To reduce the confounding effects of these language differences, future research should determine whether the results are due to language differences in interpretation or in the translation of the measure.

111.088 88 Effects of Contingency On Social Visual Engagement in Typically-Developing Infants. P. Lewis*[1], J. B. Northrup[2], J. Paredes[1], W. Jones[2] and A. Klin[1], (1)*Yale University School of Medicine*, (2)*Yale School of Medicine*

Background: Typically-developing babies, from within the first days of life, engage preferentially with social aspects of the surrounding environment. 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 others. 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.

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: We compared visual scanning for 22 typically-developing 2- to 6-month-old infants in two conditions: watching videotaped actresses (Condition 1) and live interaction with mothers (Condition 2). We disambiguated 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). Eye-tracking data were collected during each of the three conditions. 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). The eye-tracking data were then analyzed for time spent fixating on each of the four regions-of-interest.

Results: Results show that typically-developing infants significantly increase their fixation on eyes during contingent interaction with mothers (Condition 2) as compared with their responses to pre-recorded videos of actresses (Condition 1). Additionally, children increase their fixation on mouths when viewing non-contingent, pre-recorded clips of their own mothers (Condition 3).

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.

111.089 89 Identifying Atypical Development in Children Aged 12 to 36 Months. R. L. Young*, P. Williamson, G. Bradshaw and G. Choimes, *Flinders University*

Background:

Anecdotal reports suggest that the presence of behaviours indicative of autism (AD) are displayed at a very early age, with nearly half (31-51%) of all children with AD displaying abnormalities within the first year of life (Gray & Tonge, 2001). Despite this acknowledgment, a diagnosis of AD is typically not being made until a child is much older (Young et al., 2003). These delays commonly occur as a result of the inability of currently used diagnostic criteria (e.g., DSM-IV-TR; ICD-10) to identify and operationalise behaviours relevant to this age cohort. As yet, studies investigating autism during infancy have failed to operationalise behaviours of concern, the age of onset of these behaviours and the impact these behaviours have on development. For

example, lack of shared enjoyment and poor eye contact has been identified as early as 11 months, while delayed language, a diagnostic criterion outlined in the DSM-IV-TR, is often not observed until many months later (Young et al., 2003). These results indicate that behaviours indicative of AD emerge at different ages throughout a child's development with some being modified or ameliorated with maturation or intervention.

Objectives:

The aim of this study was to identify the early symptoms of the disorder and their behavioural presentation to enable us to determine the durability of these behaviours across time and the impact they have on development and prognosis. Specifically we aimed to determine the age at which behaviours commonly associated with AD reliably distinguished AD from children developing typically and children with other disabilities. Of specific interest was whether certain items or behaviours have better discriminating abilities and are of greater clinical significance at specific ages.

Methods:

The present study involved children aged 12 to 36 months. The development of children with AD was compared to an age matched typically developing group and children with an other disability such as a hearing impairment (ODD) group. Using a number of tools currently used with children of this age (e.g., ADEC, M-CHAT) behaviours were analysed according to four specified age groups.

Results:

Variations from typical development were detectable in some children as young as 12 months. In particular, response to name, functional play, and use of gestures, best discriminated between the three diagnostic groups.

Conclusions:

The present study was the first of its kind to evaluate the developmental trend of autistic behaviours within children aged 12 to 36 months. The current results suggest clear developmental differences are apparent between the three groups (AD, TD and ODD) from as early as 12 months of age with behaviours specific to autism being clearly identified. It was further evident from the current study that typical development follows a naturally progressive path with an unmistakeable distinction between the diagnostic groups emerging as early as 12 months of age with this difference becoming more apparent by 30 months of age.

111.090 90 Immediate Imitation in Infants at Low- and Heightened-Risk for Autism. N. M. Kurtz*[1], R. H. Wozniak[1] and J. M. Iverson[2], (1)*Bryn Mawr College*, (2)*University of Pittsburgh*

Background: Impairments in imitation, particularly in spontaneous imitation, are known to be characteristic of children with autism; but little is currently known about imitation in toddlers at heightened-risk for autism.

Objectives: Since autism is not typically diagnosed until approximately 2-3 years of age, our primary goal was to investigate immediate imitation in infancy to assess its potential role in early identification. To maximize the likelihood that the sample would contain children eventually receiving an autism diagnosis and to evaluate the initiation of imitative behavior in infants at heightened risk for autism, we observed younger siblings of children already diagnosed with autism (Heightened-Risk Group, HR) and compared them to later-born infants with no such family history (Low-Risk Group, LR).

Methods: Twenty-one HR and 18 LR infants at 18-months of age were videotaped for approximately 45-minutes at home in naturalistic interaction and semi-structured play with caregivers. At 36-months, HR infants were administered the ADOS-G. At that time, three HR infants (Heightened-Risk-Diagnosed, HR-D) scored above the cutoff for an autism diagnosis. Using a coding scheme developed specifically for this project, videotapes were coded for instances of Spontaneous Imitation (i.e., imitation occurring without an interlocutor's bid for imitation), Elicited Imitation (i.e., imitation

occurring following an interlocutor's Bid for Imitation), and Bids for Imitation (i.e., interlocutors' attempts to elicit imitation by the infant). Spontaneous and Elicited Imitations were further coded for Type of behavior imitated (Vocalizations, Actions on Objects, Gestures, Other Bodily Movements); and Interlocutor Bids were also coded for Type (i.e., Verbal, Action, Verbal-Action Combination), whether the infant attended to the bid, and whether the bid successfully elicited imitation.

Results: Relative to LR infants, HR infants exhibited significantly lower rates (per 10 minutes) of Spontaneous Imitation (p = .016) and also received Bids for Imitation at a significantly lower rate (p = .035). There were, however, no significant group differences in percentages of bids to which infants attended or percentages of bids that were successful in eliciting imitation. Furthermore, no significant differences were found between HR and LR infants in types of behaviors imitated either spontaneously or when elicited. Finally, the three HR-D infants produced rates of imitation which fell below the HR group medians for both Spontaneous Imitation and percentage of bids leading to Elicited Imitation.

Conclusions: Results are in line with previous research indicating reduction in the rate of spontaneous initiation of behavior (e.g., communicative behavior) in HR infants. While those HR infants eventually receiving an autism diagnosis were toward the bottom of the HR distribution in imitative behavior, they did imitate; and it does not appear, based on these data, that reduced spontaneous imitation at 18 months has strong predictive value for a later autism diagnosis.

111.091 91 Innovative Partnership for Education and Research of Autism Spectrum Disorder (ASD). E. Giarelli*[1] and J. Ruttenberg[2], (1)*University of Pennsylvania*, (2)*Center for Autism*

Background: Nurses are conspicuously absent from the roster of professionals caring for people with ASD. Pediatrics and family nurse practitioners are uniquely qualified with a set of assessment and treatment skills to provide comprehensive health care services to individuals and families. Such nurses, when given specialized training in the care of ASD can screen, evaluate, design and deliver family-centered plans of care for affected individuals. Schools of nursing and community services providers may combine their intellectual and technical resources to create a cadre of professional nurses equipped to address the increasing medical and behavioral needs of this population. The purpose of this presentation is to describe the strategic planning and products of an initiative to establish an innovative education and research partnership between the University of Pennsylvania-School of Nursing and the Center for Autism.

Objectives: The objectives of the initiative were to (1) describe a plan for a partnership between the UPENN School of Nursing and the Center for Autism (CFA) and (2) identify a agenda for community-based participatory research among nurse scientists and scholars from UPENN, clinicians from the CFA, and community stakeholders.

Methods: The planning committee obtained sponsorship from The Philadelphia Healthcare Trust in 2009 to begin an evaluations study to assess potential and explore partnership options. The team conducted a gap analysis of training experiences in the School of Nursing and nursing service needs of individuals with ASD and their families. Data included curriculum content in ASD from baccalaureate, master and doctoral level nursing courses and programs. Current research priorities proposed by the IACC were aligned with clinical data currently or potentially available through the client population of CFA.

Results: Typical for programs of nursing, only two BS level courses and one Masters level course has content on ASD and this is limited to 1.5 hours per course over 4 years. There is a conspicuous absence of nurses working with individuals with ASD and their families in community agencies and none have specialized training in ASD. Medical and treatment needs (pharmacotherapy, etc.) of children with ASD are increasing. A substantial cohort of scholars and clinicians are qualified

and interested in ASD research, and data are available to study prevention, earlier detection, lifespan perspective, and community engagement in ASD research.

Conclusions:

Over the next 5 years we will establish a *Partnership for the Integration of Care of Autism Spectrum Disorder* (PICA). The partnership will address an immediate need for a nursing work-force by offering continuing education programs; address the long-term need for a stable nursing work-force by establishing systematic education of nurses in the care of individuals with autism; and establish a program of community-based participatory research that includes a research agenda that complements the priorities of the Interagency Autism Coordinating Committee, a process for collecting; storing and retrieving data on patients and families treated at the Center for Autism; and completed pilot data to support an application for external funding. A pilot project has been developed.

111.092 92 Is There a Difference in the Amount of Direct Eye Contact in 3-Month-Old Infants Later Classified with ASD Compared to Unaffected Infants?. M. M. Abdullah*[1], P. A. Filipek[2], P. L. Horner[3] and J. T. Phan[3], (1)*University of California, Irvine*, (2)*University of Texas Health Sciences Center at Houston*, (3)*UCI School of Medicine*

Background: Recent studies in small cohorts of infants reported that decreased eye contact in 6-month old infants may predict ASD in some infants at risk (Merin et al., 2007). No one has yet investigated direct eye contact in infants at risk for ASD before age 6 months.
Objectives: To examine whether 3-month-old infants later classified with ASD differed in the amount of direct eye contact during still-face interactions compared to unaffected infants.
Methods: Twelve infants (4 males) who were predominantly Caucasian or of mixed ethnicity (42% and 42%, respectively) were enrolled in the study between age 1 and 2 months. Parents were well-educated (67% with 4 years college or greater). At age 3 months, direct eye contact during infant-parent and infant-researcher interactions were videotaped using a fiberoptic eyeglass camera in 4 face-to-face car seat conditions: (1) interaction with parent using infant-directed speech; (2) interaction with parent with a "still face"; (3) interaction with researcher using infant-directed speech; and (4) interaction with researcher with a "still face". Using Noldus Observer 9.0 software, videotaped interactions were coded for percentage of direct eye contact by trained research assistants who attained substantial inter-rater reliability with training videos (_ ≥ .72) and who were blind to later ASD classification. To obtain ASD classification, the Toddler ADOS was administered to participants at chronological and nonverbal mental age of 12 months or greater, as measured by the Mullen Scales of Early Learning (Mullen, 1995), with independent ambulation. Group differences in the percentage of direct eye contact during each interaction between children classified with ASD and unaffected children were examined using Mann-Whitney *U*-tests.
Results: Twelve infants (6 classified with ASD) completed both infant-parent interactions. There were no significant differences in the percentage of direct eye contact during either of the parent-infant interactions between the children classified with ASD and the unaffected children. Seven infants (3 classified with ASD) completed both infant-researcher interactions. There were no significant differences between groups in the face-to-face interaction with the researcher using infant-directed speech. However, children classified with ASD demonstrated greater direct eye contact during the "still face" paradigm compared to unaffected children at age 3 months (Mann-Whitney U = 0.000, p = .034).
Conclusions: Based on preliminary analyses, the "still face" interaction by an unfamiliar adult may be a provocative social disengagement scenario to which infants later classified with ASD attend significantly more than their unaffected peers. Final analyses on the full sample will be presented.

111.093 93 Temper, Breast-Feeding and the Mother's Early Experience of Taking Care of a Child Later Diagnosed with Autism: A Follow-up Study in the Danish National Birth Cohort. S. Lemcke*[1], E. Parner[2] and M. B. Lauritsen[3], (1)*Aarhus University Hospital*, (2)*University of Aarhus*, (3)*Regional Centre for Child and Adolescent Psychiatry, Aarhus University Hospital*

Background: Studies on early symptoms of autism have indicated that it is possible to identify early signs in children before the age of two years. Only few studies have used information from prospectively collected parents' interviews. Objectives: To study whether prospectively collected information from mothers on their experience of taking care of the child, breast-feeding and the child's temper during the first two years of life can predict the risk of the child later being diagnosed with Autism Spectrum Disorder (ASD).

Methods: In the Danish National Birth Cohort (DNBC) more than 70,000 women were interviewed about their child's development, behaviour and growth when the child was 6 and 18 months of age. All children in Denmark diagnosed with ASD and/or mental retardation (MR) are registered in the Danish Psychiatric Central Register or the Danish National Patient Register; thus, it is possible to identify children with ASD and MR in the DNBC. Comparison of data on children with ASD with information on the mentally retarded and the typically developing children in DNBC will provide us with distinct characteristics before the age of two years of children who later develop an autistic disorder. Data are analysed using Cox proportional hazards regression.

Results: The study is ongoing; at the age of 6 and 18 months the preliminary analyses showed no statistically significant differences with regard to breast-feeding in the characteristics of children with ASD compared with typically developing children or children with MR. With respect to the child's temper (less active than other children: HR=8.11 (95% CI: 5.26-12.5) or not a happy child: HR=2.96 (95% CI: 1.52-5.76)) and the mother's experience of taking care of the child (has been difficult: HR=3.04 (95% CI: 1.94-4.76)) statistically significant differences at the age of 18 months was found in the preliminary analyses.

Conclusions: The results indicate that in the first two years of life mothers information about deviations in the child's temper and her experience of taking care of the child are associated with the risk of the child later being diagnosed with autism spectrum disorder.

111.094 94 The Development of Adaptive Skills in Young Children with ASD -- An Examination Across One Year Using Vineland-II. N. Huai*[1], S. Ellis Weismer[2] and C. E. Ray-Subramanian[1], (1)*Waisman Center, University of Wisconsin-Madison*, (2)*University of Wisconsin-Madison*

Background: The Vineland Adaptive Behavior Scale has been an important component for diagnostic assessments, treatment planning, progress monitoring, and research on autism spectrum disorders (Chawarska & Bearss, 2008). Mental age or IQ has been found to be significantly correlated with adaptive skills (Loveland & Kelley, 1991). Researchers have consistently found that there is a significant decline in adaptive skills standard scores as children on the spectrum grow older (Fisch et al, 2002; Carter et al., 1998). In addition, levels of autism symptoms, cognitive, and language functioning affect the course of adaptive skills development (Perry, Flanagan, Geier, & Freeman, 2009). This study examines the development of adaptive skills measured by the Vineland-II within a large sample of young children on the autism spectrum.

Objectives: This study investigates the following questions: a) how do adaptive behaviors change in one year among young children with ASD? b) What are the relationships among initial mental age, calibrated autism severity score, and the magnitude of changes in adaptive behavioral skills?

Methods: Participants are 100 children on the autism spectrum who are participating in a longitudinal study on ASD. At Year 1 visit, participants (Mean Chronological Age = 31 months, *SD* = 4.37), received a battery of assessments, including the ADOS, ADI-R, Vineland-II (parent/ caregiver interview), and Bayley-III Cognitive Scale. Approximately one year later, ADOS, developmental testing, and the Vineland-II were re-administered.

Multivariate repeated measure analysis was used to examine the within-subject changes on the domains of the Vineland-II for children with and without delays on initial Bayley-III Cognitive Scale (*n* = 46 and 50,

respectively). Cognitive delay was defined as Bayley age equivalent / chronological age < .75. Partial correlation coefficients were used to examine the relationship among initial nonverbal ability, calibrated ADOS severity score (Gotham, Pickles, & Lord, 2009), and the magnitude of adaptive skill changes in the entire sample.

Results: Significant between-group and interaction effects (Group x Year) were found with both standard scores and age equivalents (_ =.05). Using domain standard scores, within-subject difference was found on Communication only (F (1, 94) = 9.59, p = .003). Using age equivalent scores, significant within-subject differences were found on Communication, Daily Living, and Socialization (ps = .000) and Year 2 scores > Year 1 scores. Simple correlations were significant among all variables at _ = .01. When Year 1 Bayley age equivalent was partialled out, the magnitude of changes from Year 1 to Year 2 on the Vineland domains were not significantly correlated with the calibrated ADOS severity score.

Conclusions: Young children on the autism spectrum make gains in communication, daily living, and socialization skills, as reflected by the increases of the age equivalent scores. The rate of domain age equivalent score change is different for children with and without initial cognitive delay. When Year 1 cognitive scores are statistically controlled, the level of autism features is not significantly related to gains in adaptive skills.

111.095 95 A Comparison of Prospective and Retrospective Methods for Measuring Regression. S. Ozonoff*[1], A. M. Iosif[1], F. Baguio[1], I. Cook[2], M. M. Hill[3], T. Hutman[4], S. Rogers[5], A. Rozga[6], S. Sangha[5], M. Sigman[4], M. B. Steinfeld[1] and G. S. Young[1], (1)*M.I.N.D. Institute, University of California at Davis*, (2)*M.I.N.D. Institute*, (3)*M.I.N.D. Institute, University of California at Davis Medical Center*, (4)*University of California, Los Angeles*, (5)*UC Davis, M.I.N.D. Institute*, (6)*UCLA*

Background: This study examined when and how behavioral signs of autism spectrum disorders (ASD) emerge in the first years of life. Most previous investigations have been retrospective, relying on parent report of earlier development or analysis of home videotape of infants later diagnosed with ASD. The existing literature suggests that behavioral signs of autism emerge in two different patterns, an early onset and a regressive course. Recently, however, the adequacy of a dichotomous classification of onset has been questioned. Questions about when and how behavioral signs of autism emerge may better be answered through prospective, rather than retrospective, studies. Objectives: The present investigation used a longitudinal infant sibling design to examine symptom emergence in the first years of life in infants at low and high risk for autism. One specific aim was to compare traditional retrospective methods of measuring regression to prospective methods. Methods: All 25 infants in the sample who were later diagnosed with ASD were matched on gender to 25 low-risk children determined to have typical development at 36 months. Prospective measures of onset, collected at 6, 12, 18, 24, and 36 months of age, included frequencies of gaze to faces, social smiles, and directed vocalizations, which were both coded from video and rated by examiners. The retrospective measure, collected at 36 months, was the ADI-R. Results: The frequency of gaze to faces, shared smiles, and vocalizations to others were highly comparable between groups at 6 months of age, but significantly declining trajectories over time were apparent in the group later diagnosed with ASD. Group differences were significant by 12 months of age on most variables. We computed 95% confidence intervals for the change from one visit to the next for the typically developing sample. Then we counted how many of the participants with ASD outcomes displayed declines in social-communication behaviors that were greater than the 95% confidence interval for change in the TD group. This analysis documented loss of skills in 86% of the sample with ASD. In contrast, only 17% of parents reported a regression in either language skills or social development on the ADI-R. Conclusions: These results suggest that behavioral signs of autism are not present at birth, as once suggested by Kanner, but emerge over time through a process of diminishment of key social-

communication behaviors. More children may present with a regressive course than previously thought, but parent report methods do not capture this phenomenon well. Implications for onset classification systems and clinical screening will be discussed.

111.096 96 A Synthesis of Existing Systematic Reviews Examining Interventions for Children and Adolescents with Autism Spectrum Disorder. D. B. Nicholas*[1] and R. MacCulloch[2], (1)*University of Calgary*, (2)*The Hospital for Sick Children*

Background: The intervention literature identifies advances in treatments for pediatric autism; however, there is ongoing uncertainty about the relative impact of various pediatric autism treatments. This literature is challenged by methodological limitations and a vast heterogeneity of population subtypes and interventional applications, inconsistencies in evaluation design, and unclear outcome targets.

Objectives: This study comprised a descriptive meta-study analysis of existing systematic reviews in the pediatric autism intervention literature, with a focus on the reported impacts of various types of intervention for children. A qualitative, synthesis review was undertaken whereby interventions were thematically reviewed and grouped into domains of intervention and presented outcomes.

Methods: This synthesis comprised a meta-study examination of systematic reviews including descriptions of approaches addressed within systematic reviews, syntheses of interventional and study characteristics, and an analysis of reported outcomes. To ascertain elements of intervention outcome and process, reviewed article content was analyzed for substantive, qualitative content and quantitative analysis. For qualitative analysis, computer software (NVivo) was utilized to assist in coding, concept identification, and theme generation (e.g., intervention components, outcomes). Trustworthiness (rigor) of findings was ensured through a process of peer debriefing and expert consultation with intervention leaders in autism. Sample and other demographic information from reviewed studies was collected and collated.

Results: The search initially resulted in 405 peer-reviewed review articles. Duplicate and irrelevant articles were first removed; ultimately resulting in a database of 283 articles. Titles and abstracts of these articles were reviewed by two blinded research coordinators, and those not matching inclusion/exclusion criteria were removed, ultimately resulting in 53 reviews. The reference list of these articles was subsequently reviewed via footnote chasing. This process of footnote chasing yielded another 14 reviews that met inclusion criteria. Accordingly, 67 reviews ultimately were included in the final review; and these reviews were subjected to coding, data extraction and synthesis analysis. Key domains of interventions reported in systematic reviews comprised: behavioral (20 reviews); pharmacological (18 reviews); social skills (10 reviews); diet/vitamin supplementation (5 reviews); non-conventional interventions (e.g., hippotherapy, music therapy, pet or animal therapy, robot interaction, and oxygen or hyperbaric therapy) (5 reviews); and communication-focused interventions (3 reviews). Systematic reviews were not found within the literature in the areas of: developmental, comprehensive educational, physiological, or psychodynamic interventional approaches.

Conclusions: The intervention literature is disparate and mixed. On balance however, the provision of intervention for children with autism is preferable to non-intervention. Domains with the most evidence to date, from systematic reviews, are pharmacological and behavior approaches. It is yet difficult to contrast the effectiveness of the various interventional approaches given varying metrics, needs, outcomes and extent of methodological rigor within primary studies. Clearly, well-designed studies and more comparative research are needed in contrasting varying approaches across ASD population subtypes.

111.097 97 Autism Diagnostic Observation Schedule- Generic (ADOS-G) with Typical Children: Evaluating Diagnostic Validity. N. L. Tanel*[1] and V. Smith[2], (1)*Bloorview Kids Rehab*, (2)*University of Alberta*

Background: The Autism Diagnostic Observation Schedule- Generic (ADOS-G) (Lord et al., 2000) is considered the current gold standard diagnostic tool for autism. There is sufficient evidence to suggest that the ADOS-G has good sensitivity and specificity and found to be better at discriminating between individuals with ASD and non-ASD than between autism and PDD NOS. However, an inherent problem with the majority of the studies examining the diagnostic validity of the ADOS-G is that few include a typical control group to demonstrate that the ADOS-G does not misdiagnose typically developing (TD) children as having ASD (Bishop & Norbury, 2002). Many of the behaviours measured within the ADOS-G have been found to discriminate between young children with ASD and TD. However, due to large variation in TD between 18 and 24 months, some behaviors measured are present in TD toddlers and may be less discriminatory.

Objectives: The objective of the current study was to examine the performance patterns of TD children on the ADOS-G and to explore the relationship of these patterns and cognitive and adaptive functioning.

Methods: Participants included 25 TD toddlers between the ages of 18 and 26 months (M= 22.76). Participants completed the Mullen Scale of Early Learning (MSEL), the Vineland Adaptive Behaviour Scale (VABS) and the ADOS- G. The ADOS-G item means and domain means of the original and revised algorithms, domain total distributions and item distributions, were analyzed to determine the range of normal scores. Correlations between ADOS-G scores and summary scores of the MSEL and VABS were calculated.

Results: A large proportion of TD toddlers demonstrated abnormalities on some of the items measured on the ADOS-G. Thirty six percent of the participants obtained a score above 'ASD cut off' on the Communication domain and 16% obtained a score above 'ASD cut off' on the Reciprocal Social Interaction domain. Twelve percent obtained a score above 'ASD cut off' on the Social Affect domain and 8% obtained a score above 'ASD cut off' on the Social Affect and Restrictive and Repetitive Behavior total domain. None of the toddlers obtained a score in the ASD or autism range on the original algorithm and two toddlers obtained a score consistent with ASD on the revised algorithms. Correlational analyses revealed significant relationships between Receptive Language (MSEL) (-.35, $p<.05$), Expressive Language (MSEL) (-.39, $p<.05$) and ADOS-G scores. Significant relationships were also found between Communication skills (VABS) (-.73, $p<.01$; -.38, $p<0.05$), Daily Living skills (VABS) (-.45, $p<.05$; -.40, $p<0.05$) and ADOS-G scores (original and revised).

Conclusions: The results of the study provide researchers and clinicians with a better understanding of how typical children perform on the ADOS-G and insight into which areas the performance of typical toddlers overlaps with individuals diagnosed with ASD.

111.098 98 Characteristics of False Positives On the ADI-R in An Adult Sample. K. S. Branch*[1], D. N. Johnson[1], L. J. Lawer[1], M. A. McCarthy[1], L. A. Plummer[1], E. S. Brodkin[1] and D. S. Mandell[2], (1)*University of Pennsylvania*, (2)*University of Pennsylvania School of Medicine*

Background: Limited research has been conducted on diagnosing adults with autism spectrum disorders (ASD). Previous studies have shown that diagnosing adults is difficult due to scarce and inconsistent information relating to the manifestation of ASD in adulthood. Symptoms of ASD in an individual may change over the life course due to maturation, environmental influences, and treatments and services. Life experiences may also cause individuals to appear to have ASD in adulthood. Current diagnostic instruments have not been validated in adult use and do not take into account the effect life occurrences may have on the presentation of ASD in adults. This may lead to a potential mistake in diagnosis of ASD in adults.

Objectives: To identify characteristics, among adults who meet ADI-R criteria for an ASD, that discriminate between true and false positives.

Methods: The sample included 322 civilly-committed patients in one state psychiatric

hospital in Pennsylvania. Nursing staff completed the Social Responsiveness Scale (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) and Conflict Tactics Scales: Parent-Child Version (CTS-PC). Chart reviews focused on developmental history, paying particular attention to age of onset and clinical features indicative of ASD. Data on medications, self-injurious behaviors, and physical/mechanical restraints were collected for each consented patient. Case conferences with two psychiatrists and the team of assessing psychologists were held for all patients. After case conferences were completed, the patients who were identified as having ASD on the ADI-R were further examined to identify differences between false positives and true positives.

Results: Case conferences as well as ADI-R and CTS-PC administration are ongoing. Twenty-two percent of patients with completed ADI-R interviews definitely or are highly to likely meet criteria for an ASD. Only 50% of subjects scoring positively on the ADI-R definitely met criteria for ASD based on record review and expert clinical judgment. Chart review found that all false positives experienced some form of abuse (physical, psychological, or sexual). In addition, all of the possible cases of ASD had a history of abuse. Only 29% of cases meeting research criteria for ASD had a history of abuse. Formal analysis of other characteristics that discriminate false positives from true positives is ongoing. To date, no differences between the false positives and true positives in patterns of responses on the ADI-R have been identified. Preliminary results indicate that false positives who have experienced abuse also have a more recent history of criminal involvement and substance abuse, while those meeting research criteria for ASD do not.

Conclusions: Even in an institutionalized adult population, the ADI-R is a useful tool. Our results suggest, however, the need for different cut-offs and to augment the ADI-R with other information, especially about physical, sexual and substance abuse history.

111.099 99 Comparison of a Broad-Based Screen Versus Disorder-Specific Screen in Detecting Young Children with An Autism Spectrum Disorder. L. D. Wiggins*[1], V. Piazza[2] and D. L. Robins[2], (1)*Centers for Disease Control and Prevention*, (2)*Georgia State University*

Background: The American Academy of Pediatrics recommends screening for autism spectrum disorders (ASDs) at the 18- and 24-month well child visits; yet ASD screening rates remain low. Some pediatricians cited inadequate time as a reason for decreased screening. We therefore examined whether a broad-based developmental screen could detect as many children with an ASD as an ASD-specific screen in general pediatric practice.

Objectives: We compared the sensitivity and positive predictive value (PPV) of the Modified Checklist for Autism in Toddler (M-CHAT) with those of the Parents Evaluation of Developmental Status (PEDS) in a sample of young children who completed a clinical evaluation.

Methods: Participants were identified from an ongoing screening study at Georgia State University (GSU) that involves administration of the M-CHAT and PEDS during a routine 18- or 24-month well child visit. If ASD risk was indicated on the M-CHAT, a member of the study team called the family and administered a follow-up interview. If ASD risk was still indicated, the family was invited for a clinical evaluation that included a cognitive and adaptive measure and several autism diagnostic measures. A licensed clinical psychologist diagnosed the children with ASD or nonASD given all available data. Performance on the PEDS did not influence whether a family was invited for the clinical evaluation.

Results: A total of 3998 children were screened with the M-CHAT; the sample was limited to 52 participants who completed both the M-CHAT and PEDS and received a clinical evaluation. Forty-seven children failed the M-CHAT and five received an evaluation because the pediatrician noted concerns on

the M-CHAT form. Forty children qualified for PEDS Path A, defined as two or more predictive concerns, and eight children qualified for PEDS Path B, defined as only one predictive concern. The mean age at the time of screening and evaluation were 21 and 26 months, respectively. Thirty children (58%) received an ASD diagnosis after the clinical evaluation. The sensitivity and PPV of the PEDS were .73 and .55 for Path A, .14 and .33 for Path B, and .93 and .58 for Paths A+B combined. The sensitivity and PPV of the M-CHAT were .93 and .60.

Conclusions: The M-CHAT detected more children with ASDs than the PEDS Path A or Path B and as many children with ASDs as the PEDS Paths A+B combined. The PPV of the M-CHAT was higher than any PEDS Path, suggesting use of the PEDS alone may result in an over-referral of ASD assessments. This point is highlighted by the fact that 968 children who passed the M-CHAT failed the PEDS Path A or B; our sub-sample of children who had concerns noted on the M-CHAT may have artificially inflated the PEDS PPV. These results support autism-specific screening in addition to general developmental screening during 18- and 24-month well child visits, to streamline referrals to ASD specialists. Moreover, given the fairly low predictive value of the M-CHAT in this study, we encourage comprehensive evaluation of all children who fail an ASD-specific screen to verify ASD diagnosis.

111.100 100 Developmental Profile of Infants with Autism. R. Maxim*[1], E. Judd[2], L. Middleton[2], L. Eversmayer[2], P. Deutsch[2], S. Stewart[1], A. Nay[1], J. Dorfman[3], J. Pan[1] and H. Matsuo[1], (1)*Saint Louis University*, (2)*Cardinal Glennon Children's Medical Center*, (3)*Washington University in St. Louis*

Background: It is unknown whether developmental screenings performed on a normal population in a community setting can identify children at risk for autism spectrum disorder (ASD) in the first year of life. Objectives: To identify the developmental profile of infants later diagnosed with ASD. Methods: Since 2007 we have trained 263 educators from Parents as Teachers programs (PAT) to observe red flags for autism and to document the developmental milestones of children enrolled in 26 PAT programs in Missouri and Illinois. 3067 children were evaluated using developmental and ASD screenings starting at 5-7 months of age. Between 5-27 months of age these children had developmental and ASD screening every 6 months. We used the Ireton Child Development Chart (ICDC) at around 6,12,18 and 24 months of age, the Red Flags for Communication Scale that is an observation scale for red flags for autism at around 6 and 12 months of age and the M-CHAT autism screening test at around 18 and 24 months of age. Since January 2009, all the 5-27 months old children that failed either the RFC or the M-CHAT were referred to our study for a developmental assessment that included standardized observation scales for autism, language, fine motor, cognitive, adaptive measures and a sensory profile. The ASD diagnosis that was based on the DSM-IV TR criteria was made by a developmental pediatrician. Results: Since January 2009 we have enrolled 8 study patients (age range of 12-27 months, Caucasians) that failed the autism screening between 11-27 months of age. T test was used to compare the early developmental profile of the ASD group (n=4, age range 22-27 months, 75% males) versus the nonASD group (n=4, age range 12-23 months, 75% males, 2 cases with language disorder, 1 case with fine motor delay and 1 case with gross motor delay). At the age of 5-7 months the ASD group had significantly lower scores on the ICDC developmental quotients in language (mean=81.5, SD=13.53) vs. the nonASD group (mean=121, SD=19.51) ($p<0.01$). At 5-7 months of age, the ICDC developmental quotients in social skills were also significantly lower in the ASD group (mean=71, SD=36) vs. the nonASD group (mean=110, SD=15) ($p<0.05$). Data on additional subjects that will be enrolled in our study over the next months will be presented. Conclusions: Defining an autistic pattern on an early developmental screening test could help to identify infants at risk for ASD.

111.101 101 Developmental Trajectories of Signs of Autism Spectrum Disorder (ASD) in Infants and Toddlers with ASD, Developmental Delay or Typical Development. M. Dereu*,

M. Meirsschaut, R. Raymaekers, I. Schietecatte, S. Van der Paelt, P. Warreyn and H. Roeyers, *Ghent University*

Background: Most research around early signs of ASD is retrospective in nature or based on high-risk populations, so little is known about the specificity of these early signs. However, some young children with other developmental disorders seem to show signs of ASD as well (many false positive screens in screening studies have other developmental disorders, e.g. Dietz et al., 2006) and at least in some children with ASD the signs only become apparent when they grow older (low sensitivity of population screening instruments, e.g. Baird et al., 2001).

Objectives: To examine the occurrence rate of these early signs over the first years of life in children with typical development (TD), in children with developmental delay (DD) and in children with ASD by comparing their developmental trajectories in amount of early signs of ASD.

Methods: Child care workers in day-care centres filled out the CESDD (Dereu et al., *in preparation*) for all children in their facility (N= 7007, age range 2 – 39 months). Children suspected of developmental problems, were assessed with the MSEL and ADOS and if necessary referred for clinical diagnosis and treatment. There were 43 children with ASD (M = 24 months, range 7 – 38) and 61 children with DD (M = 19 months, range 3 – 38).

Results: First, the occurrence of signs of ASD over time in typically developing children (n = 6909, M = 16 months, range 2 – 39) was analyzed. The total amount of early signs of ASD is very low but slightly increases over time ($R\_ = .009$, $F(1, 6901) = 64.918$, $p < .0001$; Total signs = 0.083 + 0.014*Age). Secondary, the developmental trajectories of the amount of ASD symptoms was compared across diagnostic groups (TD, DD and ASD) using ANCOVA. Age was defined as 'months from youngest ASD age' (myda; see Thomas et al., 2009). The amount of early signs of ASD significantly differed at the youngest age across groups ($F(2,7001) = 52.775$, $p < .001$). Also, for the total sample the amount of signs increased over time ($F(1,7001) = 165.125$, $p < .001$). We also found a Group x Age interaction ($F(2, 7001) = 74.863$, $p < .001$) indicating that the increase in amount of signs of ASD significantly differed across diagnostic groups. The intercepts and slopes of the regression equations showed that at the youngest age children with DD had the most signs of ASD, but the increase in signs of ASD was about four times higher in the ASD group compared with the DD group.

Conclusions: Screening for ASD in young children should be done cautiously. The younger the children, the more likely it seems, based on the developmental trajectories found in this study, that cases of ASD will be missed and the more false positives will be generated by children with DD.

111.102 102 Early Intervention for Children with Autism and Their Families: A Randomised Control Study of Child and Parent Outcomes of Home and Centre Based Programmes. D. M. Costley*, *Autism Spectrum Australia (Aspect)*

Background: Consistent with international trends there is increasing demand for early intervention (EI) for autism across Australia. The increasing need for EI is associated with a lack of empirically based evidence about outcomes for children and their families. This paper reports on an empirical study examining the effectiveness of Autism Spectrum Australia (Aspect)'s Building Blocks™ Program by a team of researchers at the University of Sydney.

Objectives: To compare the effectiveness of home-based and centre based early intervention programs for young children with autism and their families in Australia.

Methods: The study specifically compared the effectiveness of the Building Blocks™ centre based (CB) and home based (HB) programs compared with a matched group of children who were not in the Building Blocks™ program. The CB program provides a weekly parent training program concurrently with a structured play based program for a small groups of children. The HB program provides a fortnightly session. Both programs operate for 12 months. In this paper outcomes for three groups are compared: CB, HB and a

comparison (wait list) group. Program variables of interest include intensity, individual versus small group focus, context (HB versus CB), type of parent education and support. Three participant groups were recruited in 2006-7 - HB (n=31), CB (n=28), and waitlist/control (n=28). All participants were administered pre and post assessment measures. Treatment groups received intervention for 12 months. Formal and non-standardised assessments were used to measure social, communication and independent functioning outcomes for children and parent stress and quality of life.

Results: This paper reports on child and parent outcomes. Dependent variables included: Child; autism (ADOS), cognition (Griffiths), communication, (Reynell & Pragmatics Profile), independent functioning (Vineland), Developmental Behaviour Checklist (DBC): Parent/family: stress (PSI), Quality of life (Beach), and perception of competence.

Strengths of the project included: random assignment of participants to the treatment groups, a non-treatment comparison group, verification of diagnosis of autism (ADOS), pre and post measures by staff blind to the participant status, verification of treatment fidelity and recording information about additional interventions throughout the study.

Conclusions: The cost analysis suggests that the CB group program is the more cost effective with regard to outcomes, however it is important to note that a CB group was not an option for all children referred to the program. This is an important consideration given that parents and their professional advisors endeavour to choose interventions that match both child and family characteristics. Given that Building Blocks® offers a range of options and that the two treatment conditions compared in this study are similarly cost effective then this research provides support for a flexible range of programs as provided by Building Blocks®.

111.103 103 Enhanced Visual Contrast Sensitivity in Infant Siblings of Children with Autism Spectrum Disorders (ASD).
K. R. Dobkins*[1], L. J. Carver[2], E. Price[2] and N. Akshoomoff[1], (1)*University of California, San Diego*, (2)*UC San Diego*

Background: We recently reported that 6-month-old "High-Risk" infants, who are thought to carry some of the genes associated with Autism Spectrum Disorders because they have an older sibling diagnosed with the disorder, exhibit luminance (light/dark) contrast sensitivity that is significantly higher than that observed in Low-Risk control infants (McCleery, Allman, Carver & Dobkins, 2007). This finding suggests that enhanced luminance contrast sensitivity may be an early endophenotype of ASD, reflecting a genetically-mediated risk factor for the disorder. Objectives: In the current study, we investigated: 1) whether the group difference previously reported in 6-month-olds replicates in an entirely new sample of subjects, 2) whether infants who go on to develop ASD differ from High-Risk infants who do not, 3) whether group differences can be observed at an earlier time point, i.e., 3-months, and 4) whether gains in contrast sensitivity between 3- and 6-months differ between groups. Methods: The sample of 6-month-olds included 45 Low-Risk controls (infants from families without autism history, 20F, 25M) and 14 High-Risk infants (6F, 8M). The sample of 3-month-olds included 26 Low-Risk infants (11F, 15M) and 14 High-Risk infants (5F, 9M). A subset of infants were tested at both 3- and 6-months (Low-Risk: n = 17, High-Risk: n = 11). An additional 8 infants (7 High-Risk and 1 Low-Risk) went on to develop ASD (based on ADOS/ADI). Using forced-choice preferential looking, we obtained contrast sensitivities for luminance (light/dark) and chromatic (red/green) sinusoidal gratings (0.27 cycles/degree, 4.2 Hz), which are thought to preferentially activate the subcortical Magnocellular and Parvocellular visual pathways, respectively. Results: 1) For 6-month-olds, we replicated our previous findings; High-Risk infants exhibited significantly higher luminance contrast sensitivity (by about 1.6-fold) than Low-Risk infants ($p = 0.042$, two-tailed t-test), but there were no group differences in chromatic contrast sensitivity. 2) The mean contrast sensitivity of the 8 infants who went on to develop ASD was nearly identical to that of the High-Risk infants who did not develop ASD. 3) For 3-month-olds, High-Risk infants exhibited both significantly higher luminance

contrast sensitivity (by about 1.5-fold, p = 0.043) and chromatic contrast sensitivity (by about 1.7-fold, p = 0.064, MS) than Low-Risk infants. This superior performance in High-Risk infants was not due to generally enhanced cognitive performance, as confirmed by their normal Mullen Early Learning scores. 4) For High-Risk infants in the chromatic condition and Low-Risk infants in both the luminance and chromatic conditions, gain in contrast sensitivity between 3- and 6-months was consistent across subjects. By comparison, for the luminance condition in High-Risk infants, gain in contrast sensitivity between the two ages was highly variable. Conclusions: Enhanced contrast sensitivity could provide a potential endophenotypic marker associated with ASD. Because we are currently finding no difference between High-Risk infants who do vs. do not go on to develop ASD, we suggest that factors leading to development of ASD per se may include an inability to compensate for the observed atypicalities, and/or a critical combination of these and other (yet to be tested) atypicalities.

111.104 104 Sensory Disorders for Individuals with ASD: Preferances for Black Vs White Rooms. M. Boman*[1] and G. R. Mancil[2], (1)*Kelly Autism Program at Western Kentucky University*, (2)*University of Louisville*

Background: Sensory rooms, also referred to as Snoezelen rooms, have been used in many countries such as the Netherlands and Germany with individuals with severe disabilities. These rooms involves exposing individuals with sensory input within a soothing and stimulating environment using a variety of sensory stimuli. Research is limited regarding the use of these rooms, yet many programs have attested to their benefits when provided for individuals with sensory integration and developmental disabilities (Chung & Lai, 2002).

Objectives: This research focused on the outcomes for individuals with ASD who entered the black or white sensory rooms. Did the personality or mood of the individual initiate their choices of which room they entered? Did academic, communication, and social interaction increase from interactions within these settings?

Methods: The population consisted of 50 individuals from the age of 7 through college age, who voluntarily entered the rooms. These individuals were attending an after school program or were part of the college program at Western Kentucky University. They were monitored by the staff before and after they entered the room. The staff completed a questionnaire about antecedent and post behaviors. For those participants, who were able to answer a questionnaire after they left the room, the forms were made available for them to complete. Documentation was also collected regarding what type of actions the participants were performing while in the rooms (e.g., linear swing, sitting in bean bag, etc.). Heart rates were monitored for these individuals upon entering the room as well as for a five-minute interval after they left the rooms. Also, any changes in behaviors and academic performance were collected using frequency, intensity, and time duration before and after the visits to the rooms. Other variables considered included: age, gender, ability level, and diagnosis. A likert scale was implemented regarding level of changes in attitude, behavior, etc. Data information was collected every time the participants entered the room for a period of two months.

Results: Over 75% of the participants exhibited postive outcomes upon leaving the rooms. This was particularly true of the college aged students who were able to begin their work more quickly after they left the rooms. Academic performance, communication, and behaviors improved as well. Both the black and white rooms had this impact on the participants, but the white room was chosen at a higher frequency than the black room. This also was impacted according to the age and IQ level of the participants.

Conclusions: Snozelean rooms did have an impact on the academic, behavior, and communication output for some of participants diagnosed on the Autism Spectrum who made the choice to enter the rooms. This was evident regardless if the participant had been diagnosed with a Sensory Integration Dysfunction as well as

the age and ability levels. For a few individuals, the individual's became aroused to the point that it became difficult to work with the participants.

111.105 105 The Effect of Birth Order On Cognitive Ability and Symptom Severity in Children with Autism. J. G. Giles*[1], E. M. Griffith[1], M. W. Gower[1], E. H. Sheridan[1], T. Perez[1], R. A. Barry[2] and N. Adams[1], (1)*University of Alabama at Birmingham*, (2)*The Warren Alpert Medical School of Brown University*

Background: Birth order has been observed to have an effect on intelligence, not only in the typically developing population but in the autism population as well. Previous studies have found a negative relationship between birth order and intelligence in both groups along with several additional effects in the ASD population. Studies examining these effects in autism multiplex families found that birth order did in fact have an impact on intelligence and symptom severity. First-born children with autism were found to exhibit worse restricted and repetitive behaviors, but more useful phrase speech than younger siblings. However, younger siblings seemed to have better social and communication skills. These differences in cognitive ability and symptom severity due to birth order need to be examined further

Objectives: The objectives of this study are to replicate previous studies by comparing cognitive abilities and symptom severity between oldest and younger siblings and examine the effects birth order has on each category.

Methods: Archival data of individuals was obtained from 69 individuals who received an ASD diagnosis from 2006-2008 at Sparks Clinics. Only children who received a cognitive evaluation and had siblings, in addition to the ASD diagnosis, were included in this study. The ADOS was used in the ASD diagnosis and scores from the WISC-IV, DAS, and DAS-II were obtained to measure cognitive ability.
Results: It was determined that birth order did not have a significant effect on either cognitive ability or symptom severity in children with autism. There was however an interaction between the oldest and younger group's verbal and non-verbal ability scores. Also, maternal age was found to be correlated with non-verbal and verbal abilities.

Conclusions: The current finding of no birth order effect on cognitive ability, as compared to the results of previous research demonstrating lower abilities in younger siblings, can be supported by several explanations. It is possible that there is a different mechanism of action underlying the expression of cognitive ability in multiplex versus simplex families, and the current sample included only families with one child diagnosed with an ASD. Another possibility is that the genetic and biological components of autism overlay any environmental factors, thus overpowering a child's social rank in the home. Although further examination will be necessary, the presence of older typically developing children could have a protective effect on children with ASD, being responsible for the younger children in the current sample not having lower cognitive ability than other children (eg. the younger siblings with ASD benefited from having a socially-typical role model in the home).

111.106 106 The Relation Between Demographic Factors and Parental Well-Being in Parents Raising Toddlers with Early Autism Symptomatology. G. A. Levine*[1], A. H. Brown[1], A. S. Nahmias[1], P. Yoder[1], A. S. Carter[2], D. S. Messinger[3] and W. L. Stone[4], (1)*Vanderbilt University*, (2)*University of Massachusetts Boston*, (3)*University of Miami*, (4)*Vanderbilt Kennedy Center*

Background:

Parents of children with autism report higher stress and lower perceived parenting competency relative to parents of children with other developmental disorders and those with typically developing children (Bromley et al., 2004; Rodrigue et al., 1990). Identifying specific family factors associated with elevated stress and depression in this sample may help us target families in greatest need of supportive intervention.

Objectives:

The purpose of this study was to examine the relation between specific demographic features and parental well-being in a unique sample of families: those with children 25

months or younger who show early autism symptoms.

Methods:

Parental well-being and demographic characteristics were assessed in families of 55 toddlers (mean CA = 21.2 mo., range = 15.5 – 25.0 mo.) at an initial assessment of a multi-site clinical randomized trial of the Hanen More than Words intervention. Children had met a predetermined cutoff on the Screening Tool for Autism in Two-Year-Olds (STAT) and had a clinical presentation consistent with an ASD. Parental well-being was assessed using the Center for Epidemiologic Studies Depression Inventory (CES-D), Beck Anxiety Inventory (BAI), Ryff Scales of Psychological Well-Being, Parenting Stress Index-Short Form (PSI), and Maternal Efficacy Scale (MES). Demographic information, collected via parental report, included household income, parental education, and parental age.

Results:

Higher ratings of depression were associated with lower income (r = -.33, p < .05; 10.8% of the variance). Decreased parenting efficacy was correlated with lower income (r = .29, p < .05) and lower parental age (r = .33, p < .05), but only parental age uniquely accounted for variance in efficacy ratings (i.e., 10.7%). Lower self-acceptance was associated with lower income (r = .37, p < .01; 14.0% of the variance). Higher ratings on the PSI Difficult Child subscale were correlated with lower income (r = -.34, p < .05; 11.2% of the variance). Higher ratings on the PSI Parent-Child Dysfunctional Interaction subscale were associated with lower income (r = -.30, p < .05; 8.9% of the variance). Higher ratings of total stress on the PSI were correlated with lower income (r = -.28, p < .05; 8.1% of the variance). Greater anxiety was associated with lower education levels (r = -.29, p < .05; 8.6% of the variance).

Conclusions:

Results for this sample indicate that parents with fewer economic resources and less formal education are at increased risk for depression, lower perceived efficacy and self-acceptance, and greater parenting stress. 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). These results suggest the importance of providing families at socioeconomic risk with specific parent-focused supports (e.g., parent training to enhance efficacy) in addition to child-focused interventions.

111 Social Function

111.107 107 Pain Expression in Youth with ASD: Thematic Analysis of Parent Interviews. L. Goodman*, N. F. Bandstra, K. Kalousek and S. A. Johnson, *Dalhousie University*

Background: Historically, it was believed that individuals with developmental disabilities do not experience pain. It is now generally accepted that children with a variety of developmental disabilities, including autism spectrum disorders (ASD), are perfectly capable of experiencing pain. However, there has been limited empirical research on pain in ASD. Clinical impressions and anecdotal observations often suggest that people with ASD have a high pain threshold. In a recent study, we examined pain expression in ASD by employing hypothetical pain scenarios and asking parents to rate the level of pain their child would show in each situation. Results indicated that levels of pain expression rated by parents of youth with ASD did not differ from ratings of parents of typical youth. In addition to quantitative ratings, parents were also asked a series of questions to better understand how their children express pain; the current study focuses on these qualitative results. Objectives: To complete a thematic analysis of responses of parents of youths with and without ASD obtained during a semi-structured interview. Methods: As part of a larger study, 26 parents of youth with ASD and 24 parents of typically developing (TD) youth were asked: 1) How do you know when your child is experiencing pain? and 2) Do you think your child experiences pain differently than a typically developing child/other children? Interviewers wrote the parents' answers to these questions. Subsequently, two researchers completed independent paper-and-pencil thematic

analysis of the parents' responses and compared their findings. The researchers were in complete agreement for all themes and sub-themes. They differed on the number of responses assigned to 10 of the 27 sub-themes. These discrepancies were discussed and agreement was reached for all responses. Results: We found that parents of youth with ASD described pain expression by their child in ways that differed from the pain expression described by parents of TD youths. Parents of ASD youths reported that their children show overly dramatic responses, anger, or inappropriate responses to pain. The responses to pain described by the 24 parents of typical children were all considered appropriate and normative (e.g., 'moody', 'sulky', 'frustrated', etc.). Moreover, the ASD parents described the need to interpret their child's behaviour or facial expressions to know if their child is in pain. This is in contrast to parents of TD youths who stated that their children typically tell them when they are in pain or, less frequently, cry, whine, or become quiet. Lastly, some parents of youth with ASD reported that their children appeared to have a high threshold for pain, whereas others reported a high level of sensitivity to pain. All parents of TD youths said that their child experiences pain similar to other children. Conclusions: Although parents of youth with ASD reported typical levels of pain expression in our previous study, the qualitative findings of this study suggest that pain is expressed differently by youth with ASD. These findings are an important first step for future empirical studies of pain expression in ASD.

111.108 108 Parent-Child Interactions and Their Relation to Friendship Quality in Children with and without Autism: An Analysis of Joint Attention and Responsiveness. S. E. Meek*, L. T. Robinson and L. B. Jahromi, *Arizona State University*

Background: Healthy social relationships are crucial to positive child development. Previous investigations have shown that positive parent-child relationships predict a number of favorable outcomes for children including academic adjustment, popularity amongst peers, and positive long-term social outcomes (Morrison, Rimm-Kauffman & Pianta, 2003; Pianta & Harbers, 1996; Black & Logan, 1995). Engaging in joint attention is among the first interactions between children and their parents, and significantly relates to important developmental processes across early childhood, including language and social development. Parental behaviors during play activities also influence children's social development. One such parental behavior is responsiveness, which involves behaviors meant to maintain a child's engagement. Parent behavior in dyadic play interactions predicts popularity and peer acceptance in pre-school (Black & Logan, 1995). Children's social interactions with parents, therefore, may directly impact their interactions and friendships with peers, areas of notable delay for children with autism.

Objectives: To explore two dimensions of parent-child interactions (joint attention engagement and responsiveness) to understand how they relate to friendship qualities in children with autism and a comparison sample of typically-developing children.

Methods: Participants include 20 children with autism and 20 typically-developing children matched on their language age. Children had a mean age of 54.57 months (*SD* = 12.02). After taking part in an initial visit to assess developmental level, children participated in a series of laboratory tasks designed to measure social and emotional development, including a 5-minute parent-child free play interaction. Engagement states were coded as (1) coordinated engaged; or (2) unengaged (Adamson, Bakeman, Russell & Deckner, 2000). Responsiveness was coded as (1) amount of mutual play (i.e., how involved in the same activity is the dyad); (2) number of times the mother gives positive feedback (e.g. "That's right," patting child on back); and (3) the number of responses the mother gives to the child's nonverbal bids, pointing, showing, or offering (Kasari, Sigman, Mundy, & Yirmiya, 1988). Parents completed a follow-up questionnaire that included a measure of children's friendship qualities adapted from Buysse (1991).

Results: Analyses are currently underway to examine the primary study questions concerning the impact of parent-child joint

engagement and responsiveness on friendship qualities among children with autism. Preliminary findings on related variables point to an interesting pattern of findings. Specifically, on measures of child temperament related to attention and engagement (i.e., attention focusing and attention shifting), children with autism were rated as displaying significantly less focused attention and shifting ($p < .05$). On a measure of coping behaviors during interactions with peers, which may be related to peer acceptance and friendships, children with autism were rated as showing significantly fewer adaptive coping strategies when faced with challenging peer situations ($p < .10$).

Conclusions: Preliminary findings suggest a meaningful pattern of findings concerning impaired attention and engagement, and poorer adaptive coping strategies in challenging peer situations among preschoolers with autism. Further analyses will be conducted to explore whether observations of joint engagement and parental responsiveness in the parent-child interaction reveal similar group differences, and whether such behaviors relate to children's friendship qualities.

111.109 109 Predictors of Parental Self-Efficacy in Parents Raising Adolescents with ASDs. M. D. Lerner*[1], F. Martinez-Pedraza[2], N. Chae[1] and A. S. Carter[2], (1)*University of Virginia*, (2)*University of Massachusetts Boston*

Background: Parental self-efficacy has been identified as a significant variable associated with parental wellbeing and positive parenting outcomes. In particular, parents' beliefs about their parenting capacity and influence on their children's development have been associated with stress and depression experienced by parents in challenging parenting situations (Coleman & Karraker, 1998). Parents of children with autism spectrum disorders (ASDs) face unique challenges and have often reported elevated parental stress and depressive symptoms, and lower parental efficacy (Kuhn & Carter, 2006), which have been associated with child-level factors such as behavioral problems (Hastings, 2003). However, research on parental self-efficacy in ASD populations has focused on parent-reported factors in young children. Adolescents with ASDs experience increasing challenges, become more aware of their social difficulties, and explore autonomy (Seltzer et al, 2003). Identifying the relative contribution of child-level factors to parental efficacy, particularly among parents of adolescents with ASDs, would help elaborate the ongoing challenges of parents of youth with ASDs, and elucidate developmental trajectories underlying these families' self-efficacy.

Objectives: 1. To assess relative contributions to parental self-efficacy of self-reported and parent-reported characteristics of adolescents with ASDs. 2. To examine whether youth depressive symptoms moderated social skills in predicting parental self-efficacy.

Methods: Seventeen youth (12 male; ages 11 -22 years) with ASDs completed reports of their social skills (Social Skills Rating System – Child [SSRS-C]; Gresham & Elliott, 1990), depressive symptoms (Child Depression Inventory [CDI]; Kovacs, 1992), and social anxiety symptoms (Social Anxiety Scales; LaGreca, 1999). Their parents (14 female, ages 35 - 69) completed reports of child social skills (SSRS-Parent), autism-related symptoms (Social Communication Questionnaire; Rutter, Bailey, & Lord, 2005), nonverbal communication (Emory Dyssemia Index; Love, Nowicki, & Duke, 1994), and their own parental self-efficacy (Parental Self Efficacy Scale [PSES]; Bandura et al., 2001).

Results: A stepwise regression model revealed that only CDI (_ = -.54, $p < .05$) and SSRS-C (_ = -.60, $p < .05$) were significantly associated with parenting efficacy. Following Holmbeck (2002), moderation analysis of centered predictors using hierarchical multiple regression revealed significant moderation (_ = .80, $p < .05$) by child depression of the effects of self-reported social skills on parental self-efficacy. Post-hoc analyses revealed that among less depressed youth, higher self-reported social skills predicted lower parental self-efficacy (_ = -.94, $p < .01$); among more depressed youth, self-reported social skills were not

associated with parental self-efficacy (_ = .78, p = .15).

Conclusions: In contrast to expectations, only child self-reported characteristics (depression and social skills) were associated with parental self-efficacy. A moderating relationship was found; higher child self-reported social skills significantly predicted lower parental self-efficacy, but only among adolescents who reported less depression. Social skills did not enhance parental efficacy when depressive symptoms were elevated. This suggests that adolescents with ASDs who report high social skills and low depressive symptoms have parents who report more competence in affecting their children's lives. However, when self-reported depressive symptoms are high, higher social skills are not sufficient to increase parental self-efficacy. Future research should further explore child-level predictors of parental self-efficacy.

111.110 110 Preferences for Activities Embedded in a Social and Non-Social Context in Boys with High Functioning Autism Spectrum Disorder. M. C. Goldberg*[1], M. J. Allman[1], M. M. Triggs[2], M. A. Frank-Crawford[3], A. B. Carreau[3], S. H. Mostofsky[1], K. Slifer[1], M. Cataldo[1], M. B. Denckla[1], L. Hagopian[1] and I. G. DeLeon[1], (1)*Kennedy Krieger Institute, Johns Hopkins University School of Medicine*, (2)*Kennedy Krieger Institute*, (3)*Kennedy Krieger Institute, University of Maryland, Baltimore County*

Background: Autism is characterized by impairments in reciprocal social interactions and in social communication. Social interactions appear to be less rewarding for children with autism compared with typically developing (TD) children; deficient learning of social skills may result directly from deficits in responding to social rewards. Objectives: This study was designed to examine whether 8-10 year old boys with high functioning autism spectrum disorder (ASD) differ from typically developing boys (TD) in their preferences for activities embedded in a social or non-social context. Methods: Twenty boys with ASD and 20 TD boys engaged in three paired-choice stimulus preference assessments (SPAs): one consisting of 12 social activities, one consisting of 12 non-social activities, and a third preference assessment (combined SPA) consisting of 12 activities, made up of the top three social and non-social activities and the bottom three social and non-social activities identified from the single-class SPAs. A progressive-ratio (PR) analysis procedure, involving the individual presentation of each of the 12 activities from the combined SPA was also administered to assess whether boys with ASD (n=18) differ from TD boys (n=20) in the amount of 'work' they are willing to produce to gain access to social and non-social activities. Results: Analysis of variance revealed no significant group differences in the percentage of social and non-social activities selected during the combined SPA (all ps > .13). Examinations of relative rankings for social activities compared to non-social activities from the combined SPA revealed that boys with ASD prefer social stimuli to a similar extent as TD boys (Mann-Whitney U Tests, all ps > .46). Results from the PR analyses revealed no significant group differences in the break-points reflecting the amount of work participants were willing to produce to gain access to social and non-social activities (ANOVA, all ps > .35). Conclusions: Our findings suggest that boys with high functioning ASD may be similar to TD boys in their preferences for and in their responses to activities embedded in a social and non-social context. This research has implications for expanding our understanding about social and non-social rewards in autism.

111.111 111 Reliability and Validity of a Japanese of a Scale to Assist the Diagnosis of Autism Spectrum Disorders in Adults. K. Matsumoto*[1], K. J. Tsuchiya[1], M. Tsujii[2], R. A. Ritvo[3] and E. R. Ritvo[4], (1)*Hamamatsu University School of Medicine*, (2)*Chukyo University*, (3)*Yale University School of Medicine*, (4)*UCLA School of Medicine, Professor Emeritus*

Background: Diagnosing Autism and Asperger's disorder among adults has been a concern in a 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 cinfirmed, 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 can understand the meaning without confusing or difficulties, with through 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. Thirty-four volunteers were also recruited as control. In addition, 31 out-patients with different psychiatric disorders (i.e., Schizophrenia, Depressive Disorders, 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 successufully 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 usuful as a clinical scale to assist idenfification of Autism and Asperger's Disorder in adults in Japan.

111.112 112 Screening for Autism Spectrum Disorders: A Re-Examination of the SCQ and SRS. M. Huerta*[1], C. Lord[1] and E. Petkova[2], (1)*University of Michigan*, (2)*NYU Child Study Center*

Background: The current gold standard in clinical and research evaluations of Autism Spectrum Disorders (ASDs) includes the Autism Diagnostic Interview-Revised (Rutter, Le Couteur, & Lord, 2003) and the Autism Diagnostic Observation Schedule (ADOS: Lord et al., 2000). More recently, a number of screening instruments and diagnostic procedures have been introduced that include the Social Responsiveness Scale (SRS: Constantino, 2002) and the Social Communication Questionnaire (SCQ: Rutter, Bailey, & Lord, 2003). These instruments provide a large amount of information in a relatively short amount of time. However, the empirical findings on the utility of these measures have been mixed. The sensitivity and specificity of the instruments varies depending on child age and other characteristics such as language level. Given the heterogeneity of ASDs, an important next step is to examine the performance of the SRS and SCQ in specific (e.g., age by language) subsets of children with ASD. In addition, the inclusion of measures of adaptive functioning should be considered as possible way to improve the ability of the SRS and SCQ to correctly identify ASDs (see Tomanik et al., 2007).

Objectives: This study will examine the performance of the SCQ and SRS in phenotypically diverse samples of children with ASD.

Methods: The present study utilizes previously collected data. Subjects will include approximately 2,686 individuals, ages 4 to 12 years. Diagnoses of ASD were confirmed with clinical diagnostic evaluations. Measures included the ADI-R, the ADOS, the SCQ, and the SRS. Classifications based on the SCQ and SRS will be compared with clinical diagnoses. In addition, the Vineland Adaptive Behavior Scales, 2nd Edition (Vineland-II: Sparrow, Cicchetti, & Balla, 2005) will be used to assess whether the accuracy of the instruments improves when a measure of adaptive functioning is included. Correlational analyses will also be conducted to examine the validity of the SCQ and SRS as measures of ASD severity relative to the new ADOS severity metric.

Results: Results of the data analyses described above will be presented. Implications for research and clinical practice will be discussed.
Conclusions: By using a large and

phenotypically diverse sample, the results from this study will add to our existing knowledge of the SCQ and SRS and advance research on the identification of ASDs.

111.113 113 Social Responsiveness and Maternal Emotional Connectedness Predictors in Autism. M. Wheatley*[1] and D. E. Wille[2], (1)*University of Kentucky*, (2)*Indiana University Southeast*

Background: Ninety percent of mothers of children with autism report that they wish their children demonstrated more affection toward them (Hoppes & Harris, 1990). Children with autism often demonstrate affection strictly through physical means while other children demonstrate affection through verbal professions of love, helping out around the house, seeking proximity to the mother, and expressing concern for and interest in the mother. Mothers of children with autism report that their child's disability interferes with their ability to form emotional connections (Hoppes & Harris, 1990).

Objectives: The purpose of the current study is to evaluate maternal reports of socio emotional investment to her child with autism in relation to her child's social responsiveness deficits. It is expected that mothers of more severely socially disordered children will report less socio-emotional investment to that child due to difficulty in forming synchronous relations with the child. Social responsiveness predictors of mothers' socio emotional investment will be evaluated to determine areas of intervention to foster better emotional relations between mothers and children with autism.

Methods: Twenty mothers (M = 37.41 years of age, SD = 6.32) who attended support groups for parents of children with Autistic Spectrum Disorders (ASD) of 4 girls and 16 boys with ASD (M = 8.52 years of age, SD = 3.59) were surveyed.

Measures:

General Information Questionnaire. Mothers completed a general information questionnaire which consisted of questions about family income, marital status, number of children in the family, child diagnosis, and other general information items. Parental Socio-Emotional Investment.

The Parental Socio-Emotional Investment Questionnaire (Bradley, Whiteside-Mansell, & Brisby, 1997) was used to evaluate maternal feelings of attachment to two of her children. Social Responsiveness Scale.

The Social Responsiveness Scale (Constantino, & Grube, 2005) was completed only for children with ASD in order to assess the degree to which the children were able to reciprocate in social situations.

Results: Linear Regressions were used to evaluate predictors of mothers' socio-emotional investment to her child with ASD. Overall Social Responsiveness totals as well as communication deficits and social cognition deficits predicted socio-emotional investment in children with ASD. Mothers reported greater socio-emotional investment in children with fewer deficits in overall social responsiveness, $t(19) = -2.33$, $p < .05$, in communication deficits $t(20) = -3.01$, $p < .01$, and in social cognition deficits $t(20) = -2.82$, $p < .05$.

Conclusions: Areas of deficit in social reciprocity that are the most highly related to maternal reports of socio-emotional investment in children with ASD are social cognitions and communication deficits. This suggests that impairments in understanding the context of social situations and more deficits in communication most highly affect mothers' ability to emotionally connect with her child with ASD. Possible ways to help improve emotional connection between mothers and their children with ASD include providing the child with early interventions that target understanding of social context and communication skills.

111.114 114 Symptomatic Predictors of Adaptive Functioning in Children with ASD. E. H. Sheridan*, M. W. Gower, M. K. McCalla, E. M. Griffith and F. J. Biasini, *University of Alabama at Birmingham*

Background: Research has consistently shown that children with Autism Spectrum Disorders (ASD) exhibit adaptive skills that are substantially lower than would be expected on the basis of their intellectual

functioning. ASD symptomatology has potential to account for this finding. However, the specific relationship between adaptive functioning and ASD symptomatology remains unclear.

Objectives: To examine if ASD symptomatology, as measured by the Autism Diagnostic Interview-Revised (ADI-R), predicts adaptive functioning, as measured by the Vineland-II, in children with ASD.

Methods: Data were obtained through retrospective file review from routine clinical practice over a three-year period at a university-based clinic specializing in assessment and diagnosis of children with ASD. All children (N=38), age 3-7, were diagnosed with an ASD and administered the ADI-R, the Vineland-II, and a standardized measure of cognitive functioning. Separate hierarchical multiple regression analyses were conducted to determine if the ADI-R current algorithm items in the Communication and Socialization domains uniquely predicted the Communication and Socialization domains of the Vineland-II. Composite non-verbal cognitive scores were entered in the first step of the regression for both analyses.

Results: For the communication analysis, cognitive scores explained 44.4% of variance in the Vineland-II Communication score. After entry of the ADI-R Verbal Communication score at Step 2, the total variance explained by the model as a whole was 44.7%, F (2, 31) = 10.10, $p < .01$. In the final model, only cognitive scores significantly predicted communicative adaptive scores. For the socialization analysis, cognitive scores explained 15.1% of variance in the Vineland-II Socialization score. After entry of the ADI-R Socialization score at Step 2, the total variance explained by the model as a whole was 27.1%, F (2, 31) = 5.75, $p < .01$. The ADI-R Socialization score explained an additional 11.9% of the variance in the Vineland-II Socialization score, after controlling for cognitive functioning, R^2 change = .119, F change (1, 31) = 5.08, $p < .01$. In the final model, both cognitive scores and ADI-R Socialization symptoms uniquely predicted Vineland-II Socialization scores.

Conclusions: These results suggest that ASD Socialization symptoms uniquely predict social adaptive functioning, while ASD Communication symptoms do not predict communicative adaptive functioning. This finding is relevant to intervention efforts where a major effort is made to reduce symptoms with the goal of maximizing positive outcomes. It is of note that the non-verbal cognitive composite score accounted for a significant portion of variance in both the Vineland-II Communication and Socialization domains. This stresses the importance of considering the child's cognitive abilities when considering their adaptive functioning strengths and weaknesses. Future research examining how cognitive functioning and specific domains of ASD symptomatology influence the development of adaptive functioning in individuals with ASD will assist in designing individualized interventions.

111.115 115 Validation of a Peer Interaction Measure of Social Behavior for Children and Adolescents with Autism. C. Schwartz*[1], H. A. Henderson[2] and P. C. Mundy[3], (1)*Yale University*, (2)*University of Miami*, (3)*UC Davis*

Background: While all children with an Autism Spectrum Disorder have common deficits, significant individual differences in social behavior, developmental course, and adaptive outcome remain (Beglinger & Smith, 2001; Prior et al., 1998). These individual differences are seen even among the most high-functioning individuals with autism (HFA; IQ>70; Prior et al 1998) and are complicated by comorbid emotional disorders, such as anxiety and depression (Klin et al., 2000).

Objectives: To validate a social observational measure designed to capture the common social deficits associated with autism as well as individual differences related to temperament (i.e., approach/withdrawal, self-regulation), social anxiety, and social skills in children and adolescents with HFA.

Methods: A total of 58 participants (29 HFA, 29 Control) were seen as part of a larger longitudinal study examining variability in social functioning among individuals with HFA. Participants completed the self-report form of the Early Adolescent Temperament Questionnaire- Revised (Ellis & Rothbart,

2001), to assess Surgency (i.e., surgency/high intensity pleasure, shyness-reverse scored, fear-reverse scored) and Effortful Control (i.e., attention, inhibitory control, activation control). Parent- and self-report of social-emotional functioning was also obtained on the Behavioral Assessment System for Children (BASC-2; Reynolds & Kamphaus, 2004). In addition, each child in the HFA group was paired with a child in the control group to complete a Dyadic Social Interaction, composed of an unstructured conversation in which participants were instructed to get to know one another, a teaching task in which each participant was 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. Coding of videotaped tasks included time and event based codes and global ratings.

Results: A principal components analysis was used to reduce the Dyadic Social Interaction data to four factors: Social Self-Monitoring, Social Anxiety, Social Approach, and Social Skills. The HFA group exhibited higher levels of social anxiety and lower levels of approach behavior and social skills than the control group. There was no group difference on social self-monitoring. To examine the construct validity of the Dyadic Social Interaction factors, regression analyses were conducted to examine associations between the factors and related self- and parent-report measures of each construct, after accounting for diagnostic group differences. In summary, Social Self-Monitoring predicted self-reported Inhibitory Control, _=.31, *p*=.022 and Anxiety predicted self- and parent-report of internalizing symptoms, _=.23, *p*=.043. In addition, Approach behaviors tended to be positively associated with self-reported Surgency, _=.33, *p*=.058. Although observed Social Skills did not predict parent- or self-report measures of social competence, higher observed Social Skills predicted higher self-confidence, _=.36, *p*=.01.

Conclusions: These results suggest that this novel dyadic peer interaction measure may be used as an in-vivo assessment that captures both diagnostic group differences and the wide range of individual differences in social interactive behaviors that are characteristic of ASDs. The results will be discussed in terms of the unique contributions of observational measures to the assessment and treatment of higher functioning individuals with autism.

111.116 116 Visual Recognition of Social and Nonsocial Stimuli in Young Children with Autism Spectrum Disorders. J. Bradshaw*, F. Shic and K. Chawarska, *Yale University School of Medicine*

Background: Deficits in face recognition in older children and adults with autism spectrum disorders (ASD) are well documented. Recent studies suggest that in ASD difficulties in this domain can be detected as early as at 2-3 years and that these deficits are likely to be associated with atypical scanning strategies (Chawarska & Shic, 2009; Chawarska & Volkmar, 2007) and attentional processing of faces (Chawarska, Volkmar, & Klin, 2010). It is not clear however, if deficits in face recognition in toddlers and preschoolers with ASD are due to the complexity of facial stimuli or more specifically, to their social content.
Objectives: This study examined whether deficits in recognition in ASD are specific to faces, or whether they also extend to other nonsocial classes of stimuli.
Methods: Study participants were 21 children with ASD (age: M=39 months, SD=10) and 21 typically developing (TD) children (age: M=36 months, SD=7). Best estimate diagnosis was based on assessment of developmental skills (Mullen Scales) and social interaction, communication, and play skills (ADOS-G), as well as review of medical and developmental history. The Visual Paired Comparison (VPC) paradigm was used to test recognition of three classes of stimuli: common objects, complex geometric block figures, and affectively neutral faces. Visual scanning patterns were recorded using an eye-tracker. Each condition was tested with six trials, with each trial consisting of a Familiarization phase and a Recognition phase. During Familiarization, a stimulus was displayed until the child had looked at the screen for a total of 10 seconds. Following Familiarization, a 5s blank interstimulus interval was shown,

followed by the Recognition phase. During Recognition, two images were presented side-by-side for 5 seconds, one familiar and one novel. A measure of recognition, novelty preference, was calculated for each trial as the ratio of looking at the novel stimulus to looking at both the novel and familiar stimulus during the Recognition phase.
Results: There were no between group differences in total amount of time scanning the scenes in any phase or condition. The ASD group exhibited a novelty preference significantly above chance for objects (M=.57, SD=.11, t(11)=2.3, p<.05) and blocks (M=.54, SD=.06, t(13)=2.3, p<.05), but not for faces (M=.50, t(17)=-.245, p=.81). However, the TD group was able to recognize objects (M=.57, SD=.09, t(13)=2.5, p<.05) and faces (M=.60, SD=.06, t(16)=5.8, p<.001), but not blocks (M=.53, SD=.09, t(16)=1.1, p=.28)
Conclusions: Findings from this study confirm that children with ASD have a deficit in encoding and recognizing faces. In contrast to their inability to recognize faces, they were able to recognize both simple objects and complex block figures. The TD children were able to recognize objects and faces; however they found complex block patterns more challenging. These findings suggest that recognition deficits in toddlers with ASD are specific to faces and do not extend to other complex but non-social stimuli. The pattern of results has important implications for understanding social deficits in young children with ASD and for identifying candidate marker tasks for ASD in infancy.

111.117 117 New Perspectives On Joint Attention in Children with Autism and Their Siblings. P. C. Mundy*, *UC Davis*

Background: Joint attention deficits are a cardinal symptom of autism and infants at risk for autism. Several new observations have recently deepened our understanding of the significance of joint attention disturbance in autism and those at risk for autism spectrum disorders.
Objectives: This paper provides a review of recent developmental and neurocognitive research on joint attention with the intent to inform research with infants at risk for autism.
Methods: Advances in theory, typical developmental data, and neurocognitive research will be reviewed to highlight information with the potential to advance both the measurement and interpretation of joint attention data in research with infants at risk for autism.
Results: Social cognitive theory suggests that joint attention development occurs in stages. The most significant stage is thought to have a 12-15 months of age onset with the emergence of gaze alternating behavior, a measure of the intentional initiation of joint attention. New data and theory, however, indicate that gaze alternation may be reliably measured by 8-9 months. This suggests an earlier onset of a critical joint attention function which may be assessed in the first year in high risk infants. Research and theory also suggest that joint attention is part of a dynamic system whereby the onset of walking increases the spatial challenges of social attention coordination. Surmounting this challenge may be an engine of cognitive development marked regression then growth. Alternatively, the onset of walking may be one point of increased risk for the breakdown of typical development in children vulnerable to impairments in joint attention. In cognitive neuroscience new fMRI paradigms have been developed that verify theory postulating that initiating joint attention and responding to joint attention behaviors involve different constellations of cortical systems. Consistent with the theory, the former appear to be distinguished from the latter by neural activity in regions associated with motivation and reward. EEG coherence research has also provided data consistent with the hypothesis that joint attention is associated with activity in a parallel and distributed processing system spanning the frontal-temporal-parietal cortices. This research also suggests the EEG coherence measures provide a window onto asymmetries of distributed processing that contribute to differences in the joint attention capacities of people with autism and comparison groups.
Conclusions: Recent research suggests that joint attention measure may be used more effectively in the search for first year markers of social impairment in autism than some theory would predict. It may also be that the examination of joint attention during and after the consolidation of walking may be especially useful in high risk infant studies.

In addition, neuroscience lends credence to the importance of discriminating between measures of initiating and responding in joint attention in infant research. Moreover, it may be possible to use EEG coherence in conjunction with joint attention measures to good effect in assessing brain behavior relations in research with the infants at risk for autism.

111.118 118 Pilot Study of a Peer-Enacted Role Play Measure of Social Skills for Adolescents with High-Functioning Autism and Asperger Syndrome. A. B. Ratto*[1], D. L. Penn[2], L. Turner-Brown[1] and G. B. Mesibov[1], (1)*UNC-Chapel Hill*, (2)*University of North Carolina*

Background: Social skills have been identified as a high priority target of treatment and research among adolescents with high-functioning autism (HFA) and Asperger's syndrome (AS) (Tse, Strulovitch, Tagalakis, Meng, & Fombonne, 2007). While numerous social skills interventions have been developed for this population, the development of externally valid social skill assessment measures has not proceeded at the same pace (Matson & Wilkins, 2007). During adolescence, the primary context for social interaction is the peer context, particularly casual conversations (Paul, 2003). One of the most critical skills in successful conversation is responding appropriately to verbal and nonverbal social cues (Turkstra, Ciccia, & Seaton, 2003). Additionally, recognizing and responding appropriately to social cues is a frequent target of social skills interventions for adolescents with HFA and AS (Krasny, Williams, Provencal, & Ozonoff, 2003). Role play measures allow for direct assessment of these critical social interaction skills. While role play measures have been successfully utilized to assess social skills in several populations (Bellack et al., 2006; Blake & Andrasik, 1986), and as a teaching tool in autism (Krasny et al., 2003), a systematic role play measure of social skills has not been developed for ASD.

Objectives: The primary goal of this study was to pilot a peer-enacted role play measure of social skills for adolescents with HFA and AS, focused on the ability to respond appropriately to verbal and nonverbal social cues. Specific objectives included assessing interrater reliability and convergent and discriminant validity via testing in control and HFA/AS samples.

Methods: Participants included 20 participants with high-functioning autism and Asperger's syndrome and 20 undergraduate controls. Participants completed the Wechsler Abbreviated Scales of Intelligence (WASI), the Awareness of Social Inference Test (TASIT), which assesses theory of mind, and the Social Reciprocity Scale (SRS), in addition to the newly developed peer role play measure of social skills, the Contextual Assessment of Social Skills (CASS). The CASS consisted of two conversations enacted with two different trained undergraduates. In condition 1, the undergraduate demonstrated social interest through a standard set of verbal and nonverbal behaviors. In condition 2, the undergraduate displayed disinterest and boredom through corresponding verbal and nonverbal behaviors. Trained coders rated the participants' social behaviors in each condition. Participants' behaviors in each role play and change in social behavior across role plays were examined.

Results: The properties of the role play measure will be evaluated for internal consistency and interrater reliability. Linear regression analyses will be used to examine group differences in social behavior across the Interest and Disinterest conditions. In addition, criterion-related validity will be examined via Pearson correlations with verbal IQ, performance IQ, theory of mind, and SRS scores.

Conclusions: Results of this study will contribute to the field of social skills assessment in high-functioning individuals on the autism spectrum. Issues around utility, validity, and feasibility of this role play assessment of social skills will be examined in relation to existing measures of social skills for this population.

111.119 119 Positive Affect in Infant Siblings of Children Diagnosed with Autism Spectrum Disorder. J. H. Filliter*[1], J. C. P. Longard[2], L. Zwaigenbaum[3], J. Brian[4], I. M. Smith[5], W. Roberts[6], P. Szatmari[7] and S. E. Bryson[8], (1)*Dalhousie University*, (2)*Concordia University*, (3)*University of Alberta*, (4)*Hospital for Sick Children & Bloorview Kids Rehab*,

(5)*Dalhousie University & IWK Health Centre*, (6)*University of Toronto*, (7)*McMaster University*, (8)*Dalhousie University/IWK Health Centre*

Background: Although the literature indicates that children with Autism Spectrum Disorder (ASD) display flatter affect and express less positive emotion than their typically developing peers (Bieberich & Morgan, 1998), little research has examined the early development of expressed emotion in ASD. Preliminary evidence suggests that by one year of age, high-risk infants showing signs of ASD display fewer social smiles than controls (Zwaigenbaum, Bryson, Rogers, et al., 2005). However, additional research is necessary to determine whether smiling distinguishes infant siblings who are and are not diagnosed with ASD, and, if so, when these differences begin to emerge.
Objectives: To examine smiling behaviour across three time points (6, 12, and 18 months) in high-risk infants with an older sibling with ASD and low-risk control infants. Of particular interest is whether there are group differences among high-risk infants later diagnosed with ASD (ASD sibs), non-ASD sibs, and controls and, if so, when this divergence occurs.

Methods: To date, videos of 45 infants (15 ASD sibs, 15 non-ASD sibs, and 15 typically-developing controls) have been coded for displays of positive affect at 6, 12 and 18 months of age. All of the children (6 females and 9 males per group) were followed to age 3 years, at which time an independent ASD assessment was conducted using the ADOS, ADI-R, DSM-IV, and expert clinical judgement. The video clips were collected while the infants were assessed on the Autism Observation Scale for Infants (AOSI; Bryson, McDermott, Rombough, et al., 2004), a semistructured play schedule designed to measure early signs of ASD. Each 7- to 10-minute clip took place during the same portion of the AOSI assessment. The main dependent variable was the average number of seconds spent smiling per minute.

Results: A 3 x 3 (Group x Time Point) mixed repeated measures analysis of variance revealed a significant effect of Time Point ($F(2, 80) = 5.91$, $p = .004$; partial $eta^2 = .13$); children spent more time smiling as they grew older. Although preliminary analyses failed to reveal a significant effect for Group ($F(2, 40) = 1.84$, $p = .17$), effect size calculations indicate that there is a medium-to large-sized effect of this variable (partial $eta^2 = .084$), with the anticipated trend of reduced smiling in ASD sibs relative to controls at 12 and 18 (but not 6) months. No significant interaction was found between the Group and Time Point variables ($F(2,40) = .33$, $p = .86$; partial $eta^2 = .02$). Data collection is ongoing.
Conclusions: Preliminary findings suggest that by 12 months of age, ASD sibs may spend less time smiling than controls. Discussion will focus on the implications of these findings for subsequent child development and for treatment efforts.

111.120 120 Practice Models to Facilitate Participation of Children with ASD in Home, School & Community Activities. D. Sood*[1], C. Zingerevich[2] and C. Schranz[1], (1)*Governors State University*, (2)*Rady Children's Hospital*

Background: The conceptual practice models in occupational therapy guides clinical practice because they provide a framework to understand a client's participation in home, school and community activities. Evidence suggests that successful childhood participation requires a dynamic interaction between the child and the environment. There is a need to develop practice models for children with autism spectrum disorder (ASD) that reflects on the impact of the person factors (such as their cognitive, sensori-motor, psychological and spiritual development) and the environmental factors (physical, social & cultural) on the participation of the child. The International Classification of Functioning, disability and health (ICF) as well as the Person-Environment and Occupational Performance (PEOP) model highlight the importance of a child's engagement in meaningful activities. This presentation aims to present three conceptual practice models for children with ASD. **Objectives:** 1.Understand the need to develop conceptual practice models for children with ASD. 2.Explore the importance of practice models in guiding evaluation and intervention in children with ASD. 3.Analyze the interaction between meaningful

participation of children with ASD and the person and environmental factors. **Methods:** The three conceptual practice models were individually built on theory, the contemporary practice models that guide the profession of occupational therapy and the evidence from the biological, psychological, social and occupational science. It involved an extensive review of the literature as well as the classification and synthesis of the evidence from the literature. Each of the three models also identified the measurement strategies to ensure sound evaluation and planning of the interventions for children with ASD. **Results:** A critical analysis of the evidence facilitated in the understanding of the dynamic interface between theory, research, and clinical practice. The first practice model emphasizes on the role of the physical, social and cultural environmental factors on the development and the participation of children with ASD. The second practice model focuses on the impact of the sensory processing system on children's development and participation. The third practice model emphasizes the contribution of motor and cognitive functions to participation and development of children with ASD. **Conclusions:** Overall, the three practice models provide a systematic approach to address the impact of the environmental factors as well as the cognitive, behavioral, and sensorimotor factors on the participation of children with ASD. These practice models may help clinicians to guide practice and defend clinical decision making in both evaluation and intervention for children with ASD.

111.121 121 Relationship Between Individual Differences in Social Motivation and Autism Symptom Severity. A. M. Rowley*, J. S. Durocher, M. N. Hale, A. J. Margol, A. Gutierrez and M. Alessandri, *University of Miami*

Background: Children with ASDs demonstrate deficits in social relatedness, or the inherent drive to connect with others and share complementary feeling states (Rogers & Benneto, 2000). Researchers argue that autism may involve a failure to assign reward value to social stimuli (Dawson, Toth, Abbott, Osterling, Munson, Estes, et al., 2004). Failure to orient to social stimuli reflects a disturbance in the motivational mechanisms that normally draw an infant's attention to social stimuli such as faces and voices (Dawson et. al, 2004). The Autism Diagnostic Observation Schedule (ADOS) is a standardized protocol for observation of social and communicative behavior associated with autism (Lord et al., 1989). Recent additions to the ADOS have been made in an attempt to standardize scores to approximate an autism severity metric, allowing for documentation of severity as part of clinical assessment and comparisons in scores across time (Gotham, Pickles, & Lord, 2008).

Objectives: The purpose of this study is to examine the relationship between symptom severity in children with ASDs and their social motivation (or preference for adult attention). It was expected that there would be a negative correlation between ADOS severity scores and the duration of time spent interacting with the examiner in a preference for adult attention assessment (based on Dube et al., 2004).

Methods: Participants included 30 children from Miami-Dade or Broward County, FL between the ages of 2 and 5.
All children had a previous diagnosis of an ASD and met cutoffs for ASD or Autism on the ADOS and were part of a larger study on the effectiveness of an intervention targeting initiating joint attention skills. Procedures included the severity score metric of the *Autism Diagnostic Observation Schedule* (ADOS) and the *Forced Choice Preference Assessment for Adult Attention* (FC-AAR, Split Room). In the Split Room procedure, a room is divided in half with tape placed on the ground and identical toys on each side. On the attention side, an experimenter interacts with the child. On the non-attention side, an experimenter pretends to be occupied with another task (reading a book) and does not interact with the child. The child is force-exposed to each side separately for one minute; following this, the child is free to move between both sides for a five minute time period. Scoring is based on duration of time spent engaged with the examiners during the last five minutes.

Results: Results indicated a significant negative relationship between overall ADOS

severity scores and duration of time engaged with adult examiners (r= - 0.478, p= 0.010).

Conclusions: As expected, children with greater symptom severity demonstrated a lesser preference for adult attention than children with less severe symptoms, and vice versa. These findings indicate that social motivation may play an important role in autism symptom severity and have implications for clinical practice and future intervention-based research. Quantitative measures of social motivation (e.g., preference for adult attention) may be useful in identifying individual differences which may serve as predictors of positive outcomes.

111.122 122 Reliability and Validity of the Pervasive Developmental Disorder(PDD) ASJ Rating Scale(PARS). M. Tsujii*[1] and I. Tani[2], (1)*Chukyo University*, (2)*Hamamatsu University School of medicine*

Background: In Japan, government legislated "Developmental Disorders Support Act" in 2004. We have tried to make assessment tools for not only screening people with Pervasive Developmental Disorder(PDD) but also grasping support needs of them.

Objectives: A behavior checklist, the Pervasive Developmental Disorder(PDD) ASJ Rating Scale(PARS), was developed as a screening questionnaire to determine Pervasive Developmental Disorder(PDD) and also as a rating scale to evaluate the severity of a wide range of PDD symptoms. PARS was constructed by two rating, 37 toddlerhood items are evaluated retrospectively and 36 or 37 items are used for current evaluation.

Methods: 317 PDD participants and 345 non-PDD participants were assessed using PARS, and 74 PDD participants were assessed using PARS and ADI-R for these purposes. The subjects were recruited via the medical, psychological or educational institution. The study was described to the subjects and written informed consent was obtained. Diagnoses of either Autistic Disorder were made by a child psychiatrist and based on DSM-IV criteria.

Results: In this study, the reliability and validity of the PARS was tested on PDD and non-PDD samples. Interrater and internal reliability was found to be adequate. Both the toddlerhood evaluation items and the current evaluation items accurately discriminated PDD from non-PDD. The correlation between PARS and ADI-R demonstrated validity.

Conclusions: Result suggested that the PARS may be a useful screening scale for a various clinical settings.

111.123 123 Sexual Well-Being of High Functioning Adults with AUTISM Spectrum Disorders. S. Nichols*[1], S. Byers[2], S. Voyer[2] and G. Reilly[1], (1)*Advantage Care Diagnostic and Treatment Center*, (2)*University of New Brunswick*

Background: Healthy and safe sexuality for individuals with autism spectrum disorders (ASDs) is an important goal, yet it has received little empirical attention. What research has been done has focused primarily on problematic sexual behavior (Henault & Attwood, 2002). In order to be proactive and preventative, empirical studies of the sexual well-being of individuals with ASDs need to address positive sexuality development and barriers to healthy sexuality, not focus solely on problematic behavior.

Objectives: The aim of the current study is to examine a wide range of aspects of sexual functioning, with an emphasis on understanding positive sexual functioning (e.g., sexual desire, sexual esteem, sexual thoughts and fantasies). We also explored the relationship between participant characteristics (severity of social impairment, age, gender, relationship status) and sexual well-being.

Methods: Participants were 342 high-functioning adults (18-73 years) with self-reported ASDs and average to above average cognitive abilities who completed a set of online questionnaires. Of these, 79% (109 men, 161 women, 1 transgender) had been or were currently in a relationship of three months or longer; Seventy-one (44 men, 25 women, 2 transgender) had never been in a relationship. Findings will be presented for the 270 adults (non transgender) who had been in a relationship. On average, participants were 39 years old (SD = 11.0), 90% identified themselves as white, and 78%

had completed some college or graduate work. 66% were currently in a relationship. Participants completed measures assessing sexual well-being including satisfaction, desire, knowledge, cognitions, self-esteem, assertiveness, arousability, anxiety, sexual problems, sexual experience, and on-line sexual activity.

Results: Most participants (71%) identified themselves as heterosexual, and compared to normative data, participants reported poorer sexual functioning. Canonical correlation analysis was used to determine the relationship between demographic characteristics (age, gender, relationship status, severity of ASD symptomatology) and measures of sexual functioning. Three significant functions emerged. The first indicated that being in a relationship was associated with higher sexual satisfaction and more off-line sexual activity. The second function indicated that men reported less sex knowledge but more positive sexual functioning in several areas. The third function indicated that younger individuals with more severe symptoms reported less positive sexual functioning in several areas.

Conclusions: Results provide the first comprehensive assessment of the sexual functioning of adults with ASDs, and will be discussed in terms of ways to support adolescents and adults with ASDs to improve their sexual well-being.

111.124 124 The Relation Between Self-Regulation and Social Competence with Peers Among Children with Autism. L. B. Jahromi*, S. E. Meek and L. T. Robinson, *Arizona State University*

Background: It is now widely accepted that the ability to regulate one's emotions is a critical developmental task in early childhood. Researchers have acknowledged that lack of emotion regulation is a serious concern for children with autism (Loveland, 2005; Prizant, et al.,2003; Wetherby et al., 2000). Recent research has shown that children with autism demonstrate fewer adaptive affect regulation strategies than matched comparison samples (Jahromi & Ober-Reynolds, 2009; Konstantareas & Stewart, 2006). What remains to be explored are factors associated with individual differences in emotion regulation for children with autism, and the degree to which dysregulation may explain the heterogeneity in children's social outcomes, particularly their social competence with peers. Such work is significant, as even high functioning children with autism have poor peer relationships (e.g., infrequent interactions; more disruptive or non-social behaviors; Koegel, Koegel, Frea, & Fredeen, 2001; McConnel, 2000). There is a wealth of data indicating that emotion self-regulation is clearly relevant to such social relationships in typical children (Eisenberg et al., 2000; Spinrad et al., 2006; NICHD Early Childcare Research Network, 2003).

Objectives: The current study will investigate self-regulatory skills among children with autism and a comparison sample of typically-developing children in order to explore the degree to which self-regulation and dysregulation are related to children's social competence with peers.

Methods: Participants include 20 children with autism (per ADI-R) and 20 typically-developing children matched on their language age. Children had a mean chronological age of 54.57 months (*SD* = 12.02) and mean mental age of 55.37 months (*SD* = 15.31). After taking part in an initial visit to assess developmental level, children participated in a series of laboratory tasks designed to measure social and emotional development. Measures include observations of self-regulation during frustration (Locked Transparent Box and Impossible Puzzles Tasks; Goldsmith, et. al. 1999; Smiley & Dweck, 1994) and parent questionnaires, including the Child Behavior Questionnaire (CBQ), Parents' Reports of Children's Coping Reactions (Eisenberg, et al., 1993), and the Emotion Regulation Checklist (Shields & Cicchetti, 1998). Parents completed a follow-up questionnaire that included a measure of children's social competence in peer settings, the Child Behavior Scale (Ladd, 1996).

Results: Our preliminary results revealed that children with autism showed significantly greater negative expressions ($p < .05$),

poorer emotion regulation ($p < .05$), and fewer constructive regulation strategies ($p < .01$) in comparison to typical children. Interestingly, there was important variability in the scores of children with autism. Although the majority of these children showed heightened negativity, approximately 30% of the sample showed evidence of regulation. Observational coding and analyses are currently underway to explore the relation of emotion regulation and dysregulation to these children's social competence with peers in group settings.

Conclusions: Preliminary findings suggest meaningful individual differences in measures of frustration and emotion regulation among children with autism. Further analyses will be conducted to explore whether observations of dysregulation predict children's behaviors with their peers.

111.125 125 The Use of New ADOS Diagnostic Algorithms in Young Children with Williams Syndrome. F. van der Fluit*, K. M. Janke, E. K. Erdmann and B. P. Klein-Tasman, *University of Wisconsin, Milwaukee*

Background: Recent research has explored the overlap between behaviors characteristic of autism spectrum disorders (ASD) and those seen in young children with Williams syndrome. Studies using the Autism Diagnostic Observation Schedule (ADOS; Lord et al, 2000) have found that while the percentage of children with Williams syndrome (WS) who meet criteria for a comorbid autism diagnosis is relatively low, a significant proportion exhibit behavior patterns similar to those seen in children with ASDs (Klein-Tasman et al, 2009; Lincoln et al, 2007). Newly developed ADOS algorithms have been able to more effectively identify PDD in populations with developmental delays (Gotham et al, 2007). Given recent findings of ASD symptomatology in some children with WS, the new algorithm's increased ability to detect behaviors consistent with ASD in delayed populations is of interest in a WS sample.
Objectives: The purpose of this study is to examine classification of children with WS on the ADOS according to the newly published ADOS algorithms.

Methods: 29 children with WS (mean age=41.59 months, SD=8.95 months) were administered Module 1 of the ADOS and the Mullen Scales of Early Learning (MSEL). The ADOS administrations were scored according to the original and the newly published algorithms.
Results: Originally, 14/29 (48.3%) of the children with WS met or exceeded the cutoff score for an ASD (Klein-Tasman et al., 2008). With the use of the new algorithm, 16/29 (55.2%) children met or exceeded the cutoff score. In total, the classification of 10 children in the sample changed when the new algorithm was used: 4 of these children were originally classified as ASD and moved to nonspectrum, while 6 were originally nonspectrum and moved to ASD. Although a significant relationship was found between verbal ability and classification using the old algorithm cutoff scores, this relationship was not found when the new algorithm was used.

Conclusions: The use of new algorithm cutoff points identified a slightly higher percentage of children with WS who exhibit behaviors consistent with ASDs. One third of the participants with Williams syndrome changed classification with the use of the new algorithm. The new algorithm appears to be more effective at identifying social difficulties independent of language. This is especially important in WS, as studies have found that children in this population often have language difficulties early in development (Mervis & Robinson, 2000). Additional implications will be discussed.

111.126 126 The Validity of the Social Communication Questionnaire in Adults with Autism Spectrum Disorders and Intellectual Disability. W. T. Brooks* and B. A. Benson, *Ohio State University Nisonger Center*

Background:

This project expands on current research of the validity of a promising ASD screening measure, the Social Communication Questionnaire (SCQ), which has primarily focused on the psychometric properties of this measure in children. Identifying autism spectrum disorders in both children and adults who present with diverse symptoms, including challenging behavior, is a crucial step in understanding the nature of

these disorders and allocating resources to individuals who may need specific treatment and support for the associated challenges. Individuals with ASDs often require extensive life-long support, and researchers argue that continued assessment throughout the lifespan is essential for maintaining appropriate support and treatment.

Continued research on the validity of ASD screening measures is extremely important in identifying individuals who may need further assessment for autism, especially in adults who may not have been previously diagnosed before increased awareness of ASDs and introduction of sophisticated diagnostic tools. While the psychometric studies of the SCQ in children provide strong evidence that the SCQ is useful and valid, no independent studies on the validity of the SCQ among adults with ASDs were found.

Objectives:

This project examines the psychometric properties (including sensitivity and specificity) of the SCQ in a sample of 90 adults with a prior diagnosis of either 1) intellectual disability (ID) and an autism spectrum disorder (ASD), 2) ID presenting with moderate-severe challenging behavior, or 3) ID presenting with mild-no challenging behavior. This project also examines adaptive behavior profiles of individuals with autism spectrum disorders with ID.

Methods:

Adults with intellectual disability (ID) and their guardians were recruited from agencies in Central Ohio and provided consent to allow researchers to review agency records. Participants with ID nominated potential raters (caregivers or support professionals) to complete several measures to assess ASD symptoms (the SCQ and a DSM-IV Symptom Checklist), behavior problems (the Aberrant Behavior Checklist-Community), and adaptive functioning (Adaptive Behavior Assessment System – Second Edition) of participants with ID.

Results:

Recruitment is complete for the required sample at this time. Currently there is not enough data to present results, but it is anticipated that data collection and analysis will be completed in the next two months.

Based on previous research showing a decrease in the specificity of the SCQ in children who presented with challenging behavior, it is hypothesized that the specificity of the SCQ will also decrease when used to screen adults with ID and no diagnosis of an ASD, who present with moderate-severe challenging behavior. The decrease in specificity is expected to be significantly more pronounced in participants with moderate-severe challenging behavior than participants with mild-no challenging behavior. Based on previous research of adaptive skills in autism spectrum disorders and intellectual disability, it is also hypothesized that individuals with autism spectrum disorders will score lower than the comparison group on the adaptive behavior subscales of Leisure, Social, and Communication skills of the ABAS-II.

Conclusions:

Study findings will result in recommendations concerning the use of the SCQ to screen adults for autism spectrum disorders and to assess autism symptoms throughout the lifespan.

111.127 127 Mothers' Affective Responses to High- and Low-Risk Infants During Face-to-Face Interaction: Effects of Infant Risk-Status and Age. S. F. Hannigen*[1], N. J. Minshew[2] and M. S. Strauss[1], (1)*University of Pittsburgh*, (2)*University of Pittsburgh School of Medicine*

Background: Reports documenting the affective development of infants at high- (HR) and low-risk (LR) for autism have focused on the affective expression of the *infant* during adult-infant interaction paradigms (e.g., Cassel et al, 2007; Merin et al, 2007). In contrast, there is little research on the *parent's* behaviors during interactions. Baranek (1999) noted the importance of examining caregiver responses during socio-emotional interactions, as parents may be engaging in "compensatory behaviors". This idea is of particular interest in an at-risk sample where parents have prior experience

parenting a child with autism and may augment their behaviors based on this experience.

Objectives: To determine the effect of infant risk-status (HR or LR) and age (6 or 11 months) on the affective responses of the infants' mothers.

Methods: Infant-mother dyads participated in a sequence of face-to-face interaction tasks (e.g., a non-specific interaction and peek-a-boo). The non-specific (NS) interaction occurred for 2 minutes and was followed by 1 minute of peek-a-boo (PAB). This paradigm was completed with a group of 6 and 11-month-old infants at HR and LR for autism. Mothers' smiling behavior was coded using the Facial Action Coding System (FACS; Ekman, Friesen, & Hagar, 2002).

Results: A 2 (task) X 2 (risk-status) X 2 (infant age) repeated measures ANOVA analyzed the proportion of time mothers spent smiling. Results indicated that all mothers smiled more during PAB than NS interactions, $F(1, 42) = 18.351$, $p = 0.001$. Additionally, there was a near significant interaction of task, risk-status, and age, $F(1, 42) = 3.551$, $p = 0.066$. Follow-up ANOVAs indicated the following:

- 6-month-old infants: All mothers smiled significantly more during PAB than NS interaction, $F(1, 24) = 7.006$, $p = 0.014$. Mothers of HR infants smiled significantly less across the two tasks than mothers of LR infants, $F(1, 24) = 4.778$, $p = 0.039$.
- 11-month-old infants: Mothers of HR and LR infants smiled to a significantly different degree as a function of task, $F(1, 18) = 5.582$, $p = 0.030$. Mothers of 11-month-old, LR infants no longer exhibit a significant increase in smiling from a NS interaction to PAB ($t(10) = -1.392$, $p = 0.197$), however, mothers of HR infants continue to demonstrate the significant increase in smiling from a NS interaction to PAB ($t(10) = -4.731$, $p = 0.001$).

Conclusions: Mothers of HR infants appear to differ from mothers of LR infants in affective response during typical face-to-face interaction tasks and these differences shift as the infant ages. While both mother groups display more smiling during PAB than NS interaction, mothers of HR 6-month-olds exhibit less smiling behavior overall. As infants get older LR mothers begin to taper their smiling during face-to-face games, but HR mothers continue a smiling pattern characteristic of mothers who have much younger infants. It appears HR mothers may be scaffolding their infant's behavior in a way LR mothers are not.

111.128 128 Parasypmathetic Response Profiles and Adaptive Functioning in Young Children with Autistic Disorder. S. J. Sheinkopf*[1], R. A. Barry[1] and A. R. Neal[2], (1)*The Warren Alpert Medical School of Brown University*, (2)*University of Texas at Austin*

Background: Past research has suggested that children with autism show disruptions in parasympathetic responses to environmental stressors. Vagal tone (VT), a measure of respiratory sinus arrhythmia (RSA), reflects central nervous system control of heart rate which is mediated by the brainstem, and reflects the influence of the parasympathetic nervous system (PNS). Higher baseline VT is thought to indicate a readiness to engage with the social world. Changes in VT in response to environmental challenge are thought to indicate active engagement with and attention to stimuli. While some research has examined PNS functioning in autism, there has been limited research on the relations between PNS functioning and behavioral outcomes in autism.

Objectives: To determine if young children with autism show diminished VT at rest in comparison to non-autistic children, and to determine if these groups differ in their profile of responses to social challenges of varying intensity. We also sought to examine the relations between VT and measures of social and adaptive behaviors.

Methods: Children with Autistic Disorder (AUT; n = 15) and children without autism (nonAUT; n = 8) were group matched on chronological age and nonverbal IQ (2 _ - 6 _ years of age). Cognitive abilities were assessed with the Differential Ability Scales or the Bayley Scales of Infant Development.

Diagnoses were confirmed with the Autism Diagnostic Observation Schedule. Social and adaptive behaviors were assessed with the Vineland Adaptive Behavior Scales. Children were observed during a baseline period and then during a series of social events, including feigned distress reactions by a female examiner, and a stranger approach procedure. ECG was acquired during this behavioral assay. Automated algorithms were utilized to detect and correct for potential artifact in the ECG signal, and VT was calculated from the resulting ECG time series. Children were categorized as showing reductions in VT from baseline to challenge conditions ("responders") or showing increases or no change in VT ("non-responders").

Results: Groups did not differ in baseline VT or in changes in VT during social challenge. Within group analyses were conducted to compare VT responders to non-responders on measures of social and adaptive abilities (Vineland Scales). For less intrusive social conditions, responders and non-responders did not differ on Vineland adaptive behavior scores. However, for the intrusive stranger approach condition, AUT group responders showed higher mean scores on Socialization Domain than non-responders (T [10.5], p = 0.02). Group differences on the Vineland Daily Living Skills, Communication, and Motor Skills domains were not statistically significant. Within the nonAUT group, there were no statistically significant differences between responders and non-responders on Vineland Scale domain scores.

Conclusions: These results suggest that children with autism may show different patterns of parasympathetic responses to social events of varying degrees of intensity, and the individual differences in these physiologic responses are predictive of social functioning, as measured by parent report. These results will be discussed in relation to possible differences in response thresholds and implications for understanding the impact of regulatory capacity on behavioral functioning in young children with autism

111.129 129 Parental Self-Efficacy & Child Depression Predict Inflated Social Self-Perceptions in Adolescents with ASDs.

M. L. Ransone, M. D. Lerner* and A. Y. Mikami, *University of Virginia*

Background: Although challenges in social functioning are central among youth with Autism Spectrum Disorders (ASDs), research suggests that youth with ASDs may overestimate their social competence relative to adult ratings (Lerner et al., 2009) – a phenomenon known as the Positive Illusory Bias (PIB; Owens et al., 2007). Depressive symptoms have been associated with lower self-perceived social competence among youth with ASDs (Vickerstaff et al., 2007) and less bias in these social self-perceptions (i.e., less PIB) among children with ADHD (Hoza et al., 2004). Moreover, parental self-efficacy may also influence PIB. Research has found that parents who report greater parenting competency rate their child as having higher social competence and fewer behavior problems (Mash & Johnston, 1983). Because children with better social skills (Hoza et al., 2000) and fewer behavior problems (Owens & Hoza, 2003) may be less likely to overestimate their social competence (thereby displaying PIB), there is reason to believe that parental self-efficacy may be associated with PIB among adolescents with ASDs. To our knowledge, the role of depression and parental self-efficacy in predicting PIB has not been investigated in ASD populations. We hypothesize that PIB will be present in adolescents with PIB, but that higher depression and maternal self-efficacy will predict lower PIB.

Objectives: 1. To replicate previous findings of PIB in this population. 2. To determine whether child depression and parent self-efficacy influence PIB.

Methods: Fifteen youth (11 – 22 years) with ASDs completed reports of their social skills (Social Skills Rating System – Child [SSRS-C]; Gresham & Elliott, 1990), and depression (Child Depression Inventory [CDI]; Kovacs, 1992), and their parents completed reports of child social skills (SSRS-Parent) and their own self-efficacy (Parental Self Efficacy Scale [PSES]; Bandura et al., 2001). PIB was calculated using standard score discrepancies between child and parent report SSRS.

Results: Preliminary analyses revealed that CDI and PSES were not significantly correlated (r = -.35, p = .17). Matched-sample t-tests revealed significantly higher child than parent report on the SSRS (t =2.67, p = .02), indicating the presence of PIB. We conducted a multiple regression analysis, showing that higher CDI (_ = -.62; p = .01) and PSES (_ = -.64, p = .01) scores independently predicted lower PIB when entered together as predictors on the same step; no interaction effect was found (p = .50).

Conclusions: In sum, PIB was found among adolescents with ASDs, though it was relatively lower for adolescents with higher levels of self-reported depression and parent-reported self-efficacy. These results suggest that adolescents with ASDs who have *low* levels of depression and parental self-efficacy may be especially likely to overestimate their social competence. Moreover, increases in adolescent depression and parental self-efficacy only predicted PIB when considered simultaneously, suggesting that they both contribute to the presentation of PIB. Given that PIB may impede children's receptivity to social skills treatment (Mikami, Calhoun, & Abikoff, *in press*), results suggest that higher levels of parental self-efficacy may reduce that impediment, but that such a reduction may be accompanied by greater adolescent depression.

111.130 130 Parenting Stress as a Moderator of the Association Between Observed ASD Symptomatology and Related Parent-Reported Child Behaviors. S. Celimli*[1], K. K. Lyons[1], C. J. Grantz[1], P. J. Yoder[2], W. L. Stone[3], A. S. Carter[4] and D. S. Messinger[1], (1)*University of Miami*, (2)*Vanderbilt University*, (3)*Vanderbilt Kennedy Center*, (4)*University of Massachusetts Boston*

Background: Both parent report and direct observation are currently used to assess ASD symptoms. Historically, correlations among parent report and direct observation for many constructs have varied widely. In this presentation, we test the hypothesis that parental stress moderates the association between observed ASD symptomatology and related parent-reported behaviors.

Objectives: To examine parenting stress as a moderator of the association between observed ASD symptomatology and parent reports of related child's problem behaviors

Methods: Participants were 53 toddlers (mean CA = 21 months, range = 15.5 – 25.0 months) and their families from the initial assessment of *A Multi-Site Clinical Randomized Trial of the Hanen More than Words Intervention*. Included children had met a predetermined cutoff on the Screening Tool for Autism in Two-Year-Olds (STAT) and had a clinical presentation consistent with an ASD. Parent stress levels were measured using the Parenting Stress Index – Short Form (PSI-SF), which has three subscales (Parental Distress, Difficult Child, and Parent-Child Dysfunctional Interaction) and a Total Stress composite score. The Infant-Toddler Social and Emotional Assessment (ITSEA) was used to assess areas of child's difficulties and competencies as reported by parents; the STAT was used to evaluate the different behavioral domains of the child's impairments (i.e., play, requesting, joint attention, and imitation) in terms of ASD symptomatology. The Imitation/Play subscale of the ITSEA and the Play and Imitation subscales of the STAT were used for this report.

Results: Parents' report of their children on the ITSEA Imitation/Play was negatively correlated with the Total Stress and the Difficult Child and Parent-Child Dysfunctional Interaction subscale scores of PSI (r = -.31, -.31, and -.40, respectively, ps < .05). No significant bivariate correlations were found between STAT Play and Imitation and ITSEA Imitation/Play. A new variable summing the Play and Imitation domains of STAT (STAT Play/Imitation) was created for use in a first moderation analysis. In order to test the moderating effect of parenting stress variables on the relationship between observational measures of child's impairment and parental report of the child's behaviors (Aiken & West, 1991), hierarchical multiple regression analyses were conducted.

PSI Parental Distress moderated STAT Play/Imitation in predicting the ITSEA Imitation/Play. The interaction between STAT Play/Imitation and PSI Parental Distress accounted for 10% of the total variance of

parent-reported ITSEA Imitation/Play. Additional moderation analyses indicated that PSI Difficult Child and Total Stress also moderated STAT Play in predicting ITSEA Imitation/Play. The interactions between STAT Play and PSI Parental Distress, Difficult Child, and Total Stress accounted for 11%, 8%, and 9% of the total variance of ITSEA Imitation/Play, respectively. In all cases, moderation analyses indicated that the strongest associations between observed and reported child functioning occurred in parents reporting high parenting stress.

Conclusions: Higher parenting stress was associated with *greater* correspondence between observed and parent reported child difficulties with respect to play and imitation. It may be that higher levels of parenting stress lead parents to more realistically report their children's behaviors while lower levels of stress are associated with less discriminating reports of child behaviors.

111.131 131 Parents' and Child Health Professionals' Attitudes to Dietary Interventions in Autism Spectrum Disorder (ASD): Findings From a UK Survey. A. Le Couteur*[1], J. Charlton[2], E. Winburn[3], A. Cutress[2], S. Adams[4], E. McColl[2], H. McConachie[2], J. Parr[2], G. Baird[5], P. Gringras[5], A. O'Hare[6], D. C. Wilson[6] and A. J. Adamson[2], (1)*Newcastle University*, (2)*Institute of Health and Society, Newcastle University*, (3)*Tees, Esk and Wear Valley Trust*, (4)*Northumbria Healthcare NHS Trust*, (5)*Guy's Hospital*, (6)*Edinburgh University*

Background: Parents of children with ASD are implementing biomedical interventions such as special diets and dietary supplements (Millward et al., 2008), despite a lack of robust independent evaluation of these treatments (Green et al., 2006). Parents report they do not receive enough information from child health professionals (Rhoades et al., 2007) and that their decisions are more likely to be influenced by other parents, the media and internet (Mackintosh et al., 2005). One popular biomedical intervention is the gluten free casein free (GFCF) diet (Christison and Ivany., 2006). This exclusion diet is not without risks for the child and family (Arnold et al., 2003). Safe implementation of GFCF diet has significant resource implications for healthcare services (Bower 2002; Keen 2007).
A recent Cochrane review has highlighted the need for rigorous evaluation of GFCF diet; a multi-site randomized controlled trial (RCT) would require the cooperation of both parents and child health professionals.
Objectives: To investigate parents'and child health professionals' attitudes towards dietary interventions including the GFCF diet. To assess the feasibility of an RCT of this diet in preschool children with autism, and identify potential barriers and facilitators for successful trial completion.
Methods: Following a positive ethical opinion, UK parents of children with ASD and child health professionals were invited to complete a short web-based questionnaire. Recruitment will end January 2010.
Results: (Findings to date) 247 of 361 parents and 248 of 317 professionals (of these 42% were Pediatricians, 35% Child and Adolescent Psychiatrists; and 21% Dietitians and 'other' professionals) who expressed an interest have now completed the relevant versions of the questionnaire
Parents:
Just under half of parents (46%) were currently giving their child dietary supplements. 84% were aware of GFCF diet (51% of these had heard about it from other parents). A third were implementing special diets, mainly GFCF diet (81%) and all but 2 of these families were also using dietary supplements. Reported benefits for the child of GFCF diet included gut symptoms (58%), concentration and attention (46%) and communication (31%).
Three quarters of parents said they would 'definitely' take part, or would consider participating in an RCT of GFCF diet. Parents commented that they would be more likely to enroll their child knowing they would have access to a study dietitian.
Professionals:
50% of all respondents reported they did not know enough about the efficacy of the GFCF diet to advise families and 72% had been approached by parents for advice about this diet. The majority of professionals (94%) strongly supported the need for evaluation of the GFCF diet and 75% would be prepared to recruit children to a future trial.
Conclusions: These findings confirm the need

to evaluate biomedical interventions such as the GFCF diet. Facilitators and barriers towards recruitment and retention of families for a future RCT have been identified. Professionals and parents have shown support through their preparedness to refer, and willingness to participate. This study also provides important insights for the evaluation of complex interventions, including other biomedical, complementary and alternative therapies.

111.132 132 Performance by Children with ASD, Developmental Delay, and Typical Development On Delayed Non-Matched to Sample Task. D. Herman*[1], C. Maas[1], R. Landa[1] and A. Diamond[2], (1)*Kennedy Krieger Institute*, (2)*University of British Columbia*

Background: Previous literature suggests that children with ASD experience difficulty on the Delayed Non-Matched to Sample task (DNMS). In the DNMS task, children are initially presented with one stimulus covering a well that contains a reward. After a time delay, they are presented with the initial stimulus paired with a novel stimulus. During this second presentation, the reward is placed under the novel stimulus. The child must choose the novel stimulus in order to retrieve the reward. Dawson and colleagues (2001) asserted that understanding the relationship between stimuli and reward, not impairment in visual memory, compromises the performance of children with ASD on the DNMS task.

Objectives: (1) To compare performance of preschoolers with ASD, age-matched children with non-ASD developmental delays (DD), and mental-age matched typically developing (TD) children on the DNMS task. (2) To explore moderators of performance.

Methods: Participants with ASD and DD were 36 to 54 months of age; the two mental-age matched TD groups were 11 to 13 months and 26 to 28 months of age. Group membership was verified via the ADOS, ADI and Mullen Scales of Early Learning. The Communication and Social Behavior Scales Developmental Profile (CSBSDP) was used to screen for red flags for ASD in the 11- to 13-month-old group since the ADOS is not valid for children of this age. Each child received 5 pre-trial presentations of the DNMS tasks with no reward. Participants were then administered standard DNMS trials with rewards and increasing time delays based on performance. Success was defined along a two-tiered continuum: Criterion one: eight out of ten or 12 out of 15 correct trials at a 5-second delay. Criterion two: four out of five correct trials at a 30-second delay.

Results: Preliminary data suggest that the inclusion of pre-trials within the DNMS task is unifying performance on the task across all groups. Additionally, children with ASD who meet the qualifications for criterion one are more likely to also meet the qualifications for criterion two than TD controls and children with DD. Results of a chi-square analysis revealed that children with ASD were more successful at reaching criterion two, given that they had met at criterion one than were TD controls and children with DD (^{2} (1, N = 55) = 11.67, $p<0.001$, ÿ=0.46).

Conclusions: Preliminary data support Dawson's previous findings that children with ASD who meet criterion one quickly will also meet criterion two, thus confirming that visual memory does not pose a barrier in achieving success on the DNMS task. The preliminary data presented above appears to also corraborate with Dawson's finding that pre-trials with no rewards increases the performance of children with ASD's success, albeit marginally (from 50% to 60%).

111.133 133 Self-Perception, Theory of Mind, and Psychopathology in Youths with and without Autism Spectrum Disorders. K. Kalousek*, S. Whitzman, K. Strapps and S. A. Johnson, *Dalhousie University*

Background: Previous research suggests that some high-functioning people with ASD have poor insight into their autistic symptoms. There is some evidence to suggest that individuals with ASD who are more aware of their differences have greater levels of negative mood and depressive symptoms. However, this potential relationship has not been systematically investigated. It has been proposed that the level of awareness of one's autism symptoms may be related to Theory of Mind (ToM) abilities, but this potential relationship has not been examined.

Objectives: To determine if there are relationships between self-awareness and psychopathology (i.e., depression and anxiety symptoms), and between self-awareness and ToM ability, in youths with and without ASD. Methods: The Autism Spectrum Quotient (AQ; Baron Cohen, et al., 2006), a measure of autism symptom severity, was completed by 13 youths with an ASD and an accompanying parent, and by 13 typically developing youths (TD) and a parent. Participants were 9 – 19 years old. To measure self-awareness, we calculated a discrepancy score that represented the difference between parent- and self-reported AQ scores. Parents and participants also completed the Behavior Assessment System for Children-2nd edition (BASC-II; Reynolds & Kamphaus, 2004), a measure of behaviours and emotions associated with child psychopathology. Analyses focused on self-reported internalizing problems (e.g., depression, anxiety). ToM ability was measured using a brief version of the Strange Stories (Happe, 1994) that had been adapted for children. Data collection is ongoing. Results: Preliminary results indicate that parents of participants with ASD reported significantly more autistic features (higher AQs) than parents of TD participants. Parent vs. self-report AQ scores (i.e., discrepancy scores) revealed that ASD participants reported fewer autism symptoms relative to their parents. In contrast, for the TD group, parent- and self-reports did not differ on the AQ. Medium-sized, but non-significant, correlations were found between AQ discrepancy scores and the BASC-2 'Internalizing Problems' composite for both ASD ($r = .40$) and TD ($r = .33$) participants. In a separate sample of 6 youths with ASD and 7 TD participants, there was no significant difference between ToM scores for the ASD and TD group ($t = .69$, $p = .54$). However, the ASD group demonstrated preliminary evidence of a positive relationship between self-perception and theory of mind ability. That is, individuals with ASD who provided self-ratings on the AQ that were more similar to their parent's rating also performed better on the ToM task ($r = .77$, $p = .07$). Conclusions: Preliminary results suggest that greater self-perception of autism-related symptoms may be associated with more overall internalizing symptoms for individuals both with and without ASD. This relationship requires further examination as it may have important implications for understanding aspects of co-morbid psychopathology in ASD. The positive trend between self-awareness and ToM ability for ASD participants suggests that those who are better at attributing mental states to others may also have more insight into their symptoms. This suggests that there may be important links between theory of others' minds and theory of one's own mind.

111.134 134 The Relationship Between Intelligence and Teacher Ratings of Social Skills for Children with Autism. R. Aiello* and L. A. Ruble, *University of Kentucky*

Background:

Although cognitive functioning is not part of the diagnostic criteria for autism, it is often a target for intervention planning and outcome evaluation. For treatment planning, this may be problematic because educators may develop intervention goals or make educational placement decisions based on perceived abilities, rather than actual skills, of the child. For outcome evaluation, improvements in IQ scores (Smith, 2001), may not result in improvements in the core features of autism (i.e., social and communication impairments; Anderson, 2001). Behavioral interventions that impact IQ scores may be misleading because of an indirect effect of promoting test-taking strategies and encouraging behavior associated with better test performance (Lord & Schopler, 1989), rather than a true improvement on underlying cognitive functioning. Additionally, other factors such as language, attention, and motivation difficulties can affect the outcome of intellectual assessment (Leekam et al., 1997; Volden & Johnston, 1999; Wainwright & Bryson, 1996). Despite these challenges, what remains unknown is the relationship between social behaviors and intellectual functioning. Although researchers have repeatedly documented the difficulties with social skills demonstrated by individuals with autism, few have assessed whether the severity of difficulties are related to cognitive functioning. This information will help increase understanding of the multiple and

complex influences on cognitive development and of the areas of social development associated with intellectual functioning and important for intervention.

Objectives:

The purpose of this presentation is to describe the relationship between cognitive functioning and parent and teacher ratings of social skills for young children with autism.

Methods:

The *Differential Abilities Scale* (DAS) was administered to 57 children with autism and the *Early Childhood Social Skills Survey (*ECSSS; Ruble & Dalrymple, 2005) was completed by the teachers of the students. Based on the General Conceptual Ability (GCA) obtained from the DAS, participants will be divided into three groups for purposes of analyses: (a) High GCA—those whose abilities were above 85, (b) Medium GCA—those whose scores were above 70 and below 85, and (c) Low GCA—those whose scores were below 70. These groupings were chosen because individuals in each of these groups have been determined to exhibit different behavioral characteristics (Nordin & Gillberg, 1998). Additionally, the internal consistency of the ECSSS will be calculated.

Results:

Regression analysis will be used to determine the relationship between the GCAs for the different groups with teacher and parent ratings of social skills from the ECSSS. The reliability of the ECSSS will be examined by calculating the internal consistency using Cronbach's alpha, which measures reliability across items in a single test. Validity of the ECSSS will be established by calculating the relationship between items on the ECSSS and items from the Socialization domain on the *Vineland Adaptive Behavior Scales.*

Conclusions:

An analysis of the data is still ongoing; however, it is anticipated that the ECSSS will be a reliable and valid measure for assessing teacher ratings of social skills development. It is also anticipated that a moderate relationship will exist between intelligence and ratings of social skills for children with autism.

111.135 135 The Relationship of Receptive and Expressive Social Skills to Social Outcomes in Children with Attention-Deficit/Hyperactivity Disorder and Autism Spectrum Disorders. C. Demopoulos* and A. Davis, *Alexian Brothers Neurosciences Institute*

Background: Significant overlap between symptoms of Attention-Deficit/Hyperactivity Disorder (ADHD) and Autism Spectrum Disorders (ASD) has been demonstrated in previous research. While both groups demonstrate social impairments, evidence from previous research may imply a distinction in the pattern of social deficits between the two groups. Examination of receptive and expressive social cognitive skills in each group may identify factors that predict social outcomes and potentially offer insight into the underlying pathophysiology of the social impairments characteristic of these two neuropsychiatric disorders.

Objectives: To identify factors predictive of social outcomes in groups with known social skill deficits.

Methods: Participants were 88 children diagnosed with an ASD (4 females, 82 males ages 4-19 years; mean age = 9.16; SD = 4.22) and 105 children diagnosed with ADHD (42 females, 63 males ages 4-18; mean age = 9.64, SD = 3.02) undergoing assessment in a pediatric neuropsychology clinic. Receptive social skills were measured through a facial and vocal affect comprehension task, Diagnostic Analysis of Nonverbal Accuracy (DANVA-2). Expressive social skills were measured by the Pragmatic Judgment subtest of the Comprehensive Assessment of Spoken Language (CASL). Social outcomes were assessed through the teacher report Behavior Assessment Scale for Children, 2nd Edition (BASC-2) Social Skills subtest.

Analyses were planned to examine group differences relative to the standardization sample and to each other. One-sample and independent samples t-tests against the normative means were performed on the DANVA-2, CASL, and BASC-2 measures.

Regression analyses were performed to examine the relative contribution of receptive and expressive social skills to the prediction of teacher rated social competence in each group.

Results: Independent samples t-tests indicated that the performance of the ASD group was significantly less accurate than the ADHD group on the child facial [$t(191) = 2.911$, $p = .004$)] and vocal [$t(149) = 2.899$, $p = .004$)] affect recognition tasks and on the CASL pragmatic judgment subtest [$t(159) = 4.505$, $p < .001$)]. One-sample t-tests against the mean of the normative sample indicated that both groups performed significantly lower on all tasks, with the exception of the adult vocal affect task, for which the mean score of ADHD group did not differ from the normative mean. Finally, regression analyses indicated that the linear combination of predictors accounted for a significant amount of variability in teacher report of social competence in the ADHD group ($R^2 = .13$, $R^2_{adj} = .086$, $F(5,99) = 2.965$, $p=.015$), but not in the ASD group. Only partial correlations between CASL pragmatic judgment and social competence rating were significant in the ADHD regression model.

Conclusions: The significant contribution of performance on the pragmatic judgment subtest of the CASL to the prediction of social outcome may suggest that social difficulties in ADHD result from difficulties in social decision making and responding rather than misinterpretation of affective cues. This pattern was not identified in the ASD group, suggesting that social difficulties may result from different processes in ASD.

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111.136 136 A Protocol for the Disclosure of a Diagnosis of Autism by Professionals: Parent's Recommendations for Best Practice. D. W. Mruzek, E. Hebert, J. Yingling, H. Brown, C. M. Dambra and L. Hiley*, *University of Rochester Medical Center*

Background: Successful disclosure of an autism diagnosis can promote timely understanding of the disorder, prognosis, and interventions, and has implications for child and family well-being. Protocols for diagnostic disclosure have been used in other health areas to promote communication and collaboration in planning next steps. More information is needed about how a protocol could be implemented in autism diagnostic disclosure to explore the extent to which it supports families.
Objectives: The purpose of this study was to use qualitative methodology to characterize parent opinions and recommendations regarding a protocol of autism diagnostic disclosure.
Methods: Participants were 6 parents of children recently diagnosed with autism. A moderator facilitated participation in a focus group. Parents completed a follow-up questionnaire. A narrative of the focus group was audio-taped, transcribed, and coded using qualitative methods.
Results: Based on narrative data, a number of variables related to the disclosure protocol were identified by parents that contribute to or hamper understanding of the autism diagnosis and implications.
Conclusions: Results suggest that several protocol variables may be helpful in supporting parents at the time of their child's autism diagnosis. Future research will include controlled evaluation of whether use of the protocol promotes parental satisfaction and family well-being.

111.137 137 Behavioural and Physiological Effects of Weighted Vests for Children with Autism. S. Hodgetts*, J. Magill-Evans and J. Misiaszek, *University of Alberta*

Background: Sensory modulation dysfunction refers to difficulty regulating behavioural responses to sensory input in a graded and adaptive manner. Sensory modulation dysfunction is commonly reported in persons with autism and can interfere with the ability to function in daily activities. Tactile and proprioceptive input provided by weighted vests is thought to decrease sensory modulation dysfunction in children with autism, translating into improved classroom behaviour and function.

Objectives: This study systematically investigated behavioural and physiological effects of weighted vests for preschool and elementary school-aged children with autism.

Methods: Participants included ten children with autism, ages 3 to 10, in a classroom setting. All participants had low or limited language skills, significant cognitive impairment, and required an individual aide to participate in school activities. A single-case, ABCBC design was used where A =behavioural baseline without vest or heart rate monitor; B = vest with sham (unweighted) weights and heart rate monitor; C = vest with 5-10% body weighted and heart rate monitor. Observers, blinded to treatment condition, rated targeted behaviours for each participant through video taken during structured table-top activities typical of the classroom routine. Targeted behaviours included off-task and stereotyped behaviours and sitting. Visual analysis supported by percent non-overlapping data statistics was used to evaluate treatment effects. Teachers, also blinded to treatment condition, rated each child's behaviour with the Conners' Global Index following each phase of the study. Educational aides, not blinded to treatment condition, provided subjective feedback about the effects of the weighted vest for each participant. Social validity was reported by teachers and educational aides. Heart rate was collected when participants wore the vest.

Results: Objective results suggest that weighted vests were minimally to moderately effective (visual analysis and PND = 70%) in decreasing off-task behaviour in 3 participants, and possibly 2 additional participants for whom potential confounds precluded our ability to confidently say the effects were due to the vest. Weighted vests were not effective in decreasing motoric stereotyped behaviours or improving a child's ability to stay seated. Heart rate did not decrease with the weighted vest. Subjectively, all aides, who were not blinded to treatment condition, reported that weighted vests were effective in improving behaviour in all participants. All teachers and aides reported that weighted vests were appropriate modalities to use in the classroom and wanted to continue using weighted vests following the study.

Conclusions: Contrary to subjective reports, there was limited objective support for weighted vests to decrease off-task behaviour in children with autism in the classroom setting. Weighted vest use was not supported for motoric stereotyped behaviours or sitting. The theoretical basis for weighted vest use was not supported as measured here. Although weighted vests may be an appropriate modality to include as a component of intervention with some children with autism, results were not strong for any participant or consistent across participants. Therefore, if weighted vests are recommended, outcomes must be systematically evaluated. Weighted vests should not be used in isolation to improve classroom function in children with autism.

111.138 138 Child Attachment Behaviors Increase in Response to a Parent-Mediated Intervention: Initial Results From a Clinical Trial in Autism. M. R. Swanson*[1], M. Siller[2], T. Hutman[3] and M. Sigman[3], (1)*Graduate Center of the City University of New York, Hunter College of the City University of New York*, (2)*Hunter College of the City University of New York*, (3)*University of California, Los Angeles*

Background: Previous research on typically developing infants has provided correlational support for the link between parental sensitivity and child attachment behaviors (De Wolff & van Ijzendoorn, 1997). The extent to which these findings extend to populations of children with autism is controversial and unresolved (van Ijzendoorn et al., 2007). Further, the question whether the attachment behaviors of children with autism can be increased through parent education has yet to be tested.

Objectives: The current study employs a randomized clinical trial to investigate changes in child attachment behaviors after a parent-mediated intervention designed to increase responsive maternal behaviors.

Methods: Seventy preschoolers with autism (chronological age: *M* = 57.1 months, *SD* = 12.3) were randomly assigned to either the experimental group (twelve in-home parent-education sessions), or the control group (four in-home training sessions on advocacy). Data on children's attachment behaviors were only available for 41 children: 6 children did not participate in exit

assessments; for 11 children, the strange situation was not administered due to time constraints; in 12 instances, the separation was ended early because of child distress. Preliminary analyses indicate that participants with incomplete attachment data did not differ from participants with complete data on any baseline measure. Children's responses to a reunion with their mothers during an abbreviated "strange situation" were evaluated during intake and exit assessments. Observational coding consisted of qualitative ratings of two interactive behavior variables first described by Ainsworth, Blehar, Waters, and Wall (1978). The Proximity and Contact Seeking Behaviors (PCSB) variable deals with the intensity of a child's effort to regain contact with, or proximity to, their mother. Higher PCSB scores indicate that the child took initiative in achieving contact. The Avoidant Behaviors (AB) variable deals with the intensity and duration of the child's avoidance toward their mother. Highest AB scores indicate that the child did not greet his/her mother upon reunion. Excellent inter-observer reliability was established for both variables (ICC = .86-.89).

Results: To determine if the groups were similar at intake, they were compared on several child characteristics including chronological age, mental age and IQ. There were no significant differences between the treatments groups on these variables. Gains scores were computed from intake and exit assessment attachment behavior variables. Results from independent samples t tests showed a significant difference in gain scores for the PCSB: $t(39) = 2.157$, $p < .05$, where children in the experimental condition had a larger gain in PCSB scores ($M = .10$, $SD = 1.29$) than children in the control group ($M = -.81$, $SD = 1.40$). The test for change in AB was also significant, $t(39) = -2.205$, $p < .05$, where children in the experimental condition had a larger decrease in AB scores ($M = -.90$, $SD = 1.86$) than children in the control group ($M = .71$, $SD = 2.72$).

Conclusions: This research suggests that children who participate in a parent-mediated intervention that enhances maternal responsiveness exhibit more positive attachment behaviors after the treatment than children who do not receive the treatment.

111.139 139 Comparative Analysis of IMFAR Sample Sizes in Support of the National Database for Autism Research. 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 qualified researchers with access to high quality, detailed human subjects data that underlie research findings relevant to autism spectrum disorders (ASD) and to facilitate data sharing across research projects. Sharing of research data provides the opportunity for researchers to (a) use defined standards to characterize their data; (b) validate results; (c) more easily pool relevant research data acquired by others; and (d) communicate results at the appropriate time with other researchers and, if appropriate, the general public.

Objectives:

The objective of this analysis is to (a) characterize the type of research being conducted by the ASD research community to understand how NDAR may contribute to accelerating ASD research discovery and (b) provide an objective measure on the research community's progress in increasing the study sizes relevant to ASD research.

Methods:

2008 and 2009 International Meeting for Autism Research (IMFAR) presentation abstracts (779 in 2008 and 842 in 2009) were reviewed. Data collected include:

- Whether the study included human subjects or biomaterials

- Sample size of enrolled human subjects with ASD as well as controls

- Whether the study focused on NDAR relevant categories of treatment/intervention, phenotyping, genetics or neuroimaging/EEG

A priori exclusion criteria were established to confine subsequent analyses to studies most appropriate for NDAR. The exclusion criteria were that the research abstract:

- Did not involve human subjects or the number of human subjects was not reported

- Focused on the development or validation of measures/assessments

- Involved cell/animal models

- Involved a literature review, bioinformatics system review, or survey of treatment providers

- Reported on a self-selected survey population

- Had an epidemiology focus

Results:

510 (65%) abstracts from IMFAR 2008 and 574 (69%) abstracts from IMFAR 2009 were included in this analysis. In total, the average proband sample size increased from 67 to 106 subjects from 2008 to 2009. Likewise, median sample size increased from 24 to 30 subjects during this period. Standard deviation almost doubled from 118 to 330.

Category	Num '08	Num '09	Mean '08	Mean '09	SD '08	SD '09
Treatment/Int.	70	65	31	40	71	52
Phenotyping	336	382	60	100	99	340
Genetics	47	38	218	405	219	578
Neuroimaging/EEG	57	89	21	29	15	29

Conclusions:

This comparative analysis provides evidence that sample sizes for ASD studies are growing. However, relatively small samples sizes are the norm in ASD research and a large portion of ASD studies focus on phenotype data. Of particular note are the small samples sizes for treatment/intervention studies.

We suggest that the increasing ASD research community adoption of large, well characterized, high quality datasets (e.g. Simons Simplex, CPEA/STAART, AGRE) may be postively impacting the growth in average sample sizes and skewing the standard deviation in the phenotyping, genetics, and neuroimaging/EEG categories. In future years, we will evaluate the long-term impact of linking/including these datasets with NDAR in an effort to increase substantially the study sample sizes of research presented at IMFAR. It is our plan to continue to monitor this trend.

111.140 140 Demystifying Moderators and Mediators in IDD Research. C. A. Farmer*, *Ohio State University*

Background: Relative to other areas of psychosocial research, moderator and mediator analyses are sparse in intellectual and developmental disability (IDD) research. Moderator and mediator variables are necessary for understanding how and why relationships exist between variables, and are incredibly useful in treatment research. They allow researchers to hone in on causal processes and be more efficient in selecting study groups and independent variables. It is not clear why IDD research has been relatively slow to adopt the search for moderators and mediators, although several potential roadblocks are readily identified. First, the jargon of social psychology, where moderators and mediators were first widely-used, can be confusing and daunting. Second, even following the seminal Baron and Kenny (1986) paper, the distinction between the variables themselves is often confusing. Third, technical papers that describe the mechanism for testing the statistical significance of moderators and mediators appear in journals not frequently accessed by IDD researchers and are difficult for non-statisticians to understand.

Objectives: In this presentation, I will explain moderators and mediators in terms familiar to IDD psychologists, using examples from IDD literature. I will also propose that the MacArthur guidelines (Kraemer et al., 2001) be incorporated into IDD research to limit the

confusion between moderator and mediator variables, and I will describe in detail the best practice for statistical analysis of moderators and mediators. Finally, I will review the IDD literature to identify strengths and weaknesses in our current utilization of moderators and mediators.

Methods: First, rules and tips for defining, classifying, and quantifying moderators and mediators will be set forth. Second, the field will be assessed with respect to these "best-practice" guidelines. Five major IDD journals were searched for studies that investigated moderators or mediators, and the resulting articles were evaluated in the following areas: (a) publication year, (b) journal, (c) topic, (d) statistical method, (e) quantification of the mediated effect (for mediation studies), (f) criteria used for moderation/mediation (including temporal and causal relationships), and (g) "pluralism," a term used here to mean inappropriately testing the same variable as both a moderator and a mediator.

Results: Although the Baron and Kenny (1986) definitions are the most widely-used, the MacArthur guidelines (2001) represent a more useful approach to moderation and mediation. Additionally, recent statistical publications in other fields have made the quantification of moderator and mediator effects less daunting to the typical IDD researcher. Although the number of moderator/mediator papers published in the past few years exceeds previous decades, our field is still far behind others in the use of such "third variables." Only 10% of moderator analyses and 23% of mediator analyses adequately fulfilled all of the criteria set forth in this review.

Conclusions: Although moderators and mediators are very useful for understanding causal processes in greater detail than afforded by most commonly-used statistical procedures, IDD researchers have been more reluctant than others to analyze these variables. The field as a whole will advance if we expand our respective repertoires to include the recent theoretical and technical advances outlined in this paper.

111.141 141 Development and Implementation of the RUPP Parent Training Program for Children with Autism Spectrum Disorders. E. Butter*[1], C. Johnson[2] and B. Handen[3], (1)*Ohio State University*, (2)*University of Pittsburgh*, (3)*Univ of Pittsburgh School of Medicine*

Background: Parent-delivered interventions based on applied behavior analysis for children with ASDs have primarily been evaluated using single subject design methodology or small case series. While the results of these evaluations are encouraging, an important next step is to standardize interventions to allow for replication across sites in studies with large sample sizes.

Objectives: This project describes efforts by the Research Units in Pediatric Psychopharmacology (RUPP) Autism Network to assemble and pilot test a detailed manual for a structured behavioral parent training program. This was a necessary step, prior to conducting a study of the relative efficacy of drug treatment (risperidone) and combined treatment (risperidone and parent training) in children with ASDs and disruptive behavior problems.

Methods: The parent training manual was developed over a 6-month period by a group of psychologists with expertise in ASDs and applied behavior analysis. The manual drew from prior research, other parent program materials for children with autism, developmental disabilities, and other disruptive behavior disorders, and the group's own materials accumulated from many years of behavior analytic clinical and research work in the field of autism and developmental disabilities. The final parent training program consisted of 11 core sessions, 3 optional modules, and procedures for two structured home visits. The sessions include didactic materials, video-taped vignettes, and role-play activities aimed at reducing disruptive behavior and increasing learning of adaptive behavior in children and adolescents with PDD. To evaluate the feasibility of the PT manual we conducted a pilot study with 17 families of children with ASDs whose current treatment regimens were stable. Parents participated in PT sessions on a weekly basis (75-90 minutes per session) for 14 weeks, followed

by three "booster sessions," offered at two-week intervals. Two home visits were also conducted.

Results: Parental attendance at sessions (93%), satisfaction with the program (92%), and adherence to homework assignments (80%) were excellent. The mean clinician treatment integrity score across sessions and therapists was 94.2%, with a range of 80.4% to 100%. Clinician ratings of treatment integrity for the 11 mandatory PMT sessions were 95.7% congruent with reliability scoring as indicated by the video tape review. Further, the video tape review showed that mean individual therapist reliability scores across all sessions ranged from 91.7% to 97.3%. Thus, the PT therapist appeared to implement most, and in many cases all, of the critical elements of the standardized PT protocol and rated their own tendencies to follow the treatment manual accurately.

Conclusions: Initial efficacy and feasibility of this manual provided support for its utility as an adjunct treatment in the large scale risperidone vs. risperidone plus parent training intervention trial. Results from that recently concluded trial indicated that the combination of medication and parent training resulted in a greater reduction of serious noncompliant and maladaptive behavior than medication alone in children with PDD.

111.142 142 Dyslipidemia in Male Patients with High-Functioning Autism. H. Matsuzaki*[1], K. Iwata[2], S. Suda[2], K. J. Tsuchiya[2], K. Suzuki[2], K. Nakamura[2], M. Tsujii[3], N. Takei[2] and N. Mori[2], (1)*Osaka University School of Medicine*, (2)*Hamamatsu University School of Medicine*, (3)*Chukyo University*

Background: The neurobiological basis for autism remains poorly understood, but evidence is mounting in support of lipid metabolism playing a role in autism. In order to clarify the role of lipids in autism, we examined whether serum lipid profiles are altered in high-functioning autism patients (male: 6-31y.o.) enrolled in Asperger Society Japan.

Objectives: In this study, we measured serum levels of cholesterol and triacylglycerol in the 112 male subjects with high-functioning autism and 106 age-matched healthy male subjects.

Methods: The size distribution of serum lipoprotein particles was evaluated by high sensitivity lipoprotein profiling system with high-performance liquid chromatography (Skylight Biotech, Inc., Akita, Japan). Samples were diluted 20 times and analyzed at a flow rate of 350 ml/min by monitoring the concentrations of total cholesterol and triacylglycerol.

Results: The serum levels of total cholesterol and triacylglycerol in the infant subjects with high-functioning autism were significantly lower (Mann-Whitney U test: $p < 0.001$) than those of normal control subjects. In each fraction, there were significant differences in the serum levels of very-low density lipoprotein (VLDL) and high density lipoprotein (HDL) fraction. In particular, it's remarkable in VLDL fraction of triacylglycerol ($p< 0.00003$). However, there were no differences between the patients with autism and healthy subjects in serum chylomicron and low density lipoprotein (LDL)levels.

Conclusions: The association between autism and abnormal serum lipid profile suggests that individuals with high-functioning autism may be at increased risk for VLDL hypolipidemia in infancy and which might be implicated in the pathophysiology of autism.

111.143 143 Effect of Intrathecal Baclofen On Severe Tactile Defensiveness and Symptoms of Autism Spectrum Disorder. R. S. Farid*, R. Nevel and F. Murdock, *University of Missouri*

Background: This is a case report concerning a teenage patient with Autism Spectrum Disorder (ASD) and mild tactile defensiveness who had a subsequent traumatic brain injury (TBI). Prior to the TBI, the patient was independent in self care and was about to graduate high school after taking special education courses. Post-TBI he developed spasticity and his tactile defensiveness was severely exacerbated. His social and language skills, already impaired because of ASD, were markedly diminished. His severe tactile defensiveness and behavior precluded his participation in physical therapy and severely increased his required level of nursing care. He was referred to the Physical

Medicine and Rehabilitation clinic for treatment of spasticity and behavior problems.

Objectives: To report the improvements in tactile defensiveness and autism symptoms that resulted from treatment of spasticity with intrathecal baclofen.

Methods: After several conservative interventions, including oral baclofen, failed to provide significant reduction of spasticity, the patient underwent an intrathecal baclofen trial approximately 19 months after the TBI. During the trial, intrathecal baclofen reduced the patient's spasticity as desired and the patient also became more tolerant of tactile stimulation. Because of the success of the intrathecal baclofen trial for reducing spasticity, an intrathecal pump system was surgically implanted.

Results: Subsequent to infusion of baclofen by the intrathecal pump system, the patient's spasticity was significantly improved as expected. Unexpectedly, the patient's mother, personal care attendants, and the treating physician noted that tactile defensiveness and symptoms of autism exhibited by the patient also were reduced. Prior to the pump implantation, the patient's progress was severely limited and his level of dependent care was high. After implantation, he demonstrated rapid and marked improvement. Self care tasks that previously required the assistance of two helpers could be done by the patient independently or with minimal assistance. The area of most marked improvement was in the patient's ability to interact with his environment. The degree to which he became tolerant of external stimulation was excellent. His language and social skills were improved.

Conclusions: Treatment of spasticity resulting from TBI with intrathecal baclofen had the unexpected benefit of also reducing tactile defensiveness and symptoms of ASD. Baclofen is an analogue of the neurotransmitter gamma-amino butyric acid (GABA) and an agonist for GABA receptors. Disruptions in the GABA-ergic system have been hypothesized as a mechanism of ASD. The effect of baclofen on symptoms of ASD is likely due to its action on GABA receptors. Baclofen has anti-nociceptive effects and this may explain its efficacy for reducing tactile defensiveness. Additional patient studies should be conducted to determine if intrathecal baclofen has efficacy for reducing tactile defensiveness and improving social interaction and language skills.

111.144 144 Evaluation of a Sibling-Mediated Imitation Intervention for Young Children with Autism. K. Meyer* and B. Ingersoll, *Michigan State University*

Background: Children with autism have significant difficulties with social-communicative skills. Both parents and peers have been successful at implementing interventions targeting social interactions in these children. However, very few interventions have trained siblings as treatment providers. Siblings may be effective intervention providers because they serve as similar-aged peers who spend a significant amount of time with the child with autism in a variety of contexts. Previous research suggests that reciprocal imitation is a promising intervention target for children with autism.
Objectives: This study investigated (1) whether school-aged children could learn to use Reciprocal Imitation Training, a naturalistic imitation intervention designed to teach reciprocal imitation skills, with their siblings with autism, (2) whether the intervention would lead to gains in imitation and other social-communication skills in the children with autism, (3) whether the results would generalize to different settings, materials, and play partners, and maintain at follow-up, (4) whether changes seen during this intervention would be socially valid, and (5) whether the intervention would lead to changes in the sibling relationship.
Methods: This study used a non-concurrent multiple-baseline design across 4 boys with autism and 6 typically-developing siblings.
Preliminary Results: Preliminary results suggest that siblings are able to learn and use the intervention strategies with their brothers with autism. In addition, the children with autism showed some gains in imitation, language, and joint attention. However, response patterns were variable, with different children showing gains in different skills. In general, siblings generalized their

skills quite well; however, the children with autism rarely showed generalization of their skill gains. Some skill gains did maintain at follow-up for both the typical siblings and the children with autism, but patterns of maintenance varied among children. The intervention did not appear to have a clear positive or negative impact on the sibling relationship; however, both parents and typically developing siblings reported high satisfaction with the intervention, including enjoyment of the intervention, skills increases for both siblings, and an increase in the quality and/or enjoyment of playtime between siblings.
Conclusions: Overall, these results suggest that sibling-implemented Reciprocal Imitation Training may be a promising intervention for young children with autism.

111.145 145 Farm Community-Based Intervention Model in Adult Subjects with Autistic Spectrum Disorder: Not Only "After Us". A. Narzisi*[1], M. Venturi[2], M. Innocenti[2], F. Suvini[2], S. Bini[2], G. Genchi[2] and U. Caselli[2], (1)*University of Pisa – Stella Maris Scientific Institute*, (2)*AGRABAH - Associazione Genitori per l'Autismo*

Background:

Autism is a complex disorder with many contributing factors. High number of subjects, both in their childhood and adulthood, does not receive an adequate diagnosis and does not benefit from an integrated welfare pathways. Autism persist into adulthood and the majority of cases diagnosed in childhood continue to meet criteria for the disorder in early adult life.

Objectives:

Current study evaluated the effectiveness of a Farm Community model intervention for adults subjects with PDD.

Methods:

An initial cohort of 10 young adult subjects with autism, diagnosed according to DSM IV and ADOS-G criteria, is enrolled in an intervention program based on Farm Community model. As to young adults, the Farm Community model aims to be like a family: the "home-like" character guarantees, in fact, a safe, comfortable environment which permits privacy and independence at the same time but which is also configured as a focal point of activities and social relations, open to the surrounding community.

Results:

The results to date show the effectiveness of the procedures and techniques utilised. At follow-up study (after 1 year), the adult subjects have made notable progress in communication and social interaction evaluated with VABS (Vineland Adaptive Behavior Scale).

Conclusions:

The farm model intervention can produce substantial functional improvements and it is ideal for adults with Autism for many reasons: a)rural life is more simple, less stressful and safer than urban life; b) many persons with autism are more suited to life in a quiet open environment; c) a farm setting offers potential to develop skills and offer meaningful work opportunities.

111.146 146 Generating Individualized, Evidence-Based Treatment Recommendations: The Example of PECS. P. J. Doehring*[1] and B. Reichow[2], (1)*Children's Hospital of Philadelphia*, (2)*Yale Child Study Center*

Background:

Practitioners seeking to help children with Autism Spectrum Disorders (ASDs) have increasingly relied on evidence-based practices (EBP), or those interventions consistently supported by high quality, peer-reviewed outcome research. Several reviewers have recently developed rubrics for objectively evaluating the quality of outcome research, including specific standards for designating a practice as evidence-based. These efforts reflect a growing convergence regarding the general characteristics of high quality research and the number and quality of such studies needed to constitute EBP. Reviewers have been limited, however, to drawing broad conclusions about practices, because of the limited number of outcome studies, and the tendency for some studies to rely on broadly defined methods and measures. As a result, it is difficult for

individual practitioners to translate EBPs identified thus far into specific objectives for specific individuals, and so they cannot yet take full advantage of the growing body of outcome research.

Objectives:

To demonstrate a two-stage process for generating individualized, evidence-based intervention goals from methodologically sound outcome research by (a) establishing whether a given program (e.g., the Picture Exchange Communication System, or PECS) is an EBP for teaching communication and related skills, and then (b) generating specific objectives reflecting consistent patterns across studies of at least adequate quality.

Methods:

We conducted PSYCHLIT and PUBMED searches for outcome studies in which PECS was used to teach communication or improve related skills and behaviors among children with ASD, focusing on studies published in English in peer-reviewed journals. After rating studies according the Reichow, Volkmar, and Cicchette (2008) rubric, we first evaluated whether PECS is a broadly defined EBP. Selecting only studies of at least Adequate quality, we then summarized patterns of findings across at least two studies for a similar population as indicating: (a) Consistent evidence, when similar findings were obtained across all studies; (b) Some evidence when there was a generally positive, though not perfectly consistent, trend obtained across 3 or more studies, and; (c) Emerging evidence when findings were obtained by only one study examining a specific question.

Results:

Preliminary calculations of inter-observer agreement on the application of the Reichow rubric exceeded 80% for all components. Preliminary analyses of more than a dozen studies, including both group and single-case designs, indicated that PECS is an established EBP. Patterns of evidence were noted that potentially serve several different purposes: (a) the identification of goals addressing the acquisition of PECS itself (e.g., that PECS is initially mastered relatively quickly by most children, even those with little or no independent, functional communication skills; (b) addressing related skills (e.g., that improvements in PECS may be associated with improvements in some aspects of speech, and does not result in decreases in vocalization or speech), and; (c) helping to choose between PECS and other strategies according to other child characteristics.

Conclusions:

These findings demonstrate a two step approach to translating outcome research into individualized, evidence-based goals. We discuss characteristics of PECS that facilitate this approach, and some of the patterns of weakness in the outcome studies reviewed.

111.147 147 Infant Siblings of Children with Autism: Results of a Parent-Child Intervention. A. M. Steiner*[1], G. W. Gengoux[2] and K. Chawarska[3], (1)*Yale University*, (2)*Stanford School of Medicine*, (3)*Yale University School of Medicine*

Background: As prospective studies of infant siblings at increased genetic risk for Autism Spectrum Disorder (ASD) begin to identify infants who show signs of atypical social and communication development within the first year of life (Cassel et al., 2007; Zwaigenbaum et al., 2005), there is a critical need for the investigation of evidence-based treatments suitable for an at-risk infant population. Pivotal Response Treatment (PRT; L.K. Koegel et al., 1999), an evidence-based treatment developed for older children with ASD, may be particularly well-suited for treatment of infants at risk for ASD, as it has been shown to improve social communication by addressing core deficits in social motivation (R. L. Koegel et al., 1987).

Objectives: The present study investigates a developmentally-based adaptation of PRT to improve the frequency and spontaneity of critical prelinguistic communication behaviors in 12-month-old infants at risk for ASD.

Methods: Three 12-month-old infants, enrolled in a prospective study of infant

siblings of children with ASD, and their mothers were provided with 10 hours of parent-child intervention over 3 months. Each 1-hour session included instruction and clinician modeling of motivational behavioral strategies to increase the frequency and complexity of the infant's nonverbal communication, as well as opportunities for the parent to practice the techniques with in-vivo feedback. A multiple-baseline design across participants was employed. Dependent measures included frequency of child communication, communication spontaneity, and parent fidelity of implementation of treatment components.

Results: Relative to baseline, results indicated immediate increases in frequency and spontaneity of communication following introduction of the parent-child intervention. All three parents learned to independently implement the procedures with at least 75% fidelity during the course of the brief intervention. Child frequency of communication during interactions with the parent increased as parent fidelity of implementation improved. A post-treatment questionnaire indicated high levels of parent satisfaction with the procedures.

Conclusions: Results of this preliminary study provide support for 1) the feasibility of a developmentally-based adaptation of PRT, 2) the efficacy of these procedures in improving the frequency and spontaneity of prelinguistic communication in children at risk for delays in social-communication development, and 3) the efficiency of the parent education approach in teaching parents to implement procedures with fidelity. Implications of these findings for understanding developmental trajectories and treatment needs of infants at risk for ASD will be discussed, and areas for further investigation will be proposed.

111.148 148 Is PCIT An Effective Treatment for ASD?. S. F. Vess* and A. Kinsman, *Greenville Hospital System Children's Hospital*

Background: Parent-Child Interaction Therapy (PCIT) is a behaviorally-based intervention package designed for preschool-age children that emphasizes changing parent-child interaction patterns in order to improve child behavior and enhance the quality of parent-child relationships. During PCIT, parents are taught specific skills to establish a secure, nurturing relationship with their child while simultaneously increasing their child's prosocial behavior and decreasing their child's negative behavior (Bell & Eyberg, 2002). Given that the goals of PCIT are to improve the parent-child attachment relationship along with the parent's behavior management skills (Brinkmeyer & Eyberg, 2003), PCIT has garnered empirical support for treating a variety of clinical problems. Families with ASDs may benefit from PCIT by experiencing reduced parental stress, stronger parent-child bonds, improved parenting skills, decreased child disruptive behavior, and improved prosocial interactions. Recent studies have garnered support for the use of PCIT with families of children with ASDs. Solomon, Ono, Timmer, & Goodlin-Jones (2008) presented encouraging evidence regarding the efficacy of applying PCIT to the ASD population. Further, Vess and Campbell (2009) found that PCIT was effective in increasing positive parenting behavior, decreasing negative parenting behavior, and increasing child compliance to parental commands in families of children with ASDs. Parents reported greater confidence in their parenting abilities post-treatment. Significant improvement in core areas of autism symptomatology, including social approach behaviors and receptive-expressive language communication abilities, was reported by parents at post-treatment. Further, parents endorsed significant improvement in aspects of the parent-child relationship, such as attachment and involvement.

Objectives:

The current study is designed to evaluate the efficacy of PCIT in reducing conduct problems and improving parent-child relationships for preschool children diagnosed with ASDs and provide support for continued investigation in this area.

Methods: PCIT was implemented according to manualized procedures (Eyberg & Child Study Lab, 1999). Children between the ages of 2

and 6 previously diagnosed with an ASD participated in the study with their primary caregiver. Recruitment in the study is ongoing. Five families have completed treatment to date. At the time the paper is presented, it is anticipated that 20 families will have completed treatment.
A pre-post intervention design was utilized. The *Child Behavior Checklist for Ages 1 _ - 5* (CBCL; Achenbach & Rescorla, 2000) was administered pre- and post-treatment. Measures administered at each treatment session included the *Eyberg Child Behavior Iventory* (ECBI; Eyberg & Pincus, 1999) and the DPICS-III (Eyberg, McDiarmid-Nelson, Duke, & Boggs, 2005). Graduation from the PCIT program involved meeting individual CDI and PDI mastery requirements and an ECBI score of 114 or less.

Results:

Preliminary results demonstrate that PCIT is effective in changing parenting behaviors and increasing child compliance. This paper will describe the intervention program along with specific changes in (a) parenting behavior, (b) child behavior problems, (c) child compliance, and (d) parent-child interactions post-treatment.

Conclusions: PCIT shows promise as an intervention for preschool children with autism. This pilot research provides direction for therapists considering utilizing PCIT with this population and supports further research in this area.

111.149 149 Measuring and Predicting Parents' Involvement in Intensive Behavioral Intervention. A. Solish* and A. Perry, *York University*

Background:

This study focuses on parents' involvement in Intensive Behavioral Intervention (IBI) for their children with autism. Although the need for parent involvement in IBI has been emphasized by professionals in the field, little research has explored this involvement or what it entails (Kasari, 2002; Schreibman, 2000). Before future research can confirm whether parent involvement in IBI affects children's progress and outcome in therapy, we need to be able to clearly define and measure the construct of parent involvement.

Objectives:

This study aimed to reliably operationalize parent involvement in IBI. In addition, we created a model of factors influencing and predicting parents' involvement. These factors include parent self-efficacy and confidence in delivering therapy, perception of child progress, belief in the intervention (both general belief about IBI's effectiveness and belief that the use of IBI will help their child specifically), stress levels, feelings of positive change since having a child with special needs, and parents' perception of their knowledge about autism and IBI.

Methods:

Participants included 105 caregivers of children with ASD participating in behavioral intervention programs in Ontario, Canada. Parents completed the Parent Involvement Questionnaire, a questionnaire created by the authors that measures parents' involvement in IBI as well as the other six variables discussed above.

Results:

An exploratory factor analysis of 20 involvement items resulted in a good-fitting four-factor model (root mean square off-diagonal residuals value (RMR) = 0.05). Four distinct types of involvement emerged: formal IBI involvement, child program involvement, training involvement, and agency involvement. The internal consistency for each involvement factor ranged between .72 and .82.

Structural equation modeling was used to create a model of factors predicting involvement. The root mean square error of approximation (RMSEA = .078) and the standardized root mean square residual (SRMR = .072) suggested acceptable model-data fit. Direct paths were examined between involvement and three of the variables; belief, stress, and self-efficacy. Self-efficacy emerged as the only direct significant predictor of involvement (path coefficient = 1.07), as the direct effects of stress and

belief on involvement were not significant. Thus, while belief does not directly influence parents' involvement, belief in IBI indirectly influences involvement through its relationship with self-efficacy. Similarly, parents' level of stress is not directly influencing their involvement; however, parents' stress can indirectly affect their involvement via stress' negative impact on parents' feelings of self-efficacy.

Conclusions:

The present study reliably operationalized involvement, which can contribute to needed research examining whether parent involvement directly impacts children's progress in therapy. Furthermore, results add support to the importance of providing services to parents with children in IBI programs. In particular, such opportunities should focus on ways to help parents increase their self-efficacy about participating in their children's programs, strengthening their belief in the effectiveness of the intervention, and helping them to cope with the stress accompanying raising a child with autism. By targeting these areas we can ultimately encourage parents to become more involved in their children's intervention programs.

111.150 150 Mother-Child Engagement: The Co-Construction of Narratives in Intervention Contexts for Young Children with Autism. A. M. Mastergeorge*, *University of California, Davis/M.I.N.D. Institute*

Background: Parents and young children create and sustain narrative interactions in their participation in socially engaged contexts in everyday interactions. In clinical interactions these narratives can be contrived in order to maximize social interactions, and are most evident in young children diagnosed with autism. In clinical interactions, narratives can be considered a 'window' into the development of conversational practice. Development of narrative practice involves the triadic coordination of attention between self, other and events—a hallmark of difficulty for young children with autism (Adamson, 1995; Tomasello,1995; Trevathen & Aitken, 2001). While narrative development includes ordering experience that is dialogic, dynamic, and includes affective engagement, few studies have delineated the parent's role in interaction contexts or the trajectory of narrative development. Objectives: This paper examines the conversational narrative chains of mother-child interactions in clinical interaction interventions with their young children recently diagnosed with autism. The purpose of this paper is twofold: (1) to investigate the development, co-construction, and trajectory of narratives in mother-child interactions in an in-home intervention; and (2) to further our understanding of the development of narrative and conversational "moves" or practices in the context of engagement. Methods: Fifteen dyadic mother-child interactions were videotaped over a period of sixteen weeks. Children were between 25-44 months of age with a mean age of 32.5 months, and were matched on developmental ages on the Mullen Scales of Early Learning. All videotaped interactions were transcribed verbatim for mother and child interactions involving specified play routines. Specific narrative structures were coded to examine the use of questions, statements, or stories, and function to initiate, confirm, disconfirm, or elaborate in the clinical contexts of the interaction. Rating scales (Mahoney, Boyce & Spiker, 1996; 1999; Mahoney & Wheeden, 1998; 1999) were used to code maternal sensitivity, responsivity, and reciprocity as well as child persistence, interest, cooperation, initiation, joint attention and affective engagement. Results: A mixed-method approach was used to analyze the conversational structures over the sixteen week intervention. Exemplars of the dyadic narratives are described as thematic routines developed over the intervention period. Each dyad developed and sustained interaction stories that were created in the conversational practices. Maternal sensitivity and reciprocity were significantly correlated with the child's joint attention and initiation of conversation from pre-intervention to post-intervention ratings. Further, results from a Wilcoxon Signed Ranks text showed a significant increase in observed child joint attention ($z = -2.23$, $p=.03$), a significant increase in the proportion of maternal praise ($z= -1.93$, $p =.05$) to their child from the total

verbalizations during the mother-child structured play contexts, and a significant decrease in the proportion of maternal commands ($z = -.77$, $p=.05$) from the pre-intervention to post-intervention assessment. Conclusions: These results provide evidence that engagement routines should be established in the context of meaningful activities that are dynamic in nature in order to understand narrative trajectories. Further, engagement appears to be a mediator for reciprocity, sensitivity, and embedded in the quality of the intervention in mother-child interactions that facilitate and sustain the narrative development and structure.

111.151 151 A Pilot Study of Group CBT Targeting Anxiety in Children with Asperger Syndrome. J. A. Weiss*, M. A. Viecili, J. A. MacMullin, J. Summers and Y. Bohr, *York University*

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 often ill-equipped to offer psychotherapeutic treatments to this population, and specialized supports are difficult to find. Few group treatments for mood and anxiety disorders in children with AS have been published.

Objectives: This pilot study examines the effectiveness of a manual-based group cognitive behavior therapy (CBT) program, Coping Cat (Kendall & Hedtke, 2006) for use with children with AS, and suggests ways to adapt the treatment to better suit the needs and abilities of this population.

Methods: Two groups of 5 children (in total, 9 males and 1 female, 8-12 years of age) participated in a 12-week CBT program. Along with a lead therapist who facilitated the group, each child was paired with their own graduate student therapist for the entire treatment, in order to support their unique behavioral and cognitive needs and facilitate group cohesion among participants. Approximately four weeks prior to the first session, participants completed youth baseline measures, including the Wechsler Abbreviated Scale of Intelligence (WASI; Weschler, 1999), Revised Children's Manifest Anxiety Scale (RCMAS; Reynolds & Richmond, 1979), and Autism Diagnostic Observation Schedule (ADOS; Lord, Rutter, DiLavore, & Risi, 2002). Parents completed the Brief Child and Family Phone Interview (BCFPI; Cunningham, Pettingill, & Boyle, 2000), Autism Spectrum Questionnaire for Children (AQ Child; Auyeung, Baron-Cohen, Wheelwright, Allison, 2007), Screen for Child Anxiety Related Disorders (SCARED; Muris, Merckelbach, Schmidt, & Mayer, 1999), and Child Behavior Checklist (CBCL; Achenbach, 1991). Participants and youth will complete many of the same measures post program to allow for a pre-post comparison on levels of anxiety and other externalizing and internalizing behaviors (CBCL, SCARED, BCFPI, and RCMAS).

Results: Pre-intervention, all participants had Full Scale IQ estimates in the Average to Above Average range (M = 109.1, SD = 16.3), met criteria for Autism Spectrum Disorder using the ADOS, and received a diagnosis of AS from a psychiatrist or psychologist. On the CBCL, 90% of children scored within the Clinical range on the anxiety/depression scale (overall M = 79.7, SD = 7.6), 80% on the social problems scale (M = 74.9, SD= 6.4), and 100% on the obsessive-compulsive scale (M = 79.0, SD = 6.9). On the parent report measure of anxiety (SCARED), 100% were reported to have clinically significant levels of an Anxiety Disorder. The intervention is currently ongoing, and the poster will present post intervention scores as well as qualitative data about what parents and children thought was helpful about the group and what could be changed.

Conclusions: There is evidence that CBT can be a useful mode of intervention for helping children with AS with regard to problems with mood. Further research is needed to develop tailored group therapy programs that capitalize on the strengths of children with AS, and support their difficulties.

Acknowledgments: This research was supported by Linda Brightling, Abby Solish, Alissa Levy, Julie Koudish, Jill Shuster, and Megan Ames.

111.152 152 Advantages of CAI for Single Word Comprehension and Grammar Production Training. F. Hurewitz*[1] and K.

Boser[2], (1)*Drexel University*, (2)*Individual Differences in Learning, Inc*

Background: Several controlled studies have recently demonstrated increased learning benefits from computer aided instruction (CAI) for children with autism in areas such as functional, play and pragmatic skills. Potential benefits of CAI in language instruction include data automatization, modeling, ease of information presentation and immediate feedback delivery for more individually directed learning. The social-communicative nature of language highlights the importance of research regarding the advantages of 'individualized' instruction in using CAI compared to more natural language learning contexts.

Objectives: We report two experiments that examine individualized benefits and efficacy of CAI for language instruction for 1) single word comprehension and 2) sentence level production in children with autism

Methods: Experiment 1) reports a 10-week study using Cosmo's Learning System (CLS) software (from Anthrotronix, Inc.) with six 'low-verbal' children with autism, aged 6-12 years. Subjects received two half hour sessions a week focused on developing identification of auditory and written words (e.g., prepositions, shape, color) and also following directions and discrimination of size/ amount. CLS included leveled cueing, rewarding animations and automatized progress through levels. Experiment 2) reports a 6 week study using GrammarTrainer(GT) software to instruct eleven 9-17 year-old individuals with autism. Training was conducted daily for 20 minutes. GT teaches syntax production through progressive exposure to written grammar increasing in complexity from small phrases to complex sentences. Training begins with easier recognition-style responses and increases in difficulty to full elicited production of constructions. All responses are 'keyed' in via word buttons. Students were verbal, but showed weaknesses in language production, particularly syntax and morphology.

Results: Experiment 1) A computerized assessment was created to evaluate initial skills, progress on CLS and generalization to new questions. All subjects improved and generalized on post-test in all areas tested except color identification. Lower functioning subjects focused on easier problems and completed less content. More verbal subjects improved an average of 20% in comprehension of prepositions, following directions and with written words. Relative size/amount improved but students had difficulty understanding the concept 'same'. All subjects showed an increase in the number of trials completed and required less prompting in later training sessions. Experiment 2) All students improved across time and in pre-, progress and post testing of novel items. As hypothesized, the students using GT showed significant improvement on the morphemes subtest of the Comprehensive Assessment of Spoken Language (CASL), but did not improve on measures of vocabulary (e.g. PPVT-IV), or on the pragmatics subtest of the CASL. This shows that writing-based delivery of CAI may generalize to spoken language syntax.

Conclusions: CAI may be one way to improve necessary language exposure and feedback through increased repetition otherwise difficult to implement in more 'natural' learning settings for children with autism. These experiments support generalization of specific language skills in CA instruction, but CAIs must be well-matched to student profiles and skills.

111.153 153 Assessing Peer-Related Social Interest in Preschool-Aged Children with Autism. G. G. McGee* and M. J. Morrier, *Emory Autism Center, Emory University School of Medicine*

Background: Diagnosis of an Autism Spectrum Disorder (ASD) relies on use of the ADOS (Lord et al., 2003) and ADI-R (Rutter et al., 2003) to assess behaviors associated with *DSMIVTR* criteria. Criteria also requires an assessment of a child's "development of peer relationships" (APA, 2000), yet there are no behavioral observations dedicated to this observation. Most evaluators rely on parental reports of children's social interest, through the ADI-R and/or Vineland (Sparrow et al., 2005). Although parent report can be reliable

for out-of-school settings, gathering behavioral information during peer social interactions is lacking. Wing and Gould (1979) originally classified children with autism by their interest in other people, yielding three classifications (passive, avoidant, active but odd). A modified assessment using Wing and Gould's classifications targeting peer interest is needed.

Objectives: To describe a standard protocol for assessing peer-related interest in children with autism as Avoidance/Escape, Toy-Related Interest, Active but Odd.

Methods: Participants included nine preschool-aged children with autism and nine typical preschoolers. Videotaped probes were obtained during various arrangements of play activities. Condition 1: ALONE offered highly preferred toys, no requirements for peer proximity, and no prompts/rewards for social interaction. Condition 2: OUTDOOR RECESS assessed naturally occurring peer proximity and social contacts during outdoor recess. During Condition 3: PRIMED PEER PROXIMITY children were redirected to stay within 3-feet of typical peers, but received no prompts/rewards for social interactions. During Condition 4: PRIMED SOCIAL CONTACT children were required to stay within 3-feet of typical peers, and typical peers were rewarded for frequent social bids. Peer interest was assessed via (a) proximity to peers across conditions, (b) and conditional probabilities.

Results: Differences between children with and without autism were evident for the percent of intervals children watched or interacted with peers across Conditions 2, 3, and 4. Classifications of social interest were accurate for 8 of 9 children with autism as validated by clinical judgment and more extensive data samples. Three children with autism were classified as AVOIDANT due to displayed levels of peer proximity below the mean and bottom range for both typical children and other children with autism. Three children with autism were classified as having a TOY RELATED INTEREST based on probabilities for "Given child focus on peer, what is the probability child focus on a toy?" approximated typical children and far exceed the range of children with autism. Three children with autism were classified as having an ACTIVE BUT ODD based "Given a social bid from a peer, what is the probability of a verbal response given?", and on peer responsiveness far exceeding mean for children with autism and lower than normal ongoing rates of social bids from peers.

Conclusions: Peer-related social interest was accurately classified in 89% of children based on data gathered during probe conditions. These classifications suggest that differing peer-related treatment protocols may be effective in remediating these social difficulties. Combined with the ADOS and ADI-R, this standard protocol for effective assessment of peer-related social behavior may be used to accurately identify children with an ASD.

111.154 154 Children's Friendship Training, Play Date Improvement and Generalization to School for Children with Autism Spectrum Disorders. F. Frankel* and R. Myatt, *UCLA Semel Institute for Neuroscience & Human Behavior*

Background: Our STAART study examined the efficacy of a manualized parent-assisted social skills intervention (CFT) compared with a delayed treatment control group (DTC) to improve social skills among rigorously diagnosed second to fifth grade children with autism spectrum disorders. Targeted skills included conversational skills, peer entry skills, developing friendship networks, good sportsmanship, good host behavior during play dates, and handling teasing. Our recently reported results revealed that most parent measures of social skill and play date behavior, child measures of popularity and loneliness showed significant post-treatment improvement in the CFT group in comparison with the DTC group. Most measures showing significant post-treatment improvement continued to do so at 3-month follow-up. A notable exception to this pattern of positive findings was teacher reports of withdrawal in the classroom, a significant problem for subjects. Despite teacher reports of improvement in 54.2% of children in the CFT group, group differences were not significant. Objectives: Our initial treatment hypothesis was that improvement in quality and frequency parent-supervised play dates would improve peer acceptance at school. The present analysis was intended to test this working hypothesis.

Methods: The original design was to administer the intervention only to the CFT group between Time 1 and Time 2 conduct a 3-month follow-up of the CFT group while administering the intervention to the DTC group between Time 2 and Time 3. This permitted increasing sample size by combining results of the CFT group after Time 1 with the results of the DTC group after T3. A Stepwise regression analysis was performed on the combined sample. Demographic variables (Grade in School, Vineland ABS total score, WISC-III-R Verbal IQ, Autism Symptom Screening Questionnaire scores) and general social skill indices (parent report Social Skills Rating Scale subscales) were used to predict teacher-reported withdrawal on the Pupil Evaluation Inventory.
Results: Decreases in conflict on play dates and increases in engaging behaviors (chasing/running, imaginary play and talk) resulting from CFT were the only measures that accounted for a significant proportion of the variance in improvement in teacher-reported withdrawal.
Conclusions: The results confirmed the treatment hypothesis that improvement in quality and frequency parent-supervised play dates would improve peer acceptance at school. These results suggest that modules which further enhance the parent role in supervising play dates may lead to more improvement in peer acceptance at school.

111.155 155 Efficacy of Methylphenidate Treatment in Children with Asperger Syndrome and ADHD Comorbidity. C. Porfirio, G. Giana*, A. Benvenuto, B. Manzi, S. Benedetti and P. Curatolo, *Tor Vergata University*

Background:
Several studies have reported relatively high rates of comorbidity between Asperger Syndrome (AS)/Autistic Spectrum disorders and Attention Deficit and Hyperactivity, attention and emotional processes, Disorder (ADHD), although nowadays the DSMIVTR and ICD10 exclude inattentive and/or hyperactive-impulsive children with Autistic Spectrum Disorders (ASD) from a diagnosis of ADHD. Individuals with AS may have a range of behavioral symptoms such as hyperactivity, impulsivity, short attention span, aggressiveness. Furthmore, many children with AS often are initially misdiagnosed with ADHD. Psychostimulant medications, such as Methylphenidate (MPH), are considered pharmacological goal treatment in children with ADHD. The broad overlapping between ADHD and autistics spetrum symptoms can be explained by a common neurobiological dysfunction of dopaminergic system, given that dopamine plays a key role on behavioral, cognition, selective implicated both in the pathogenesis of autism and ADHD.
Objectives:
The purpose of this study was to evaluate the responsiveness and the effects of MPH on the core symptoms of ADHD in children with AS trough a retrospective analyses.
Methods:
The clinical sample included 13 male subjects, aged between 8-12, with AS and an additional diagnosis of ADHD. All the patients have been treated with MPH during a period of 6-12 weeks; dosage was based at approximately dose of 0,2-0,4 mg/Kg/die. Before medication exposure, all children have been submitted to cardiological visit, ECG and blood analysis. We also routinely monitor height and weight, hematologic analysis, blood pressure, and heart rate during medication exposure.
Results:
10 of 13 subjects (77%) have shown a significant clinical improvement with in the Clinical Global Impression (reduction > 2), and in the Conners' Parent and Teachers ADHD Index. Three patients have experienced adverse events during the first weeks of treatments: 2 patients showed dysphoria, agitation, anxiety and mood instability and 1 patients showed decrease in appetite and irritability. The severity of these side effects have required the interruption of the treatment.
Conclusions:
MPH reduces symptoms of ADHD in children with Asperger syndrome; symptoms of ADHD are common in Asperger/autistic popoulation and MPH emerges as one of the best empirically validated treatments for the target of ADHD symptoms. Finally,we did not observe any exacerbation of repetitive behaviors, in contrast to the common belief that MPH may worsen stereotypies in autistic children. The best goal will be in defining predictors of response for each individual to

this medication and in documenting effectiveness on cognitive and social domains and long-term outcomes. In this ways, pharmacogenetic studies may be informative in this regard.

111.156 156 Examining the Use of Multiple Cues as a Necessary Component of Pivotal Response Training. S. Reed*[1], A. Stahmer[2], J. Suhrheinrich[1] and L. Schreibman[1], (1)*University of California, San Diego*, (2)*Rady Children's Hospital*

Background: Previous research indicated that responsivity to simultaneous multiple cues is difficult for many children with autism. Therefore, teaching attention to multiple cues has been considered a 'pivotal behavior' in Pivotal Response Training (PRT). Clinicians report that this aspect of PRT is difficult to implement and may not be developmentally appropriate for all children. To inform best practice, this study first examined the age at which typically developing children attend to simultaneous multiple cues, then assessed responsivity to multiple cues in children with autism above this age.

Objectives: The developmental appropriateness and necessity of training response to multiple cues (via conditional discriminations) in Pivotal Response Training will be examined and discussed.

Methods: Participants included 35 typically developing children ages 19 to 50 months and 16 children with autism ages 39 to 89 months. Each typically developing child completed a discrimination learning assessment. Children were taught to discriminate one compound stimulus (comprised of color and shape) from another (different color and shape). Children subsequently were tested on individual components of the training stimuli and child responses to each of the components were assessed as the dependent measure. Overselectivity was defined as correctly responding to one stimulus feature (i.e., shape vs. color) with 80% or better accuracy and a level of response at least 30% less than that to the second feature. Based on the age at which typically developing children were able to reliably respond to multiple cues, children with autism above this developmental age were assessed to determine whether they remained overselective.

Results: Typically developing children ages 19-26 months were unable to successfully complete the tasks and/or acquire the original discrimination. A majority of children ages 28-35 months showed overselective responding to one feature. In contrast, data indicated that children over 36 months of age consistently displayed response to the simultaneous cues. Therefore, the discrimination learning assessment was conducted with children with autism at a developmental age above 36 months, as determined by standardized tests and/or psychologist report. Of the 15 children with autism ages 39 to 89 months who completed the assessment, five children displayed overselectivity. These five children range in age from 4 years, 6 months to 6 years, 11 months and represent a range of ability levels. One of the children with autism was unable to complete the assessment due to non-compliance. The majority of children with autism (9 of 15) displayed normal selective attention similar to their typically developing peers.

Conclusions: Findings are consistent with and expand upon previous research. Teaching responsivity to multiple cues is not developmentally appropriate until a child with autism reaches a functioning level of 36 months. There appears to be a sub-group of children with autism who have difficulty responding to simultaneous multiple cues. Assessment of the type of tasks necessary to improve this ability in this sub-group of children with autism is the next step in this research.

111.157 157 How to Develop An Effective Intervention through the Participatory Research Process: A Case Example in An Executive Functioning Intervention in High-Functioning Autism Spectrum Disorders. L. G. Anthony*[1], L. Cannon[2], K. Alexander[2], M. A. Werner[2], K. Register Brown[1], J. Rutledge[1], J. Wintrol[3] and L. Kenworthy[4], (1)*Children's National Medical Center, George Washington University Medical School*, (2)*Ivymount School*, (3)*The Ivymount School*, (4)*Children's National Medical Center*

Background: Cognitive and behavioral inflexibility is a commonly observed associated feature of high-functioning autism spectrum disorders (ASD). Interventions

aimed at improving flexibility are limited and not commonly implemented in home and school settings. We have developed a school-based intervention to improve flexibility in students with ASD, the Enhanced Flexibility Intervention (EFI). Our team set out to develop this new intervention using a participatory process informed by a theoretical framework that emphasizes real world interventions to remediate executive function (EF) deficits in ASD through: cognitive training, self regulatory scripts, and faded practice and cueing in home and classroom settings.

Objectives: 1) Apply the principles of the participatory framework process of intervention development to ASD
2) Develop an innovative classroom intervention targeting flexibility in children with ASD
3) Evaluate the feasibility of the intervention by examining preliminary pilot data

Methods: This project represents the partnership among key stakeholders including clinical researchers, special educators, parents of children with ASD and individuals with ASD to develop an intervention that addresses the core EF component of flexible thinking, while also building other, supporting EF skills. We developed the EFI manual and materials through a participatory research framework (including focus groups, needs assessments, classroom observations, intensive collaboration with the Ivymount School Model Asperger Program and feedback from participants, parents and interventionists). We also conducted a preliminary test of the intervention with 16 children comparing the change in multi-modal assessments from pre- to post-intervention.

Results: The participatory process defined the structure of the intervention, how the intervention was delivered during the school day, what teaching methods should be used, and streamlined the lessons. The resulting intervention is feasible and acceptable to participants (with an over 90% completion rate), proving the achievability of using an intensive participatory process, including adults, adolescents and children with ASD to develop a new intervention. We will present the resulting EFI manual, with a focus on how the participatory process shaped the development of the manual. We will also present the results of a preliminary test of the intervention with 16 children comparing the change in multi-modal assessments from pre- to post-intervention. Post-intervention data, including classroom observations, questionnaires, and a new measure assessing EF, especially flexibility, in a socially-demanding context (observing groups of four children working together to complete tasks) will be completed in January to March 2010 and will available for presentation at the conference.

Conclusions: Our approach to developing this intervention was an innovative combination of a participatory process and a theory-driven method based on our knowledge of the complex EF deficits and effective intervention techniques in ASD. Because EF deficits are primarily expressed, and best assessed, in real-world settings, such as classroom, home and social settings, it was essential that we test and modify interventions in a real-world setting and that the intervention be administrable by teachers and other school personnel; thus it was an ideal intervention to develop with a participatory model. This project has implications for future ASD intervention development using a participatory process.

111.158 158 Identifying the Active Ingredients in Intensive Behavioural Intervention Programs for Children with Autism.
A. Perry* and J. Koudys, *York University*

Background: Research demonstrates that a subset of children with autism show significant improvements following Intensive Behavioural Intervention (IBI), while other children demonstrate more modest gains. Given the heterogeneity of the population, variable outcomes are not unexpected. This variability is likely attributable to a combination of child, family and treatment characteristics, the impact of which remain poorly understood. Although several child and family characteristics have been linked to best outcome, research on treatment variables has focused nearly exclusively on quantitative treatment aspects, such as

treatment intensity and duration. Little exploration into qualitative treatment variables has occurred. Despite the lack of systematic review, a variety of treatment characteristics are believed to be integral to effective IBI, such as well trained/highly supervised staff and parent involvement. However, more research needs to be done to precisely identify the "active ingredients" of treatment.

Objectives: The purpose of this research is to identify treatment variables associated with best outcomes, as well as identify variables linked to less optimal outcomes. Further, a comprehensive review of the literature will be presented, including classification of studies based on methodological rigour (i.e., randomized controlled trial, comparison group, pre-post comparison).

Methods: This poster presents findings from an exhaustive review of the IBI literature, including analysis of efficacy and effectiveness studies conducted in the past 20 years. Studies were reviewed independently by two people and rated according to methodological rigour. Studies were also independently coded on 13 treatment variables (e.g., model/amount of supervision, treatment setting). Treatment effect sizes were determined for four outcome measures, cognitive and adaptive level, severity of autism and communication. Associations between effect sizes (dependent variables) and treatment characteristics (independent variables) were then determined.

Results: Majority of studies used pre-post comparison designs with no control group or involved non-random assignment comparison groups. Several studies provided insufficient information about treatment variables preventing detailed analysis on some treatment characteristics (e.g., type/fidelity of parent involvement). Few studies reported on the impact of treatment on autism symptoms preventing an analysis of this outcome variable. Treatment provided in "Home AND Community/School Settings" or "Integrated Settings" was associated with significantly larger cognitive and language outcome effect sizes. Adaptive skills showed the reverse pattern with significantly larger effect sizes associated with children receiving treatment in "Home Only". Studies which measured treatment fidelity were associated with significantly larger IQ effect sizes. While supervision conducted live with the child and therapy team was associated with larger effect sizes for cognitive skills, adaptive skills showed the reverse pattern (i.e., larger effect sizes associated with indirect supervision). Finally, the largest IQ effect size was associated with frequent (i.e., <weekly supervision).

Conclusions: Although several treatment characteristics were associated with significant effect size differences for cognitive and adaptive level and language skills, the pattern was inconsistent. Further, variability in outcome data collected and descriptions of treatment characteristics limits analysis. Future research should include standardized outcome measures and report treatment characteristics in sufficient detail to enable cross study comparisons and effect size analysis.

111.159 159 Integrating Treatment Strategies for Children with Autism. A. B. Cunningham*[1], L. Schreibman[1] and A. Stahmer[2], (1)*University of California, San Diego*, (2)*Rady Children's Hospital*

Background: In practice, many practitioners integrate various treatment techniques into comprehensive treatment programs for children with autism. Indeed, researchers have hypothesized that incorporating multiple treatment methods into a comprehensive program and customizing it in terms of individual needs should increase overall treatment effectiveness. However, very little data are available to inform specific methods for integrating approaches. In particular, highly structured behavioral treatments (e.g., Discrete Trial Training; DTT) and naturalistic behavioral treatments (e.g., Pivotal Response Training; PRT) may be differentially effective at targeting different skill areas. Structured and naturalistic models have often been compared, but no studies have suggested empirically-tested methods for integrating them into comprehensive treatment programs. It may be that they accomplish different goals and are mutually

beneficial, and that their effectiveness depends on individual child characteristics.

Objectives: To identify methods of tailoring comprehensive treatment programs to the individual needs of different children with autism.

Methods: Preliminary data for three children with autism (18-36 mos of age), who participated in a single-subject alternating treatments design, are presented. Expressive and receptive language targets were selected from the MacArthur CDI. Target items were subdivided according to form (i.e. noun, verb, adjective), developmental appropriateness, and child preference (for objects only). Words were then randomly assigned to treatment conditions. Children received three one-hour sessions of in-home treatment per week, including 30 minutes each of DTT and PRT. Order of teaching procedures was randomly determined on the first day of the study and counterbalanced across subjects. Data are reported on rate of learning, word acquisition and generalization, as well as child disruptive behavior.

Results: Preliminary data indicate that participants made gains in the acquisition and generalization of the target items taught via DTT and PRT. Children demonstrated distinct patterns of responding to DTT and PRT. Word acquisition and generalization, as well as rates of learning and disruptive behaviors during treatment sessions varied depending on the treatment method used and word form of focus. Potential predictor variables useful in deciding treatment appropriateness a priori will be discussed. Fidelity measures indicated that the interventions were implemented accurately.

Conclusions: These data corroborate with other studies emphasizing the importance of treatment individualization and begin to suggest specific methods for tailoring treatment programs to individual child needs. The strengths and weakness of DTT and PRT are not as explicit as previous research may suggest. Effectiveness may vary depending on child variables, as well as curriculum area focus. This line of research also offers a model for future research designed to establish an empirical basis for combining intervention methods into comprehensive treatment programs for children with autism.

111.160 160 Investigation of the RUPP Parent Training Program for Pre-School Children with ASDs and Disruptive Behavior.

K. Bearss*[1], L. Scahill[2], C. Johnson[3], B. Handen[4] and T. Smith[5], (1)*Yale Child Study Center*, (2)*Yale University School of Medicine*, (3)*University of Pittsburgh*, (4)*Univ of Pittsburgh School of Medicine*, (5)*University of Rochester*

Background: Autism Spectrum Disorders (ASDs) are characterized by deficits in social interaction, impaired communication, and repetitive behavior affecting as many as 20 children per 10,000. In addition, 50 to 70% of children with ASDs have co-occurring behavioral problems such as tantrums, aggression, and noncompliance and most show deficiencies in adaptive functioning. As the number of identified cases of ASDs has grown, so have the challenges for serving this group of children and their families. Parent training is an intervention that has received much interest due to the central role parents have in promoting the development of their children with autism and the need for strategies to alleviate the high burden these parents face.

Objectives: With early intervention being key to optimal outcomes for children with ASDs, this study describes the development of a downward extension of the 24-week Research Units in Pediatric Psychopharmacology-Parent Training (RUPP-PT) manual. The RUPP-PT program was developed with school-age children in mind. This study aimed to develop a structured, exportable parent training manual for preschool-age children (ages 3-0 to 6-11) with ASDs and mild to moderate behavioral problems and then evaluate its feasibility and preliminary efficacy.

Methods: Study investigators adapted the RUPP-PT program to insure it was appropriate for preschool age children. Modifications included changing text so that discussion examples were age appropriate and recreating video vignettes to reflect common behavioral issues encountered with preschool age children. Sixteen families with a preschool age child with ASD and disruptive behaviors were then enrolled in an open label pilot trial of the updated PT program. Primary outcomes of interest included a) changes in

the parent-rated Aberrant Behavior Checklist – Irritability and Hyperactivity Subscales and Home Situations Questionnaire (HSQ), which are designed to assess the degree of the child's irritable and noncompliant behavior; and b) improvements on the Vineland, which is designed to assess the child's communication, socialization, and daily living skills.

Results: To date, 13 families have completed treatment, 2 terminated early, and 1 remains in treatment. Subjects include 7 children with autism, 9 with PDD-NOS. Mean age is 4-11 years. 81% are Caucasian, 14% Latino, 7% other. Most (63%) have an IQ above 70. None are on medication. After 24 weeks of PT, mean scores on the parent-rated Home Situations Questionnaire (HSQ) for the 11 families changed from 3.1 ± 1.1 to 1.3 ± 1.2 ($p < 0.001$; 59% reduction), mean scores on the parent-rated Aberrant Behavior Checklist (ABC) Irritability subscale changed from 17.3 ± 9.6 to 7.5 ± 6.3 ($p < 0.001$; 57% reduction), while age equivalent gains on the Vineland ranged from 6 to 13 months. Eighty-eight percent of families enrolled completed the 6 month intervention and parents attended 94% of the 11 core sessions.

Conclusions: Preliminary data from this study provide support for the effectiveness and acceptability of a structured parent training manual for young children with autism. Results from this study were utilized to support a recently funded large-scale multi-site randomized trial of this parenting intervention compared to a parent psychoeducational control group

111.161 161 Parent Stress Related to Infants at-Risk for Autism Spectrum Disorder. G. W. Gengoux*[1], A. M. Steiner[2] and K. Chawarska[3], (1)*Stanford School of Medicine*, (2)*Yale University*, (3)*Yale University School of Medicine*

Background: The literature documents higher levels of stress in parents of children with autism spectrum disorder (ASD) compared to parents of typically developing children and children with other developmental disabilities, with stress levels strongly related to child behavior (e.g., Davis & Carter, 2008). Though it is well-established that siblings of children with ASD are at increased risk for developing ASD themselves, very little is known about the parenting experience of raising an infant at high risk for ASD (HR-ASD). Specifically, research has not yet documented levels of parent stress in this unique parent population, nor has it examined how stress pertaining to an older child with ASD may affect parent impressions of their HR-ASD infant.

Objectives: The current study explores parent reports of levels of stress and concern regarding their HR-ASD infant, and the relationship between these concerns, HR-ASD infant behavior, and reported stress related to the older sibling diagnosed with ASD.

Methods: Participants included 53 parents of HR-ASD and Low Risk (LR; no genetic risk for ASD) infants. At 12, 15, and 18 months of age, all parents completed the Parenting Stress Index (PSI) and the Parental Concerns Sheet (PCS), a likert-scale questionnaire which probed level of parental concern regarding child development and parental observation of developmental delay. Parents of HR-ASD infants also completed a PSI in regards to their older child with ASD.
Results: Preliminary results revealed that parents of HR-ASD infants did not report overall higher overall levels of parenting stress regarding their infant than parents of LR infants. However, emerging trends suggest that some parents of HR-ASD infants were more likely to evidence defensive responding on the PSI, indicating a tendency to underreport stress related to their HR-ASD infant. Furthermore, despite limited reports of stress related to specific child behaviors on the PSI, when asked about general developmental concerns (PCS), parents of HR-ASD infants reported more frequent and severe concerns ($p = .03$; $p < .000$, respectively) than LR parents. In addition, among HR-ASD parents, 69% of parents who did not observe any specific developmental challenges with their child, nonetheless reported significant levels of parental concern ($p = .01$).

Conclusions: Results indicate that parents of HR-ASD infants do not generally report significant levels of stress related to specific

child behaviors, but evidence significant levels of concern related solely to their child's risk-status. Higher levels of defensive responding among HR-ASD infants indicate that it may be difficult for parents to report stress relating to their infant's behavior. Results will be discussed in terms of implications for parent-child interaction, parent support, and early intervention.

111.162 162 Potential Behavioral Precursors to Autism Spectrum Disorders in NICU Graduates. J. M. Gardner*, B. Z. Karmel, I. L. Cohen, P. M. Kittler, E. M. Lennon, L. D. Swensen, R. L. Freedland, M. J. Flory and E. London, *NYS Institute for Basic Research in Developmental Disabilities*

Background:

Infants with obstetric/neonatal complications who typically are admitted to neonatal intensive care units (NICUs) have ~ 2-fold risk for Autism Spectrum Disorders (ASDs). Our longitudinal studies of NICU graduates from birth follow development of regulatory influences on multiple domains including attention, motor skills, social communication, temperament, and cognition. We present behavioral data from the neonatal period through later infancy in NICU graduates later diagnosed with ASDs to help identify patterns in neurodevelopment specific to these infants and/or ASD.

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) 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 neurobehavior (RNNA), arousal-modulated visual attention (AMA), focused attention and distractibility, exploration in a novel environment, and cognitive and motor performance. Comparisons to early behaviors in term nursery infants later diagnosed with ASDs also will be presented.

Results:

In analyses controlling severity of brain pathology and maternal education, ASD infants exhibited behavioral deficits starting in the newborn period. The RNNA showed more visual asymmetry, upper extremity tone problems, and less decrease in number of NB abnormalities between hospital discharge and 1 month. AMA was atypical out to 4 months, with more attention to faster stimuli (like younger infants). Attention deficits and less habituation to distractors during focused attention were noted by 10-13 months, with fewer referencing the examiner or looking at toys, and many spending most of the time looking at distractors. Behavior in a novel environment after 1 year showed repetitive stereotypic movements, lack of toy play, and an atypical positive approach to a 2-ft robot. Scores on BSID-II MDI and PDI declined as early as 7-10 months, which typically only occurs in infants with the most severe brain pathology.

Conclusions:

Infants later diagnosed with ASD may form a distinct sub-group of NICU graduates, with atypical visual, motor, and regulatory development. They have a unique behavioral profile, with slower resolution of neonatal problems and development, visual system deficits involving early asymmetry, poor regulation, stimulus-bound attention, and impaired ability to habituate, and motor as well as cognitive impairment starting much earlier than expected. Such deficits may underlie their lack of transition to higher-level visual function that, with deficits in regulation underlying inappropriate reward and motivation systems, produce disinterest in and inadequate processing of social stimuli and events. Whether such behavioral patterns are specific to later diagnosed NICU infants, share common features or are

distinct from other ASD cohorts, will be addressed.

111.163 163 Training-the-Trainer: An Effectiveness Study of Pivotal Response Training in School Settings. J. Suhrheinrich* and L. Schreibman, *University of California, San Diego*

Background: Pivotal Response Training (PRT) is an evidence-based, naturalistic behavioral intervention for children with autism. Teachers have been effectively trained to implement PRT, but effective training is time consuming and expensive. An alternative may be providing training to existing school district staff on how to train teachers and evaluate the teachers' use of PRT. To increase the availability and sustainability of training in PRT, this study employed a train-the-trainer model while working with school district staff and classroom teachers.

Objectives: The purpose of the study was to assess the effectiveness of a train-the-trainer protocol for PRT.

Methods: Three school district behavior specialists (trainers), nine special-education teachers, and 18 students with autism (3-8 years old) participated. Participants made up three training groups, each with one trainer, three teachers and six students. A multiple baseline design was used, and data were obtained via weekly classroom observations during baseline, treatment, post-treatment and follow-up. During the treatment phase 1) trainers attended a 15 hr training workshop on how to implement PRT, assess PRT implementation and provide feedback to others, 2) staff trainers conducted a 6 hr workshop with the three teachers in their training group, and 3) staff trainers, teachers, and students participated in 6 additional observations. During each observation, the teacher worked with each student, individually, for 10 minutes while the trainer observed. Then the trainer provided feedback to the teacher for 10 minutes. Each observation was videotaped and later coded to examine teacher implementation of PRT, trainer assessment of PRT implementation, and student behavior. Follow-up data were collected 3 months after the completion of the treatment phase.

Results: All three trainers successfully completed the trainer training, including correctly implementing all PRT components, assessing fidelity of implementation of PRT and providing feedback. After completion of this training, the trainers' implementation of training procedures was more varied. Six teachers learned to correctly implement all components of PRT while the other three teachers made more limited progress. Teachers demonstrated consistent patterns of learning with some PRT components being implemented correctly more often than others. Seven of the nine teachers completed the follow-up procedures. Three made some improvement in their ability to implement PRT, one maintained her ability to implement PRT, and three declined in their ability to implement PRT.

Conclusions: The train-the-trainer method resulted in notable gains by the participants. Results indicating where specific adaptations to the training model would likely lead to further effectiveness will be discussed. While some teachers maintain or improve their skills over time, others may lose these skills and benefit from additional training in the form of a "booster session."

111.165 165 Advancing Social-Communication and Play in Preschoolers with Autism: Initial Findings From a Classroom-Based Intervention. B. Boyd*[1], L. Watson[1], T. W. Lenhardt[1], J. Dykstra[1], K. Berry[1], G. T. Baranek[1], E. R. Crais[1] and S. Odom[2], (1)*University of North Carolina at Chapel Hill*, (2)*University of North Carolina*

Background: Children with autism spectrum disorder (ASD) have deficits in social-communication and play, which has implications for later developmental outcomes. Current interventions for social-communication and play deficits in ASD primarily are designed for implementation in clinic or home-based settings (Kasari, 2006; Schertz & Odom, 2007). There is a need for comprehensive interventions specifically designed for use in public school classrooms as children with ASD spend a great deal of time in school settings. The *Advancing Social-Communication and Play (ASAP*) intervention was developed to increase the social-communication and play skills of preschoolers with ASD served in public school

classrooms. The ASAP treatment has 2 context components—implementation in one-on-one and group classroom settings, and 2 content components—focus on social-communication and play skills

Objectives: To present preliminary data on the effects of ASAP, when implemented by preschool teachers and school-based therapists, on the social-communication and play behaviors of 3 preschool-aged children with ASD.

Methods: Single case design methodology was used to investigate the effects of ASAP on the child's social-communication and play skills, as it allows experimental control to be established with small N studies. Specifically, a multiple baseline across participants design was used. Three participants (ages 3 – 5) diagnosed with ASD participated in the ASAP intervention. The ADOS was used to confirm diagnosis and the Mullen was used to determine baseline levels of cognitive functioning. For each child, the classroom teacher, classroom assistant, and/or the speech-language pathologist (SLP) participated in the treatment. The SLP implemented the 1:1 component of the intervention and the classroom teacher or assistant implemented the group component in the classroom. Prior to implementation, the classroom team attended an initial training and on-going coaching was provided by research staff to support fidelity of implementation. Behavioral raters coded intervention sessions in vivo to examine treatment effects. Coders used a hand-held computer to collect data during a 10 minute observation period. A 10 second partial interval coding system was used to collect data, whereby at the end of each interval coders indicated whether the target behavior occurred.

Results: Across the 3 children, the percentage of time children displayed social-communication (i.e. initiating behavior requests or joint attention) or play (i.e. functional or symbolic) skills in the baseline condition was low (soc-com M=6.2%, range= 4-10.4%; play M=3.9%, range=.4-10.9%). Mean rates of behavior for the group only intervention component were 3.8% (range=1.5-7.5%) for social-communication and 10.4% (range=.4-28.4%) for play. Mean rates of behavior for the group component when combined with the 1:1 component were 12.3% (range=5.4-17.6%) for social-communication and 17.3% (range=9.9-28.4%) for play. Interobserver agreement and fidelity data also will be reported.

Conclusions: As expected with single subject data, there was individual variability in treatment response to the ASAP intervention. In general, it appears that combining the group and 1:1 components resulted in better outcomes for the 3 children, although across conditions there were infrequent displays of the targeted behaviors. However, school-based personnel were able to implement the intervention with good fidelity, which shows promise of longer term sustainability.

111.166 166 Asperger Male Teens' Use of Relaxation Strategies and Selection Preferences: Which Strategies for Which Stressors?. D. S. McLeod* and D. A. Lucci, *Massachusetts General Hospital*

Background: It is well documented that stress management is an important life skill for individuals with Asperger's Syndrome (AS) and Nonverbal Learning Disabilities (NLD). Often these individuals have heightened levels of stress, have difficulty reporting their stressors and do not use relaxation strategies (RS). Successful efforts to address these concerns would likely lead to increased self-management of stress and ultimately healthier lifestyles and better emotional functioning.

Objectives: To demonstrate that through the use of technology (PDA) and direct instruction about stress teens would increase self-awareness in recognizing their stressors and demonstrate the use of RS they prefer and do not prefer in relationship to specific stressors.

Methods: Nine adolescent males: 8 diagnosed with AS and 1 diagnosed with NLD, ADHD and Sensory Integration Dysfunction; ages 14.6 – 16.6 with a mean age of 15.1, each had average to above average IQs on the WISC-IV. Each participant was enrolled in a therapeutic summer program. They were assigned to one group staffed by two adult

counselors. Teens were admitted through an interview and submission of the following documents: school records, psychological reports and completion of our social checklist and the Walker-McConnell Scale of Social Competence and School Adjustment.

The clinical program included instruction in stress management that included ten RS (e.g. deep breathing, visualization, yoga etc.), fourteen stressors (e.g. unexpected change, perseverative thinking etc.) and fifteen different physiological signs of stress (e.g. tension in chest, perspiring etc.). Teens recorded their use of RS and their stressors using an Apple iTouch. Staff concurrently recorded their own perspective on each teen for comparison purposes.

Data was collected across 5 settings (Start of Day, Morning, etc.) and during specific activities (e.g. "Science of Me", "Social Thinking", etc.). Each setting and activity had its own set of data collection questions. The full data set was used to perform statistical analyses.

Results: Of all the RS taught, only deep breathing (DB) and visualization (VI) were consistently used by the teens. There was a significant positive correlation between use of each of these strategies and each of the following stressors: unexpected change, unmet expectation and perseverative thinking. There was a significant negative correlation between use of each of these strategies and their feeling forced to do an activity.

Conclusions: Male AS teens may prefer deep breathing and visualization strategies over the use of other strategies. Further analysis will be needed to determine whether this preference is based on this specific training program or if there is some specific reason why this group prefers these strategies. Teens used these strategies when met with unexpected changes and when their own thinking became perseverative. The negative correlation between RS and feeling forced to do an activity might perhaps be understood by the teens' negative emotion about being "forced" to do an activity interfering with their decision-making about the use of an otherwise employed RS.

111.167 167 Assessing the Impact of Pivotal Response Training (PRT) Group Therapy On Parenting Stress and Empowerment Levels. M. B. Minjarez*[1], E. M. Mercier[2], S. E. Williams[1] and A. Y. Hardan[1], (1)*Stanford University School of Medicine/Lucile Packard Children's Hospital*, (2)*Durham University*

Background: Rates of autism spectrum disorders have increased in the United States, with recent data indicating that 1.1% of children are now being diagnosed with these disorders. With children being diagnosed as young as 18 months of age, the need for services is increasing. Research has demonstrated that parents can effectively deliver treatment models such as PRT, which may also have a positive psychological impact on parents themselves. In a previous study by our group, parents were able to learn PRT procedures in a group format and their children showed correlated language gains. As parents are becoming more integrated into intervention programs there is a growing need for research to focus on the impact of such programs on parent functioning in addition to assessing child outcome measures.

Objectives: In the present study, we build upon our previous findings, and examine whether participating in a parent training PRT group influenced parent overall functioning by affecting their levels of stress and empowerment.

Methods: Seventeen families (24 parents) participated in a 10-week therapy group designed to teach parents the use of PRT, with a specific focus on child language gains. The independent variable was parent participation in a 10-week PRT parent training group. The dependent variables were, 1) Scores on the Parenting Stress Index/Short Form (PSI/SF) and 2) Scores on the Family Empowerment Scale (FES). The PSI/SF and FES were completed at baseline and post-treatment and paired samples t-tests were used to analyze changes in these dependent variables.

Results: Findings indicated that parents experienced reductions in stress and

increased empowerment from baseline to post-treatment. Parents reported statistically significant reductions in stress after the therapy group as measured by changes in the Total Stress Score [t(23) = 2.84, p <.01] and the Parent-Child Dysfunctional Interaction subscale score [t(23) = 3.89, p <.01] of the PSI/SF. Differences between baseline and post-treatment were also observed on the PSI/SF Parent Distress [t(23) = 1.85, p =.08] and Difficult Child [t(23) = 2.02, p = .055] subscales, but did not reach statistical significance. Parents also experienced increased empowerment after the therapy group as measured by changes in the three scores derived from the FES: Family Level Empowerment [t(20) = -5.96, p <.001], Services Level Empowerment [t(20) = -4.12, p <.001] and Community Level Empowerment [t(20) = -5.4, p<.001].

Conclusions: Findings from this pilot study suggest parents experienced reductions in stress, especially as related to parent-child interactions, and increases in empowerment after participating in a PRT parent training group. These findings support that parents may experience positive psychological benefits from participating in parent education programs related to caring for their child with autism. Findings are analyzed in light of previous research on psychological functioning and coping in parents of children with disabilities. Our preliminary findings suggest that future controlled studies are warranted to further examine the efficacy of this treatment model and explore the impact on parent functioning.

111.168 168 Behavioral Flexibility in Autism and Asperger Disorder: The Impact of Intervention On Child, Parent, and Family Functioning. C. E. Lin*, R. L. Koegel and L. K. Koegel, *University of California, Santa Barbara*

Background: Restricted interests and repetitive behaviors (RIRBs) comprise one of the diagnostic criteria for autism spectrum disorders (ASD). Considerable evidence indicates that the manifestation of RIRBs is pervasive and associated with persistent interference with the social, communicative, and adaptive functioning in children with ASD. In addition, children's engagement in RIRBs has been associated with limiting family activities and disrupting family interactions.

Objectives: The current study examined the effectiveness of a parent-implemented self-management intervention to target higher-order RIRBs (i.e., restricted interests and repetitive behaviors) in children diagnosed with an autism spectrum disorder. The intervention incorporated an empirically supported, motivation-based behavioral intervention for autism spectrum disorder—Pivotal Response Treatment. Furthermore, changes in children's behavioral flexibility were examined in relation to child affect and RIRB symptoms, child and parent engagement, parent affect and confidence, and overall family functioning.

Methods: A non-concurrent multiple baseline across participants time series research design was implemented with measures collected longitudinally to assess the effectiveness of a parent-implemented self-management intervention on child, parent, and family measures. Children diagnosed with autism and Asperger Disorder aged 4 to 6 participated in the study.

Results: The results indicate that improvements in behavioral flexibility, along with collateral gains in observed child affect, parent and child engagement, observed parent affect and confidence, global measures of child RIRB symptoms, and family functioning occurred with the implementation of the intervention. Evidence of the generalization of intervention effects was observed.

Conclusions: Interventions to address impairments in behavioral flexibility may provide insight into the impact of expanding the behavioral repertoire of children with ASD and how doing so may play a pivotal role in the overall well-being of children and their families.

111.169 169 Developing Innovative Ways to Measure and Communicate Autonomic Arousal in Autism Spectrum Disorders. M. S. Goodwin*, *Massachusetts Institute of Technology*

Background: The Autonomic Nervous System (ANS) is a control system in the body with far-

reaching influences, including maintenance of heart rate, digestion, respiration rate, and perspiration that mediates regulation of emotion, shifting of attention, sleep, signaling of anticipation and salience, biasing of memory, and more. A number of investigators over the past 30 years have recorded ANS activity in individuals with Autism Spectrum Disorders (ASD) to assess physiological responsivity during attention and habituation tasks, while exposed to social and sensory stimuli, and when engaged in self-injurious and repetitive behaviors. Unfortunately, however, there are several methodological issues associated with these studies that cast doubt on the reliability, validity, and generalizability of the data obtained. For instance, the majority of ANS studies to date use obtrusive equipment that require individuals to sit still while multiple wires are adhered to their chest or fingers, limiting the number of participants who can comply with the procedures and thus contribute data to a study. ANS observations are also undertaken primarily in unfamiliar research laboratories that are potentially stress inducing, and are often limited to short intervals of measurement that may or may not represent a person's true ANS patterns when going about everyday activities. Data from these studies are also often averaged across persons so that no individual profiles are retained, obscuring the heterogeneity of response patterns across individuals.

Objectives: This presentation will briefly discuss the clinical utility of recording ANS responsivity in ASD, review findings to date in this area, describe the abovementioned methodological issues, and demonstrate a novel platform being developed in the MIT Media Lab for sensing sympathetic and parasympathetic autonomic data comfortably off the wrist and ankle without wires or boxes.

Methods: The wireless autonomic recording system captures: (1) Electrodermal activity, which provides a sensitive measure of changes in sympathetic arousal associated with emotion, cognition and attention; (2) Heart rate and heart rate variability that provides information related to the sympathetic and parasympathetic branches of the ANS; (3) Temperature; and (4) Motor movement and posture changes through 3-axis accelerometery. The 3-axis accelerometer and temperature sensors provide information about a person's activity and account for the influence of motion and environmental temperature on electrodermal and cardiovascular signals.

Results: & Conclusions: Monitoring autonomic reactivity using comfortable, wireless, wearable packages could enable new *in situ* experimental paradigms and address some of the shortcomings associated with traditional methods of recording the ANS in persons with ASD. For instance, these sensors could enable longitudinal studies of individuals that yield data beyond the traditional "snapshot" timeframe, providing new insights on within-person, within-group, and across-group differences over time, and capturing phenomena of interest that are hard to replicate in laboratory settings, e.g., panic attacks. Measuring and communicating ANS patterns that precede, co-occur, and follow an event could also provide rich data enabling new ways to anticipate, intervene on, and ultimately prevent problem behaviors.

111.170 170 Early Communication Correlates of Language Development and Autism Symptomatology in Toddlers at-Risk for ASD. C. J. Grantz*[1], K. K. Lyons[1], S. Celimli[1], P. Yoder[2], W. L. Stone[3], A. S. Carter[4] and D. S. Messinger[1], (1)*University of Miami*, (2)*Vanderbilt University*, (3)*Vanderbilt Kennedy Center*, (4)*University of Massachusetts Boston*

Background: Early nonverbal behaviors, such as initiating and responding to shared attention and requesting objects or actions, show associations with verbal language and autism symptomatology. Understanding the relationship between nonverbal social communication, verbal language, and autism symptomatology has implications for assessing early interventions in toddlers exhibiting symptoms of autism spectrum disorders (ASD).

Objectives: Investigate the relationship between nonverbal and verbal social communication and autism symptomatology in toddlers at-risk for ASD.

Methods: Forty-nine toddlers (mean CA 21 months, range 15-30 months; 8 females) who met a predetermined cutoff on the Screening Tool for Autism in Two-Year-Olds (STAT) and had a clinical presentation consistent with an ASD were enrolled in *A Multi-Site Clinical Randomized Trial of the Hanen More than Words Intervention*. Toddlers were administered the Early Social Communication Scales (ESCS) and Mullen Scales of Early Learning (MSEL) as part of the initial assessment. The ESCS was coded (Mundy et al., 2003; Yoder & Fey, 2008) to capture toddler-initiated joint attention (IJA), response to joint attention (RJA), toddler-initiated behavioral requesting (IBR), and weighted frequency of infant communication (WFC), a measure of intentional gestural and verbal communication. The MSEL language subscales yielded raw score measures of expressive (MSEL-EL) and receptive (MSEL-RL) language abilities; the STAT indexed autism symptomatology.

Results: ESCS variables—IBR, IJA, WFC, and RJA—were intercorrelated, *r*s ranged from |.33| to |.48|, *p*s<.05, with one exception: IBR was not significantly correlated with IJA. Symptomatology and language variables—STAT total score, MSEL-RL, and MSEL-EL—were significantly correlated, *r*s ranged from |.45| to |.66|, *p*s<.01. IBR and WFC were associated with STAT total score, MSEL-RL, and MSEL-EL, *r*s ranged from |.38| to |.60|, *p*s<.01. RJA was associated with STAT total score, r=-.35, p<.05, and MSEL-RL, r=.33, p<.05. IJA was not significantly correlated with STAT total score or language subscales of the MSEL.

ESCS variables with a significant univariate association with STAT, MSEL-EL, or MSEL-RL were entered as simultaneous predictors in regression equations to identify unique predictors of autism symptomatology and language abilities. No unique predictors of STAT total score were found, although WFC (p=.07, partial R^2=.06) approached significance, F=3.75, p<.05, adjusted R^2=.19. IBR (p<.01) and WFC (p<.05) each demonstrated unique associations with MSEL-RL, F=8.10, p<.01, adjusted R^2=.37, IBR partial R^2=.17, WFC partial R^2=.06, and with MSEL-EL, F=9.99, p<.01, adjusted R^2=.43, IBR partial R^2=.24, WFC partial R^2=.05

Conclusions: The strong associations between IBR and MSEL-EL and MSEL-RL indicate the significance of requesting behaviors to language abilities in toddlers. The associations between WFC and MSEL-EL and MSEL-RL indicate that intentional gestural and verbal communication is also a significant indicator of language abilities at this age. Both IBR and WFC exhibited significant univariate associations with the STAT, suggesting that deficits in requesting and intentional social communication are significant, if not unique, predictors of autism symptomatology among toddlers displaying autism symptoms. Understanding the associations between verbal and nonverbal communication and autism symptomatology will provide the building blocks for later tests of treatment efficacy in this *Multi-Site RCT of the Hanen More than Words Intervention*.

111.171 171 Early Intervention for Children with Autism: Which Factors Impact Service Approval?. R. M. Seijo*, L. H. Shulman, M. D. Valicenti-McDermott, K. Hottinger, T. Fried, D. J. Meringolo and N. Tarshis, *Albert Einstein College of Medicine*

Background: Autism affects children of all ethnicities, races and socio-economic levels. Treatment with a program of early and intensive behavioral intervention has been associated with best outcomes for children with autism. Early Intervention(EI) is a federally mandated entitlement program for children birth to 3 years that provides free therapeutic services to eligible children and their families. The services a child is approved for through the EI program are documented in the Individualized Family Service Plan(IFSP). Previous analyses have shown that certain groups of children are at risk for delays in initiation of therapeutic services.

Objectives: To determine clinical and demographic factors impacting on services approved at IFSP for children with autism from a diverse inner-city population.

Methods: Retrospective chart review of all children diagnosed with Autism Spectrum Disorder by a multidisciplinary evaluation at a

University Affiliated EI program and whose families participated in an IFSP at the center from 2007 to 2009. Data included: age, gender, ethnicity, dominant home language, maternal country of origin, level of maternal education, medical insurance coverage, child's cognitive standard score(SS) and Childhood Autism Rating Scale(CARS) score. The types and intensity of intervention approved for each child at IFSP were also collected including: hours per week of applied behavioral analysis(ABA), speech therapy, occupational therapy, physical therapy, family training, and school program. Statistical analysis included Chi-Square, independent T-test, and correlation.

Results: Seventy children meeting inclusion criteria were identified. Demographics: **mean age at IFSP**: 25.4±5 months(mo)(12-36mo); **gender**: 75% boys; **ethnicity**: 10% white, 45.7% hispanic, 28.6% black, 15.7% other; **dominant home language**: 58% monolingual English, 25% bilingual Spanish/English, 9% monolingual Spanish, 9% other; **maternal country of origin**: 64% of mothers were born in the United States; **maternal level of education**: 30% of mothers were college graduates; **medical insurance:** 49% had Medicaid and 51% private insurance. Clinical data: 53% had a cognitive SS ≥70. Mean CARS score was 34±4 (range of 26-48).

Children older than 24mo at IFSP were approved for more hours of ABA per week (11.97±6.3 vs. 8.48±6.7, p=0.03). Children with higher CARS scores were approved for more hours of ABA per week (r=0.248, p=0.04) and those with CARS scores above 40 were more likely to be approved for >10 hours of ABA than those with CARS scores <40 (67% vs. 29%, p=0.05). There was also a trend for children with cognitive SS<70 to be approved for more hours of ABA per week (12.1±6.4 vs. 9.3±6.5 hours, p=0.08). There was no significant difference in the amount of ABA approved in terms of maternal country of origin, maternal education, medical insurance coverage, ethnicity, or dominant home language. There were no differences in the intensity of other services by demographic characteristics.

Conclusions: In this sample, greater intensity of behavioral intervention was approved for children with increased severity of autistic symptomatology and age greater than 24mo at IFSP. There was a trend towards increased behavioral intervention for children with ASD with lower cognition (SS<70). Other demographic factors (including Spanish home dominant language and ethnicity) did not affect intensity of services approved.

111.172 172 Effect of Lenalidomide On TNF-Alpha Elevation and Behavior in Autism. M. Chez*, T. Donnell, C. Parise and R. Low, *Sutter Neuroscience Institute, Sacramento Medical Center*

Background: Autism currently affects 1:100 births. Research has shown markers of neuroglial inflammation with elevated cytokines. Elevation of tumor necrosis factor-alpha (TNF-_) in the CSF vs. serum in patients with regressive autism has been reported. Lenalidomide (Revlimid®) is an oral immunomodulatory agent predicted to modulate elevated TNF-_ levels.

Objectives: This study was to determine if lenalidomide safely reduces CSF and serum tumor necrosis factor-alpha (TNF-_) and correlates to improved behavior and speech function in children with autism spectrum disorder who have elevated CSF and serum TNF-_ levels.

Methods: Six males (6 to 12 years) with elevated TNF-_ were included in this open label trial and received Revlimid® 2.5 mgs per day for 12 weeks. CSF and serum TNF-_ were measured before baseline and at 12-weeks post treatment. The Expressive and Receptive one-word tests, and the Childhood Autism Rating Scale (CARS) were obtained at baseline, 6-weeks, and at 12-weeks in all subjects. Repeated measures t-tests were used to compare pre and post test differences.

Results: The CSF-TNF-_ declined an average of 57% from 80.5 ±41.03 to 38.0 ± 31.27 (P = 0.065) in four children who completed the study at 12 weeks. Serum TNF-_ showed decline of 57% (92.50 ± 68.92 to 40.25 ± 44.53 (P = 0.048). At the 6-week follow-up, language in the 4/6 patients with initial

expressive language as indicated by an ADOS module of 2 or 3 was analyzed. Mean receptive language in the 4 children increased from 50.00± 19.5 to 57.75 ± 19.03 (P = 0.049) and showed decreased symptoms of autism based on the CARS scores (baseline 37.38, SD±4.11 vs. 6 weeks 34.50±4.92, P = 0.090). Patients also had Clinical Global improvement (CGI) ratings by the primary investigator at each visit and also at 6 and 12 week points. The CGI data for socialization and expressive and receptive speech improved in all 4 patients above at 6 weeks, and 3 patients at 12 weeks.
Side effects included rash causing two patients to drop out of study. One patient was dropped out of study after eight weeks for transient drop of absolute neutrophil count of 1200 (safety cutoff 1500).

Conclusions: This study successfully looked at a novel mechanism for autism with regression using elevated TNF-_ markers in CSF and serum and treatment with oral TNF-_ inhibitor lenalidomide. This study shows clear clinical lowering of TNF-_ in both serum and CSF in 4 patients completing 12 week study. Despite the small number of patients, 4/6 patients with measurable language improved by one-word vocabulary testing with receptive language showing statistically significant and clinically meaningful changes by 6 weeks of treatment. CARS improved on average by greater than 2 points. Although some measures did not reach significance statistically, this was probably due to low number of patients. Larger and placebo controlled studies looking at TNF-_ treatment in autism patients with elevation in CSF and/or serum is warranted.

111.173 173 Efficacy of An Outpatient Social Skills Training for Individuals with ASD and Their Parents. S. Woolsey Duvall*, D. Hill, B. Lopez, M. Moriarta and N. Mody, *University of New Mexico*

Background: Autism spectrum disorder (ASD) is characterized by impairment in social relatedness, deficits in communication skills, and repetitive or restrictive interests or behaviors. Research has demonstrated that these social impairments continue into adulthood unless the individuals receive targeted treatment. In order to evaluate the efficacy of a time limited outpatient treatment approach for children with ASD, this study implemented the PROGRESS Curriculum (PROGram for Remediating and Expanding Social Skills) which includes a social skills training program for children with ASD and a co-occurring parent group.

Objectives: The purpose of this study was to evaluate changes in social skills functioning following a social skills group for children with ASD. Additionally, the social skills ratings of teachers, parents and children with ASD will be compared.

Methods: Six families of children with ASD were recruited for this study and diagnosis was confirmed with the ADOS. The Social Skills Rating Scale (SSRS) was administered as part of a larger battery. The SSRS provides a broad, multi-rater assessment of social behaviors influencing the child's development of social competence and adaptive functioning at school and at home. Informed consent was obtained from all parents and verbal assent was obtained from children prior to participation. Children participated in a 20-week social skills group with a co-occurring parent group (combination of psychoeducational and CBT approaches used). Data on social skills functioning was collected pre-intervention (week 1), mid-intervention (week 10), post intervention (week 20) and at a 3 month follow-up from children, parents, and teachers.

Results: Parents reported a statistically significant improvement in their child's social skills by the end of the intervention, $t(5)=4.98$, $p=.004$. No statistically significant differences were found in social skills reported by the teachers, $t(4)=1.70$, $p=.17$, nor the children's self reported social skills $t(5)=.89$, $p=.41$. Additionally, children with ASD reported themselves as having higher social skills compared to the ratings of their teachers and parents.

Conclusions: The current study found some support for the efficacy of a 20-week outpatient social skills group with a concurrent parent training component in improving the social skills of children with ASD. Parents reported the most improvement in their child's social skills. Additionally, only parents reported a significant improvement in

their children's social skills. The small sample size of the study might have limited our ability to find significant effects in the teacher and child groups. It is also possible that parents observed improved social skills in their children because the parent training component of the program taught the parents to be more effective at engaging their children. Though children did not report an increase in their social skills over the course of the intervention, at all time points children with ASD perceived their social skills to be well above their functional abilities (as rated by parents and teachers). Future directions include increasing sample size, evaluating how to improve generalization of social skills from a group setting to the child's everyday environments, and the effects of aggrandized self-perception of social skills in children with ASD.

111.174 174 First Year Intervention for Infants at Risk for Autism – Initial Feasibility and Acceptance. S. Ahmed*[1], M. W. Wan[1], M. Elsabbagh[2], M. H. Johnson[2], J. Green[1] and .. The BASIS Team*[3], (1)*The University of Manchester*, (2)*Birkbeck, University of London*, (3)*BASIS*

Background: Studies of high risk infants (A-sibs) show estimated recurrence rates of 5-30% for the broader autism phenotype. Prospective studies are elucidating emerging behavioural[1] and brain function atypicalities[2] in the latter part of the first year in infancy. The "interactive specialisation" (IS) model[3] within cognitive neuroscience suggests that the "social brain" develops through an active process of postnatal interaction with the environment. Our group has found evidence of perturbation of parent-infant in relation to these early atypicalities[4]. It has been argued that intervention in infancy carries promise of altering the early trajectory of autism[5]. These considerations have led us to undertake a parent-mediated intervention to enhance the social interactive environment for A-sibs from 10-14 months. This is only the second study internationally to initiate an intervention prior to 12 months. Review of acceptability and feasibility of such an intervention is therefore crucial.
Objectives: To report on the initial feasibility and acceptability to parents of the parent-mediated video-aided home based intervention from 10-14 months.
Methods: Siblings of autism probands are recruited within the context of British Autism Study of Infant Siblings (BASIS); a UK collaborative research network.
The intervention design derives from a combination of developmental theory and the best current evidence for effective interventions for parent-child interaction in typically developing infants at high and low risk, as well as in pre-schoolers with autism. Video-aided techniques are used to enhance parent-infant interaction.
Results: Detailed interviews have been conducted with participating parents and questionnaires filled out before and after the intervention. These assessments ascertain:
· parental expectations of and attitudes towards an intervention of this nature
· acceptability of the sessions with respect to content, duration, frequency
· acceptability of the home practice expected
· wider impact of intervention on parental attitudes and family factors
The qualitative data from the first families to take part in the intervention will be described.
Conclusions: Early findings from the pilot study reported here give insight into parental acceptance and feasibility of parent-mediated intervention with infants at high risk of autism.

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111.175 175 Incorporating Technology Into a Pilot Cognitive Behavioral Therapy Group Treatment for Adolescents with High Functioning Autism Spectrum Disorders. A. Blakeley-Smith*[1], J. Reaven[2], E. Leuthe[2], K. Culhane-Shelburne[1], E. Moody[3] and S. Hepburn[2], (1)*JFK Partners, University of Colorado Denver School of Medicine*, (2)*University of Colorado Denver School of Medicine*, (3)*University of Colorado Denver, Anschutz Medical Campus*

Background:

Adolescents with autism spectrum disorders (ASD) face the same developmental challenges as their peers, but their lives are complicated by the core deficits of ASD, as well as increased risk for anxiety (Farrugia & Hudson, 2006). To date, there are no published psychosocial studies that target anxiety reduction in adolescents with ASD (White et. al, 2009). There is a critical need for anxiety specific interventions for this age group as they are on the cusp of living independently, attending institutions of higher learning, and/or entering the working world (Broadstock et al., 2007), and clinical anxiety symptoms can interfere with independent functioning in these areas. The purpose of the current study was to extend a manualized family-focused CBT group treatment designed for children with ASD and anxiety (Reaven et al., 2009) to adolescents, incorporating the use of technology (i.e., a Personal Digital Assistant; PDA). Given the complexity of adolescents with ASD, the addition of technology may potentially be an innovative way to enhance the portability of CBT techniques to everyday life.

Objectives:

- To develop and assess the initial effectiveness of a pilot group intervention in reducing symptoms of anxiety in adolescents with ASD.
- To examine adolescents' compliance in using a PDA to assist with a) self monitoring of anxiety symptoms, b) as a guide for CBT strategy use, and c) to document graded exposures.

Methods: Twelve adolescents participated in the 14 week intervention and: (a) met criteria for an ASD, as confirmed by the ADOS (Lord, et. Al, 2002); (b) had a Verbal IQ of 80 or above; and (c) exhibited clinically significant symptoms of anxiety, as measured by Anxiety Disorders Inventory Schedule for Children, Parent Report (ADIS-P; Silverman & Albano, 1996). Each adolescent received a PDA and was coached in its use throughout the intervention.

Results:

Results from the ADIS-P indicated that pre-treatment, 11 of the 12 participants met diagnostic criteria for 2-6 psychiatric diagnoses (mode=4); post-treatment, 11 of the 12 participants met criteria for 1-4 psychiatric diagnoses (mode=3). Post-treatment ratings on the Clinical Global Impressions Scale for the participants' primary anxiety diagnoses indicated that 2 of the 12 participants were "very much improved", 3 were "much improved," 4 were "minimally improved," and 3 were "no change." All adolescents engaged in self-monitoring of anxiety symptoms and graded exposure documentation via their PDAs.

Conclusions:

Results of the pilot study indicated that 75% of the adolescents who participated in the group CBT intervention displayed reductions in anxiety symptoms. These results represent a preliminary, but important step in the development of efficacious CBT interventions for high school students with ASD. In addition, while all adolescents used their PDAs for self-monitoring and to record their exposure practice, variability was noted in their use. Benefits and challenges related to the use of the PDA will be discussed and the relationship between PDA compliance and anxiety symptom reduction will be explored. Study limitations include the lack of a comparison group and the small sample size.

111.176 176 Psychosocial Treatment Effects of the PEERS Social Skills Intervention for Young Adults with Autism. A. Gantman*[1], S. Kapp[2] and E. Laugeson[1], (1)*UCLA Semel Institute for Neuroscience & Human Behavior*, (2)*UCLA*

Background: Deficits in social skills acquisition and generalization are frequently the most significant challenges for children

and adults with Asperger's Disorder/High Functioning Autism (AD/HFA). Social difficulties can lead to significant impairment in daily living, vocational skills, social relationships, and psychological functioning. This area continues to be highly understudied in treatment research for young adults with AD/HFA. Few studies have examined the difficulties these individuals endure during this highly socially, emotionally, and physically demanding period of their lives. Findings suggest that only about 15% of adults with AD/HFA have reciprocal friendships, and even fewer are in long-term romantic relationships. It is believed that lack of social skills in young adults with AD/HFA may lead to more isolation and lack of interpersonal relationships, vocational difficulties, victimization and exploitation, and increased psychopathology, such as higher rates of depression and generalized anxiety. 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 in young adults with AD/HFA.

Objectives: To test the efficacy of an adapted evidence-based social skills treatment intervention for young adults with AD/HFA, by looking at the acquisition of social skills, development of interpersonal relationships and treatments effects on psychological well being.

Methods: The intervention, known as PEERS for Young Adults, consisted of 14-week evidence-based caregiver-assisted social skills treatment program for transitional AD/HFA youth 18-22 years of age. 23 participants and their caregivers were randomly assigned to a treatment or delayed treatment control group. Weekly 90-minute treatment sessions, consisted of didactic social skills lessons, modeling, role-playing, behavioral rehearsal and homework. Didactic lessons targeted: conversational skills; peer entry/exiting strategies; choosing appropriate friends; planning/implementing get-togethers; dating etiquette; handling peer rejection; avoiding peer exploitation/victimization; and resolving conflicts.

Results: Preliminary analyses reveal that participants in the treatment group significantly improved their psychosocial functioning along a number of domains in comparison to the delayed treatment control group. Significant differences along the domains of emotional regulation, social and dating anxiety, loneliness, and locus of control were also observed between participants with AD/HFA and neurotypical and clinical populations.

Conclusions: Findings suggest that the use of PEERS for Young Adults, an adapted manualized caregiver-assisted social skills intervention, is effective in improving the social competence and friendship/relationship skills of young adults with AD/HFA, suggesting that caregiver involvement in treatment for this population continues to be vital for skill acquisition and generalization of social skills.

111.178 178 Social and Pre-Linguistic Behavior in Infants at Risk of ASD Improves Following Behavioral Intervention. L. K. Koegel*, *University of California, Santa Barbara*

Background: Although some progress has been made in diagnosing ASD in infants, little intervention research for this population has been published. Interventions designed to increase the social and pre-linguistic behaviors of this populating may be problematical because infants are not expected to verbally communicate, have limited receptive language, and lack a large repertoire of strategies to initiate social interactions.

Objectives: The purpose of this study was to assess whether naturalistic interventions that have been effective with toddlers with autism could be adapted for infants under the age of 1 year. This manuscript presents preliminary data from an intervention program designed for infants that exhibited symptoms of ASD (e.g., failure to respond to name, avoidance of eye contact, lack of social smile, and preference for toys over people).

Methods: Two infants (4 and 7 months) participated in this study. Both infants had been referred by independent physicians for symptoms of ASD. Motivation-based intervention components shown to be

effective for older children (e.g., using child-preferred activities, task variation, and systematic interspersal of acquisition and maintenance tasks) were adapted to be appropriate for infants. Sessions were implemented by one of the infants' parents following parent training. Sessions were once per week for 1 hour. A multiple baseline across participants design was used to evaluate the effects of the intervention on social engagement. Dependent variables included affect, frequency of eye contact between parent and child, and total number of ASD symptoms using the Autism Diagnostic Scale for Infants (AOSI). Affect was rated using measures of happiness and interest. Five point Likert scales were created to identify behavioral indicators of interest (e.g., score of 1 assigned for looking away from parent or activity, score of 5 assigned for alert and active responding) and of happiness (score of 1 for crying or tantrums, score of 5 for laughing or smiling).

Results: Both participants showed stable low levels of interest and happiness in baseline and steady improvement in interest and happiness during intervention. Improvements in affect were maintained at 6 month follow-up. During baseline, both participants rarely engaged in eye contact with parents. During intervention frequency of eye contact was increased. Increased eye contact was maintained at 6 month follow-up. Mean number of ASD symptoms at baseline for both participants was 12 (range, 10 to 14) and was reduced to 4 for participant 1 and 1 for participant 2 following intervention.

Conclusions: The results of this study suggest that components of naturalistic interventions previously used for older children, also were helpful in increasing positive affect, and improving eye contact in 2 infants referred for symptoms of ASD. The results are discussed in terms of early intervention in infancy and developmental trajectories for children that show early signs of ASD.

Keynote Address Program
112 Adopting Evidence-Based Practice for Children with Autism: What Will It Take?

Speaker: B. Burns *Duke University*

Invited Educational Symposium Program
113 What Really Matters: Measuring Outcome and Addressing the Needs of Adolescents and Adults with ASD

Moderator: P. Howlin *Institute of Psychiatry*

This symposium addresses current and past trends in assessing variously defined outcomes in adolescents and adults with ASD. Autism-specific features, comorbid psychopathology, independent living skills, family resources, and demographic variables come together to influence outcome after the childhood years. Moving beyond categorical diagnoses and standard measures of functioning such as IQ, we discuss measurement issues related to diverse dimensions of impairment and success, as well as subsequent service provision for individuals with ASD and their families.

113.001 The Transition to Adulthood for Individuals with ASD and their Families. J. L. Taylor*, *Vanderbilt Kennedy Center*

The transition out of high school and into the adult service system for individuals with ASD is a time of immense change and uncertainty. New data will be presented examining the transition process for these young adults and their families, focusing on post-transition outcomes.

113.002 Incorporating Family and Demographic Variables in Outcome and Intervention Research. T. Carr*, *University of Michigan*

Individual outcome may be conceptualized as the result of transactional relationships between individual, family, and community variables. The utility of outcome measures assessing such variables will be discussed and implications for service development explored.

113.003 The Developing Phenotype: Measuring ASD Features Beyond Childhood. S. L. Bishop*, *Cincinnati Children's Hospital Medical Center*

ASD diagnostic criteria are derived mainly from observations of school-aged children, and thus may not adequately reflect symptoms that are most relevant for individuals as they enter adulthood. Approaches to measuring ASD-related impairments will be discussed in terms of

their ability to describe a full range of social-communication outcomes for adults.

113.004 Assessment and Treatment of Co-occurring Psychopathology. K. Gotham*, *University of Michigan*

Differential presentation of mood and anxiety disorders in ASD complicates measurement of these common comorbidities. New data on the situational and psychosocial predictors of these disorders will be presented and indications for services discussed.

Cognition Program
114 Cognition 2

114.001 Can the Raven's Progressive Matrices Intelligence Test Be Solved by Thinking in Pictures?. M. Kunda*, K. McGreggor and A. K. Goel, *Georgia Institute of Technology*

Background: Both children and adults with autism spectrum disorders (ASD) often perform better on the Raven's Progressive Matrices intelligence test than on multi-domain intelligence tests like the Wechsler scales, whereas typically developing individuals do not show this pattern. Given the strong visual abilities of many individuals with ASD, one hypothesis explaining these data is that individuals with ASD can use visual strategies to solve the Raven's test, which consists entirely of visual analogy problems, but such visual strategies are successful only on the visual portions of broader tests like the Wechsler scales. In line with this hypothesis, a recent fMRI study showed that, relative to typically developing controls, a sample of individuals with ASD displayed increased neural activity in the extrastriate visual cortex and decreased activity in prefrontal and parietal regions while solving the Raven's test.

Objectives: Even though the Raven's test consists of visual problems, most information processing accounts assume that people solve it using verbal, rule-based strategies, and behavioral evidence from typically developing individuals supports this view. However, this study aims to examine, from an information processing perspective, whether visual strategies can also be used to successfully solve the Raven's test. A positive result will 1) show that the hypothesis of certain individuals with ASD solving the Raven's test visually is computationally feasible, and 2) provide a computational basis for making behavioral predictions to further test this hypothesis.

Methods: Two computational models were developed that try to solve problems from the Raven's test using visual strategies. In contrast to existing computational accounts that require the translation of visual (i.e. pixel-based) representations of Raven's problems into propositional (i.e. verbal-symbolic) descriptions, both visual models operate directly on the given visual inputs from the test. The first model uses affine transformations to predict the answer for a given problem, and the second model automatically converts each problem into fractal image representations and chooses the best-fit answer based on a measure of fractal similarity. Both of these models have been tested on portions of the Raven's Standard Progressive Matrices test and on similarly constructed visual analogy problems.

Results: Both the visual affine model and the visual fractal model have successfully solved significant numbers of Raven's (or similar) visual analogy problems. For example, the affine method correctly answers about 60% of the problems on Set B from the Raven's Standard Progressive Matrices test, and the fractal method correctly answers about 70% of these problems.

Conclusions: Two different computational models can successfully solve many problems from the Raven's Progressive Matrices intelligence test using visual strategies. These results offer a new information processing basis for the hypothesis that, unlike typically developing individuals who use verbal strategies, certain individuals with ASD might solve the Raven's test visually. In further work, these models will be used to generate behavioral predictions to distinguish whether an individual is using visual as opposed to verbal strategies on Raven's-type problems.

114.002 Effectiveness and Relevance of a Reading Intervention as a Function of Students' Characteristics for High-Functioning

Students with Autism Spectrum Disorder. C. Roux*, E. Dion, D. Landry and M. S. Arcand, *University of Quebec in Montreal*

Background: Learning to read is a challenge for many high-functioning students with autism spectrum disorder (ASD), especially when it comes to understanding the meaning of texts (e.g., Whitehouse & Harris, 1984). Indeed, their reading comprehension appears to be below their reading fluency levels on standardized testing (Nation, Clarke, Wright & Williams, 2006).
Regrettably, evidence-based reading interventions for students with ASD are almost completely inexistent (see Chiang & Lin, 2007 for a review), and reading comprehension problems continue to impede on these students' school success and social and professional integration.

Objectives: The objective of this study is to examine the effectiveness of a reading intervention and to determine whether this intervention is effective for a wide range of students with ASD.

Methods: Forty-three students diagnosed with ASD were randomly assigned to a control condition (N = 20; regular classroom activities) or to an intervention condition (N = 23; reading intervention: three 30 minute sessions per week for four months). The intervention was offered in small groups (three or four students) by a research assistant. Reading vocabulary, paragraph main idea identification and text structure were targeted. The instruction was explicit, structured and interactive. Fidelity of implementation was monitored through direct observations. Students were assessed on researcher-developed measures of instructed vocabulary, general comprehension (recall) and main idea identification. Reading assessments were conducted individually. Interrater reliability was performed for at least 25% of the assessments.

Results: Mean comparisons of control and intervention students indicate that the intervention is highly effective, with effect sizes (*d*) varying between 0.60 (general reading comprehension) and 0.80 (instructed vocabulary). Among students' pretest characteristics (mastery of basic reading skills, performance IQ, receptive vocabulary, oppositional behavior), only oppositional behavior appears predictive of the degree to which students benefited from the intervention, with students rated as oppositional by their teachers benefiting less.

Conclusions: Interestingly, the results of this study seem to indicate that it is possible to significantly improve the reading comprehension of a wide range of students with ASD, including those with limited basic reading skills or oral vocabulary or relatively low IQ. These results have implications for the development of future reading interventions.

114.003 Multisensory Processing of Emotion Expression in Autism and Asperger Syndrome. G. Charbonneau[1], O. Collignon[1], M. Nassim[2], M. Lassonde[1], L. Mottron[2], F. Lepore[1] and A. Bertone*[2], (1)*Centre de Recherche en Neuropsychologie et Cognition (CERNEC), Université de Montréal, Canada*, (2)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*

Background: The ability of nonautistics to recognize emotional expression through voice and facial affect usually leads to the correct interpretation of others' feelings, representing a fundamental cognitive ability for the effective regulation of social interactions. Although limitations in the expected, overt behaviors typically associated with the processing of emotion represents a core "symptom" of the autistic spectrum, empirical evidence using ecologically-validated stimuli and methods is rather limited.

Objectives: To assess atypical processing of facial and vocal affect in the autistic spectrum, using a recently validated set of ecological stimuli comprised of dynamic visual and auditory (non-verbal) vocal clips of emotional expression (Belin et al., 2008; Simon et al., 2007).

Methods: Twelve autistic, 10 nonautistic, and 11 Asperger syndrome participants matched for chronological age, full-scale IQ, gender, and handedness were asked to distinguish between facial and vocal affect stimuli representing disgust and fear as quickly and accurately as possible. Participants were presented with stimuli expressing fear or

disgust (produced by trained actors) either visually (dynamic facial expression), audibly (non-linguistic vocal clip), or bimodally. For bimodal presentations, the same emotion was presented in both modalities for congruent conditions, while different emotions were presented in the two modalities for incongruent conditions. Signal-to-noise ratio scores for both visual and auditory signals resulting in an 85% discriminability (fear vs disgust) level of performance were also collected using the QUEST adaptive staircase method. In a second part of the experiment, the same procedure was repeated for each participant using visual and auditory information whose saliency was adjusted for (i.e., equally salient) based on thresholds previously obtained using the QUEST adaptive staircase.

Results: Results demonstrate a tendency for less efficient processing of emotional expressions in all conditions for the autistic group, but not the Asperger group, when compared to controls. Moreover, autistic participants necessitated an increased signal-to noise ratio to discriminate at an 85% correct level between fear and disgust. For incongruent bi-modal conditions, only autistic and Asperger participants preferentially categorized the affective expression using visual cues, suggesting a strong visual dominance for the processing of dynamic emotion information.

Conclusions: Our results suggest a reduced ability to categorize dynamic emotion expressions in autism, whether via visual or auditory channels. We are presently assessing whether the nonlinear probabilistic summation for the congruent bi-modal condition will differ in autistic spectrum and control groups by looking for a violation of the "race model" (an indicator of the level of neural integration of different sensory-emotional information) before and after equating the saliency of auditory and visual information for each participant. This is an important methodological consideration since we will be able to dissociate whether a putative impairment in multisensory emotion processing is contingent on less efficient processing in either of the perceptual channels.

114.004 Cognition and Social Behaviour in Adults with Asperger Syndrome. M. Stothers* and J. Cardy, *The University of Western Ontario*

Background: In 1995, Klin and colleagues described a convergence of features in individuals with Asperger Syndrome (AS), an Autism Spectrum Disorder, and Nonverbal Learning Disability (NLD), a learning disorder defined by deficits in visual-spatial organization. The comparison was focused on the debate over whether AS is distinguishable from high-functioning autism, and subsequent research has had the same goal. With no multiple participant studies directly comparing adults with AS and NLD, the relationship between these disorders remains unclear. Behaviourally, individuals with AS and NLD demonstrate atypical social behaviour and difficulty adapting to novelty. Cognitively, they are reported to have difficulties with gestalt perception, or the perceptual integration of constituent parts to make a meaningful whole.

Objectives: This study explored commonalities in and differences between perceptual processes in adults with AS and NLD. The primary goal was to determine whether individuals with AS and NLD share underlying perceptual integration deficits that a) distinguish them from typical adults, b) impair their ability to communicate in social situations, and c) are evident regardless of whether they are manipulating verbal or nonverbal material. A second goal was to determine whether deficits in perceptual processes differ by degree or kind in individuals with AS and NLD.

Methods: A sample of typical adults was compared to adults with a community diagnosis of AS or NLD on social and gestalt perception tests. Their performance was compared on a verbal test of social behaviour interpretation (Dewey, 1991), and two types of nonverbal tests. The first set of nonverbal tests necessitated gestalt integration for successful completion; that is, they could not be solved using fragments. This set included puzzle assembly, figure copying, and two gestalt closure tasks. The second set of nonverbal tests could be solved using either a step-by-step approach or gestalt integration. This set included embedded

figures, matrix reasoning, and two versions of a block design task.

Results: Participants with AS or NLD had lower scores on tests of perceptual integration and social behaviour interpretation than comparison participants. The deficit appeared to extend beyond test format, with lowered scores evident on both nonverbal tests of gestalt perception and verbal tests of social behaviour interpretation. Moreover, there was a trend for members of both clinical groups to score more poorly on tests that demand gestalt perception than on tests that can also be solved correctly with an analytic approach. Typical participants did not show this pattern, and the trend was more apparent for those with AS than NLD.

Conclusions: Results suggested that adults with AS and NLD may be distinguished from typical adults using tests of gestalt integration. Adults with AS appeared to compensate better than those with NLD on nonverbal tests that can be solved analytically. Both clinical groups had difficulty with tasks that required gestalt perception, including social behaviour intepretation. Differences in scores for nonverbal tests of gestalt integration suggest that with careful consideration of the degree to which such tests may be solved analytically, the disorders may be distinguished from each other.

114.005 Implicit Learning Impairments in Individuals with Autism and First Degree Relatives. C. J. Smith*[1], J. M. Silverman[2], C. M. Lang[3] and A. S. Reber[4], (1)*Southwest Autism Research & Resource Center*, (2)*Mount Sinai School of Medicine*, (3)*Montefiore School Health Program*, (4)*Graduate Center at CUNY*

Background: The neurobiology of autism spectrum disorders (ASD) likely affects learning and perception of information from the environment such that development is pervasively delayed. Implicit learning (IL) is a complex cognitive process that occurs primarily without conscious effort. Such a process may be crucial for typical development of communication and socialization skills, and impairments in these skills are core deficits associated with ASD. Thus, impairments in the implicit system may be associated with the onset of this complex developmental disorder. If individuals with autism demonstrate IL impairments and their first degree relatives demonstrate similar impairments, then IL performance may serve as an endophenotype to facilitate genetic studies. Previous investigations of implicit processes in individuals with ASD have demonstrated conflicting results, thus it is unclear whether the underlying implicit processes are disturbed or if specific tasks or stimuli affect learning processes. Implicit functioning needs to be further investigated in individuals with ASD and their family members. Objectives: To examine the stimulus-related performance differences of individuals with autism and their first degree relatives on two IL tasks. Methods: In the sequence reaction time task (SRT) stimuli are presented in a sequence. Subjects learn the sequence largely without conscious effort and their reaction time decreases. When the sequence is replaced with random presentation of stimuli, RT increases, and when the sequence returns RT decreases again. Two tasks were designed for the present study. One presented a sequence with facial expressions of emotions, and the other presented the sequence with images of furniture. Both tasks presented ten stimuli in a complex sequence, ten times per block for five learning blocks. The sixth block was random presentation. In the seventh block, the sequence was restored but it was presented with different images of the same context (emotions or furniture). Individuals with autism and aged matched controls were tested on both tasks. Parents, other first degree relatives, and age matched controls were also tested on both tasks. Results: There were no significant between group performance differences in the learning and random phase of each SRT task. In the seventh block on the facial expression task the RT for the autism group increased from the RT for block 6. In the seventh block of the furniture task, the RT for both the autism group and the first degree relative group increased from the RT for block 6. Conclusions: These results suggest autism-related familial IL impairments associated with the transfer of complex information that is implicitly learned. Both the autism group

and the relative group had slower RT to the sequence when presented with novel stimuli. Their knowledge of the sequence implicitly acquired during the learning phase of the experiment was not applied when the same sequence was presented with novel stimuli. The autism group demonstrated this impairment in both tasks while the relatives demonstrated this impairment only in the furniture task. Both groups may share a similar underlying impairment, but the relatives may be able to overcome this impairment with expertise for specific stimuli (i.e. facial expressions).

114.006 Metacognitive Awareness of Face Processing in High Functioning Autism. C. Hileman*[1], H. A. Henderson[1], L. C. Newell[2], M. Jaime[1] and P. C. Mundy[3], (1)*University of Miami*, (2)*Indiana University of Pennsylvania*, (3)*UC Davis*

Background: Previous research has focused on face processing ability in individuals with High-Functioning Autism (HFA). However, limited research is available on the degree to which individuals with HFA have a metacognitive awareness of their own face processing abilities.

Objectives: 1) To compare the performance of children with HFA and children with typical development (TD) on a basic face processing task of affect selection. 2) To compare the correspondence between accuracy of affect selection and confidence in affect selection for HFA and TD children.

Methods: Twenty-eight HFA children and 25 TD children viewed 56 pictures of faces. The faces were revealed in a piecemeal fashion, and children were instructed to guess the affect of each face as quickly and accurately as possible and then rate their level of confidence in that affect selection. Half of the faces had an inverted orientation, and half of the faces had an upright orientation. For half of the faces, the eye region was revealed early and the mouth region was revealed late; for the other half of the faces, this order was reversed.

A two-level HLM model was used to examine the data, with face stimulus trials nested within persons. At Level 1, the variables confidence, face orientation, and order of facial features were examined as predictors of accuracy of affect selection. At Level 2, the variables diagnostic group, gender, verbal IQ, and age were examined as predictors of the intercept and slopes of the Level 1 model.

Results: At level 1, there was a significant effect of confidence on accuracy of affect selection, $t(51) = 7.03$, $p < 0.01$, such that as participants' confidence level increased, the accuracy of their affect selection also increased. There was a significant effect of face orientation on accuracy of affect selection, $t(2863) = -10.29$, $p < 0.01$, such that participants were more likely to be accurate on upright faces than inverted faces. There was a significant effect of order of facial features on accuracy of affect selection, $t(2863) = 3.38$, $p < 0.01$, such that participants were more likely to be accurate when the mouth region of the face was revealed early than when the eye region was revealed early. At level 2, there was a significant effect of diagnostic group on the relation between confidence and accuracy, $t(51) = -3.99$, $p < 0.01$, such that TD participants with a one-unit increase in confidence were more likely to be accurate on their affect selection than HFA participants with a one-unit increase in confidence.

Conclusions: HFA children were just as accurate as TD children in identifying the affect of facial expressions. However, HFA children didn't have the same degree of metacognitive awareness of the accuracy of their affect selections as TD children. These results suggest that teaching metacognitive awareness of social skills may be an important component of interventions, in addition to teaching the social skills themselves. The effectiveness of interventions with HFA children may improve by targeting both a particular skill and metacognitive awareness of that skill.

114.007 Object Individuation in Autism. K. O'Hearn*[1], S. Franconeri[2] and B. Luna[1], (1)*University of Pittsburgh School of Medicine*, (2)*Northwestern University*

Background: Seeing multiple objects at the same time – object individuation – is crucial for mature visual processing. The present studies examine object individuation, and the

effects of grouping on individuation, both of which may differ in autism. In particular, people with autism may be less sensitive to grouping information than controls.

Objectives: We examined whether people with ASD could individuate as many objects as typically developing people, and whether they were as sensitive as controls to grouping information in an individuation task.

Methods: We tested 38 high functioning individuals with ASD (9 to 29 years old) and 38 typically developing individuals matched on IQ, age and sex using two well-established tasks that examine parallel individuation of multiple elements: rapid enumeration of 1 to 4 objects and multiple object tracking (MOT) of 4 objects. In separate 'grouping' conditions, the arrangement of elements varied, influencing the difficulty of the task. We hypothesized that individuals with autism would be less sensitive to the grouping of objects regardless of whether it helped or hurt typical adults.

Results: Individuals with autism exhibited poorer performance than typically developing individuals on the rapid enumeration and MOT task across age on both tasks with 4 objects. However, the developmental pattern differed when enumerating 1 to 3 objects. With these smaller numbers, the performance differences emerged with age, reflecting that developmental improvements evident in typical adolescents were not present in the group with autism.

We then examined the effect of grouping on performance. When the elements were in a dice pattern in the enumeration task, performance improved in both groups but this improvement was *more* striking in the group with autism. Similarly, when common motion was used to link two targets together in the MOT task, the common motion helped everyone but helped people with autism more than typically developing people. A slightly different pattern was evident when the elements were grouped together in a way that typically hurts performance (enumerating concentric squares, tracking targets that are linked to distracters by common motion). In this case, the groups were affected similarly by the grouping manipulation in both tasks.

Conclusions: Individuation of multiple elements is impaired in autism, indicating that it utilizes a distinct process from visual search tasks that are relatively strong in ASD. The results suggest there is a lack of late development in autism in the parallel processing of small numbers of elements. Additionally, attentional processes supporting the serial individuation of larger numbers of elements appeared abnormal throughout development. In contrast to our hypothesis, we found that individuals with autism are as sensitive as controls to grouping information – in fact, grouping that helps performance typically actually helped people with autism more than controls, providing the support needed to elevate performance to a more typical level. This indicates that grouping information is perceived and utilized by individuals with autism on tasks that measure sensitivity to the individual elements. Together these findings indicate that the visual processing of objects, and its developmental course, is unique in autism.

114.008 Training Children with Autism Spectrum Disorders to Pass Theory of Mind Tasks Using Thought Bubbles. J. M. Paynter* and C. C. Peterson, *The University of Queensland*

Background: Impairments in theory of mind (ToM), in autism spectrum disorders (ASD), have received much attention (see Baron-Cohen, 2001). Recently, research has investigated whether these impairments may be amenable to change. This has relevance both practically and theoretically in terms of informing understanding of the mechanisms by which ToM may be acquired. Previous research has used a range of visual strategies to assist children with ASD to pass ToM tasks. Early research using photo or picture-in -the-head strategies (e.g. Swettenham, Baron-Cohen, Gomez & Walsh, 1996; McGregor, Whiten & Blackburn, 1998) demonstrated some success in improving pass rates in the trained task, but showed less success in generalisation to untrained tasks. More recently, the "thought bubble" method proposed by Wellman et al (2002) showed promise in improving pass rates on both the trained task and some

generalisation. This method taught children with ASD that mental states were like thought bubbles, a convention universally recognised in children's cartoons. Thought bubbles were used to demonstrate and teach theory of mind concepts. However, despite promising findings, with improvements on the trained changed location false belief as well as on a deceptive contents false belief task, this study suffered from limitations. Perhaps most notably, it lacked a control group. Given that in a more recent training study Fisher and Happe'(2005) found significant improvements in their control group in a similar deceptive contents false belief task, further research into thought bubbles is required.

Objectives: The current study sought to extend upon Wellman et al's (2002) study by including a control group, adding a delayed follow-up test session to assess durability of training effects and including an empirically validated developmentally scaled ToM scale (Wellman & Liu, 2004) as an outcome measure to assess generalisation.

Methods: Twenty-four children with ASD participated; 17 completed training and seven comprised a non-intervention control group. Training was based around Wellman et al's (2002) method around five stages, over two to four training sessions. All children completed pre/post standard false belief tasks and Wellman and Liu's (2004) scale tasks. Nine children from the experimental group and the entire control group also completed a three week delayed follow-up session.

Results: The trained group showed significant improvements on false belief total score, as well as on Wellman and Liu's (2004) scale. Improvements were maintained at follow-up. The control group did not show any significant changes on either scale.

Conclusions: This research lends further support to the growing body of evidence that children with ASD can be taught to pass ToM tasks. It adds specific support to the thought bubble method as a promising strategy to promote social-cognitive reasoning, which allowed for some generalisation beyond the trained task. This was maintained, at least in the short- term. Although in its preliminary stages, the thought bubble method shows great potential as a valuable tool worthy of further research to increase understanding of the mechanisms by which ToM may be acquired, and ultimately as a practical resource.

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115.001 Haploinsufficiency of Shank3 Leads to Impairments in Synaptic Transmission and Plasticity. J. D. Buxbaum*, T. Sakurai, O. Bozdagi, X. Wang, Q. Zhou, D. Papapetrou and P. R. Hof, *Mount Sinai School of Medicine*

Background: SHANK3 is a synaptic scaffolding protein that is important for glutamate synapse formation/maturation in cultured neurons. Alterations in SHANK3 have been implicated in 22q13 deletion syndrome characterized by developmental delay and severe speech impairment. Recently, rare mutations in SHANK3 as well as copy number variation at this locus have been found to be associated with autism spectrum disorders (ASD). Objectives: In order to clarify the role of SHANK3 involvement in ASD pathogenesis and ASD phenotype, we have developed and characterized Shank3 knockout mice. Methods: Synaptic transmission, plasticity and spine morphology was examined using combined patch-clamp whole-cell recording, two-photon time lapse imaging and extracellular recording of field excitatory postsynaptic potentials at Schaffer collateral-CA1 synapses in acute hippocampal slices prepared from Shank3 heterozygous mice and control littermates. Results: Since all human cases of SHANK3 haploinsufficiency are heterozygotes, we focused our analyses on heterozygotes. In heterozygotes, Shank3 gene expression levels are about half of that of wild type littermates. Heterozygotes and born and grow without any obvious abnormality. Electrophysiological characterization using hippocampal slices prepared from these animals demonstrated that both the amplitude of miniature excitatory postsynaptic currents from hippocampal CA1 pyramidal neurons and the input-output curve for Shank3 heterozygous mice were significantly lower than those in control mice suggesting a reduction in basal transmission due to a postsynaptic effect. However in Shank3 heterozygous mice the

frequency of miniature excitatory postsynaptic currents were significantly higher in comparison with the control mice and paired-pulse ratio was decreased which revealed a potential presynaptic role. We next examined the effect of Shank3 deficiency on synaptic plasticity and spine modification. Long-term potentiation (LTP) induced either with theta burst pairing (TBP) or high frequency stimulation was impaired in Shank3 heterozygous mice with no significant change in long-term depression (LTD). Only transient spine expansion was observed in Shank3 heterozygous mice while persistent expansion was seen in spines from control mice after TBP. Conclusions: These results indicate that reducing Shank3 expression level leads to alterations in synaptic transmission and plasticity that would predict behavioral phenotypes, related to learning and memory. Currently, we are characterizing Shank3 heterozygous animals behaviorally. Supported by the Simons Foundation and the Seaver Foundation.

115.002 Autism Models Based On Synaptic Adhesion Molecules Neurexin and Neuroligin: Molecules and Potential Treatments. C. M. Powell*, *The University of Texas Southwestern Medical Center*

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. More recently, copy number variations in neuroligin 1 have also been linked to autism. We have recently characterized mouse models lacking neurexin 1, 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 successfully 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 and neurexin 1 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.
Neurexin 1 knockout mice show a similar increase in grooming behavior along with reduced excitatory synaptic transmission in the somatosensory cortex.

Conclusions: The neuroligin-3 R451C knockin mice and neurexin 1 knockout mice are among the first, genetically accurate models 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, both models exhibit a decrease in the excitatory to inhibitory synaptic balance via disparate mechanisms.
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.

115.003 mGluR5 and Preclinical Treatment of Fragile X Syndrome in a Mouse Model. G. Dolen*, *Stanford University School of Medicine*

Background: Fragile X is the leading inherited cause of mental retardation and monogenic autism. The disease has been modeled in mice by molecular genetic manipulation of the Fmr1 gene (Fmr1 KO). This gene encodes the Fragile X mental retardation protein (FMRP) and is turned off in human patients with Fragile X. FMRP is an RNA binding protein found in the post-synaptic compartment of neuronal synapses, where is thought to negatively regulate local protein synthesis. The major excitatory neurotransmitter used at central nervous system synapses in mammalian brain is glutamate, and several subtypes of glutamate receptors are found at the post-synapse. Of these the metabotropic glutamate receptor 5 (mGluR5) is unique for its ability to couple activation by glutamate to post-synaptic signaling cascades, including induction of local protein synthesis. Indeed, many of the long-term consequences of mGluR5 activation, including a form of synaptic plasticity called mGluR-LTD, are protein synthesis dependent. Furthermore, mGluR-LTD is exaggerated in Fmr1 KO mice, and is no longer protein synthesis dependent. These findings raise the possibility that the pathogenesis of Fragile X results from dysregulation of mGluR5 mediated protein synthesis, and that this imbalance might be corrected by downregulating mGluR5 mediated signaling.

Objectives: To test the theory that Fragile X results from dysregulation of mGluR5 mediated protein synthesis, and that downregulation of mGluR5 could correct Fragile X phenotypes in Fmr1 KO mice.

Methods: Genetic interaction between Fmr1 and Grm5 (the gene that encodes mGluR5) was tested by generating mice of four genotypes (Wild type, Fmr1 KO, Fmr1 KO/Grm5 Heterozygote, and Grm5 Heterozygote) and comparing phenotypes relevant to the disease (including protein synthesis,mGluR-LTD, in vivo ocular dominance plasticity, behavioral learning and memory, seizure susceptibility, pathologic dendritic spine morphology, abnormal growth trajectory, and macroorchidism) across genotypes.

Results: Seven of eight Fmr1 KO phenotypes tested showed rescue in the Grm5 knockdown background, consistent with genetic interaction between Fmr1 and mGluR5. This interaction implicates mGluR5 as a therapeutic target for the treatment of Fragile X.

Conclusions: These results provide evidence for the use of mGluR5 antagonists in the treatment of Fragile X. Moreover, mGluR5 signaling cascades interact with a number of synaptic proteins, many of which have been implicated in autism, raising the possibility that therapeutic targets identified for Fragile X may have efficacy in treating some, if not all, other causes of autism.

115.004 Genetic and Functional Analyses Support a Role for CYFIP1 in Autism Spectrum Conditions. O. Bozdagi*[1], T. Sakurai[1], G. Cai[1], L. Ospina[1], N. Takahashi[1], M. Pilorge[1], J. Glessner[2], H. Hakonaron[2], L. Pepa[1], L. Soorya[1], P. J. Gonzalez[3], E. Manghi[4], L. A. McInnes[1] and J. D. Buxbaum[1], (1)*Mount Sinai School of Medicine*, (2)*Center for Applied Genomics*, (3)*Hospital Nacional de Niños "Dr Sáenz Herrera"*, (4)*University of Illinois at Chicago*

Background: The 15q11.2 region has been implicated in autism spectrum disorders (ASDs) associated with 15q11-q13 duplications and in Prader-Willi and Angelman syndromes. Within the recurrent, minimal copy number variation (CNV) region of 15q11.2 there are at least 5 genes, including CYFIP1 (cytoplasmic FMRP interacting protein 1). CYFIP1 is a critical part of a complex that includes fragile X mental retardation protein (FMRP) that regulates mRNA transport and translation at the synapse, controlling critical aspects of activity-dependent protein synthesis. Objectives: In the current study we examined the 15q11.2 region in ASD and studied the function of the Cyfip1 gene using mice with a disruption of the Cyfip1 gene. Methods: We made use of genome-wide single-nucleotide polymorphism (SNP) arrays to screen for

CNVs in patients with ASDs. CNVs in 15q11.2 were confirmed by multiplex ligation-dependent probe amplification (MLPA). Mice with a disruption in Cyfip1 were generated from gene-trapped embryonic stem (ES) cells. Mice were characterized using quantitative polymerase chain reaction (qPCR), immunoblotting, behavior, and detailed electrophysiology in the hippocampus. Results: A survey of 184 unrelated patients with ASDs identified 3 CNVs in 15q11.2, including a de novo deletion and two inherited duplications, all affecting the genes in the interval (TUBGCP5, CYFIP1, NIPA2, NIPA1, and WHAMML1). CNV at 15q11.2 was not observed in pseudo-controls derived from untransmitted parental chromosomes. These findings suggest a role for one or more genes in 15q11.2 in ASD, with the important association of CYFIP1 with FMRP highlighting altered dosage of this gene as a very likely candidate for ASD-associated phenotypes. Mice with a disruption of one copy of Cyfip1 (heterozygotes) showed reduced expression of Cyfip1, with no change in expression of the structurally and functionally related Cyfip2. With hippocampal electrophysiology, there were no significant differences in input/output function, paired-pulse facilitation, or various forms of long-term potentiation among the genotypes. Remarkably, metabotropic glutamate receptor-dependent long-term depression (mGluR-LTD), whether induced by paired-pulse low frequency stimulation or with the mGluR agonist DHPG, was enhanced in the heterozygotes and was independent of protein synthesis. Application of both mGluR5 and mGluR1 antagonist to slices from Cyfip1 heterozygous mice reversed the increase in mGluR-LTD. Preliminary behavioral studies suggest abnormalities in extinction in a fear-conditioning paradigm. All of the phenotypes be observed in the Cyfip1 heterozygotes are similar to those observed in mouse models of Fragile X syndrome. Conclusions: Our genetic studies are consistent with a role for 15q11.2 gene dosage abnormalities in ASDs, as well as other psychiatric conditions. Mice lacking one functional copy of Cyfip1 show enhanced mGluR-LTD that is independent of protein synthesis. This observation provides a mechanism by which gene dosage abnormalities of CYFIP1 can alter synaptic plasticity and function and implicates shared mechanisms between Fragile X syndrome and loss of a functional copy of CYFIP1. Our studies with combined mGluR1 and mGlu5 antagonists to reverse these synaptic deficits provide a potential therapeutic target in CYFIP1 dosage abnormalities and also indicate that a combined therapy may be more effective in Fragile X syndrome.

115.005 Dissociation Between Sociability and Anxiety in Juvenile Balb/Cj Inbred Mice, a Model of Low Sociability. A. S. Kreibich*, M. Torre and E. S. Brodkin, *University of Pennsylvania*

Background:

Many individuals with autism spectrum disorders (ASD) show both reduced sociability (reduced tendency to seek social interaction), and disabling anxiety symptoms, but the biological relationship between sociability and anxiety is not well understood. Mouse model systems are useful for experimentally testing the relationship between sociability and anxiety. Relative to C57BL/6J mice, BALB/cJ mice show certain behavioral endophenotypes relevant to ASD, including low levels of sociability and high levels of anxiety-related behaviors in non-social tests.

Objectives:

We hypothesized that the low sociability of BALB/cJ mice is related to their generalized high level of anxiety, and that pharmacologically reducing anxiety in BALB/cJ mice would increase their level of social interaction.

Methods:

To test this hypothesis, we treated BALB/cJ mice with the anxiolytic chlordiazepoxide (CDP), and then measured levels of sociability in a social choice test and anxiety-related behaviors in a non-social paradigm, the elevated zero maze.

Results:

Contrary to our original hypothesis, we found that treatment with an anxiolytic medication, CDP (a benzodiazepine), reduces anxiety-related behavior in a nonsocial task, but also significantly decreases sociability. In

contrast, treatment with a GABA inverse agonist, beta-carboline does not affect sociability or anxiety.

Conclusions:

These findings indicate that decreasing generalized anxiety does not increase sociability in this model system, suggesting that sociability and nonsocial anxiety-related behaviors are subserved by distinct neural circuitry. Future studies will use this mouse model system to further elucidate the neural circuitry and mechanisms that subserve sociability vs. nonsocial anxiety-related behaviors. These mechanistic studies may provide new pharmacologic targets for treating social withdrawal and/or anxiety symptoms in ASD.

115.006 Deficiency of Engrailed 2 (En2) Produces Abnormal Development of Forebrain-Projecting, Monoamine Neurotransmitters Systems and Depression Related Behaviors. L. Lin*[1], P. Sonsalla[1], P. G. Matteson[2], J. L. Silverman[3], J. N. Crawley[3], J. H. Millonig[2] and E. DiCicco-Bloom[1], (1)*Robert Wood Johnson Medical School*, (2)*UMDNJ-Robert Wood Johnson Medical School*, (3)*National Institute of Mental Health, National Institutes of Health*

Background:

Association of patterning gene *EN2* with ASD has been replicated independently in multiple datasets, supporting *EN2* as an ASD susceptibility gene. We are using mouse models to define *En2* developmental functions. Since *En2* is expressed in embryonic mid/hindbrain regions where forebrain-projecting monoamine neurons originate, we examined neurotransmitters norepinephrine (NE), serotonin (5HT) and dopamine in *En2* knock out (KO) and wild type (WT) mice. In previous study on postnatal day 21 (P21), KOs exhibited reduced forebrain monoamines, with changes in NE greater than 5HT, and increases in hindbrain. These results raise two questions: what are the developmental mechanisms of forebrain deficits? What are the behavior consequences?

Objectives:

Identify mechanisms mediating reduced forebrain monoamine neurotransmitters and characterize behavioral effects.

Methods:

Neurotransmitter levels were assessed using HPLC. Levels of TH protein were detected using western blotting, and axonal fibers were quantified using TH immunohistochemistry and Z-stack image analysis. Porsolt forced swim: Mice were placed in 20cm Plexiglas cylinder containing 12cm water. Immobility was measured every 5s during the last 4min of a 6min test, with observer blind to genotype. Tail suspension: Mice were suspended over a visually isolated area by the distal tail and immobility scored every 5s for 6min.

Results:

Overall, during development, monoamine neurotransmitters in *En2* KO mice were increased in mid/hindbrain regions but decreased in forebrain structures. NE exhibited the greatest changes, with levels elevated 40-70% in brainstem/cerebellum and reduced 30-60% in hippocampus from P7 to P21 (N=15). However, by adulthood, P60, NE deficits were diminished, with 23% reductions ($p<0.05$) in hippocampus and no differences detected in hindbrain, suggesting partial developmental recovery. Regarding mechanisms, changes in NE levels were paralleled by those in biosynthetic enzyme protein, TH, which was decreased 50% in hippocampus and increased 60% in cerebellum at P21 ($p<0.05$). Further, TH protein deficits were paralleled by changes in axonal innervation: TH fibers were reduced 73.2% in the KO at P21 ($p=2.74E-12$), and also displayed mild recovery by P60 (to 59.2%). Significantly, we also detected sex-dependent differences in both neurotransmitters and behaviors. While NE levels in adult cerebral cortex did not differ between KO and WT littermates, sex-specific analysis revealed that male KOs retained a 26.5% reduction ($p<0.05$). Behaviorally, the male but not the female *En2* KOs displayed significantly higher levels of immobility than WT littermates on the depression-related forced swim test, coinciding with sex

dependent NE deficits, whereas tail suspension was unaffected.

Conclusions:

Development of forebrain-projecting monoamine systems is disturbed in the *En2* KO, producing elevated levels in mid/hindbrain regions and reduced levels and axonal fibers in forebrain structures. These forebrain deficits, reminiscent of human ASD, partially recover as development proceeds. Thus *En2* may regulate axonal innervation and/or neurotransmitter system development. Further, with age, transmitter system abnormalities and depression related behaviors were sex-dependent, potentially relevant to the male preponderance of ASD. These observations provide one mechanism by which hindbrain patterning gene abnormalities may affect development of and connectivity to the forebrain, likely reflecting known monoamine effects on proliferation, survival and differentiation.

115.007 Long-Lasting Behavioral Interaction Between Perinatal PBDE Exposure and *Mecp2*$^{308/+}$ Mutation. R. O. Vallero[1], M. S. Golub[1], J. K. Suarez[1], R. Woods[2], T. A. Ta[1], A. L. George[1], I. N. Pessah[1], R. F. Berman[1] and J. M. LaSalle*[1], (1)*University of California at Davis*, (2)*University of Caifornia at Davis*

Background: Rett syndrome is an autism-spectrum 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. A mouse model with a truncation of *Mecp2* (*Mecp2*^{308}) has described social behavioral defects, but does not show the severe neurological phenotype of the *Mecp2* null RTT mouse model, and thus is a useful mouse model for genetic and epigenetic risk for autism-spectrum neurodevelopmental disorders. 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, particularly in genetically susceptible individuals.

Objectives: To test potential genetic, epigenetic, and environmental interactions by perinatal chronic low-dose exposure to the organic pollutant BDE-47 in an animal model with genetic risk for social and cognitive deficits.

Methods: *Mecp2*$^{308/+}$ dams bred to wild-type C57Bl6J males were exposed daily to BDE-47 (0, 0.03, or 0.1 mg/kg/day orally) for 10 weeks (4 weeks pre-mating, 3 weeks in utero, 3 weeks lactation). Female and male pups (*Mecp2*$^{308/+}$, *Mecp2*$^{+/+}$, *Mecp2*$^{308/y}$, *Mecp2*$^{+/y}$) from the control and low dose treatment groups underwent behavioral testing for sensory/motor neurodevelopment, social behavior (ultrasonic vocalization, social novelty, social barrier interaction), motor behavior (motor challenge, activity chamber), anxiety (elevated plus maze), sensory processing (prepulse inhibition), and learning (Morris water maze). Behavioral endpoints were analyzed with ANOVA separately by sex using genotype and BDE-47 treatment as independent variables and including the interaction. Following behavioral tests, mice were sacrificed and brain and other tissues remove for epigenetic analyses.

Results: The 0.1 mg/kg/day BDE-47 exposure negatively impacted fertility and litter survival specifically in *Mecp2*-mutant but not wild-type C57Bl6J mice, suggesting an increased genetic susceptibility of *Mecp2*-mutant mice to BDE-47 in reproductive success. Independent BDE-47 effects were limited to early pre-weaning developmental tests with significant effects on sensory neurodevelopment and ultrasonic vocalizations. In contrast, *Mecp2* genotype effects were predominant in juvenile and adult tests showing significant defects in social behaviors and activity. Significant BDE-47/*Mecp2* interaction effects were ameliorating for ultrasonic vocalizations and social interaction time, but compounding for adult spatial learning, specifically in the heterozygous females.

Conclusions: The combination of a genetic risk factor and perinatal exposure of a common organic pollutant showed a long-lived compounding effect on spatial learning behavior of female offspring. Because of the specificity of interaction effects in females, X chromosome inactivation and other

epigenetic mechanisms involving MeCP2 are further being investigated.

115.008 The Timing of Prenatal Immune Challenge Determines the Extent of White Matter Microstructural Anomalies Relevant to Autism. G. M. McAlonan*[1], Q. Li[1], C. Cheung[1], R. Wei[1], V. Cheung[2], E. S. K. Hui[1], P. Wong[3], S. E. Chua[1] and E. X. Wu[1], (1)*University of Hong Kong*, (2)*Hong Kong Polytechnic University*, (3)*Cornell University*

Background: Imaging and neuropathological studies point to the onset of pathology in neurodevelopmental disorders such as autism early in fetal life. White matter connections appear to be disrupted, leading to altered functional connectivity during higher-order cognitive processing. We have previously reported diffusion tensor imaging (DTI) evidence of microstructural pathology in our clinical studies of autism, but direct evidence for a fetal trigger of these brain structural differences is sparse. Epidemiological studies implicate maternal inflammation during prenatal life as an environmental risk factor for autism in the offspring.

Objectives: In this study we tested the hypothesis that maternal immune activation causes post-natal white matter microstructural anomalies in offspring relevant to schizophrenia or autism. We examined the effects of maternal inflammation in early and late gestation on white matter microstructure in the offspring using advanced small animal in-vivo MR-DTI.

Methods: We used an mouse model of maternal immune activation (MIA) by the viral mimic PolyI:C administered in early (day 9) or late (day 17) gestation. A novel application of automated voxel-based morphometry (VBM) of in-vivo MRI data mapped fractional anisotropy (FA, directional diffusion of water) across white matter pathways of adult offspring. Region-of-interest manual tracing was used to confirm FA changes in selected white matter tracts. In addition we conducted a preliminary immunohistochemical exploration of the oligodendrocyte marker CNPase to determine whether myelination processes might contribute to any changes in FA observed.

Results: FA was lower in MIA exposed offspring throughout fronto-striatal-limbic circuits and in the corpus callosum. Regions with lower FA were more extensive in the early exposed group. In both groups there were regions with increased FA but again, these were more extensive in the early exposed group. Preliminary immunohistochemical evidence revealed reduction in the oligodendrocyte marker CNPase in mice exposed to MIA, consistent with a white matter structural insult affecting myelination

Conclusions:

The present results provide direct experimental evidence that prenatal inflammation causes white matter microstructural abnormalities analogous to those found in autism. Maternal inflammation earlier in gestation precipitates more extensive changes in offspring, suggesting that the fetus is more vulnerable to environmental insults early in development.

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116.001 Compensatory Strategies in Locating Referential Object in Children with ASD: The Contribute of An Eye-Tracker Paradigm. R. Fadda*[1], G. Doneddu[2], T. Striano[3], A. Chessa[4], A. Salvago[2], G. Frigo[2] and A. Liberati[5], (1)*University of Sheffield*, (2)*Azienda Ospedaliera Brotzu*, (3)*Hunter College*, (4)*Linkalab, Complex Systems Computational Laboratory*, (5)*University of Cagliari*

Background: Gaze direction detection plays an important role in socio-communicative development. Accurate eye gaze judgement appears problematic for individual with autism (Gepner et al., 1996; Sweetenham et al., 2001; Webster & Potter, 2008). However, the basic geometric understanding of gaze direction seems to be preserved in ASD (Leekam et al., 1997). Thus evidence concerning the eye gaze direction detection abilities in individual with Autism Spectrum Disorders (ASD) needs to be further investigated. Recently, researchers focused on tracking eye movements to better understand the strategies used to perform

these tasks and detect possibly atypicity (Klin et al., 2002).

Objectives: Investigate if children with ASD are sensitive to the orientation of an adult's eye gaze in relation to an object which is within the child's field of view.

Methods: We compared on an eye-gaze detection task 30 children with ASD (20 M; 10 F), aged between 2-8yrs (mean=4; DS=1,7), IQ Leiter-R=73 (DS=22), and 30 TDs (12 M; 18 F), age-matched. The stimuli were presented with Tobii T60 Eye Tracker and were a modified version of the ones used in Hoehl, Reid, Mooney, and Striano (2008): an adult looking either toward or away from an object that was depicted on eye-level next to the adult's head. There was a second object on the other side of the adult's head. We defined 4 areas of interest for all the stimulus images: eyes, gaze target, no gaze target, screen-others (that is the area of the screen external to the other AOI). In order to define the strategies used to perform the tasks we considered Fixation Count (FC: the number of times that the child fixate an AOI), Time of First Fixation (TFF: how long it took to the participants to fixate an AOI for the first time) and Observation Length (OL: the total time in seconds for every time a person has looked within an AOI).

Results: The results show that ASD children looked more times outside the AOI (FC screen-others=34%) than controls (FC screen-others=22%) and less to the eyes (FC eyes ASD=22%; FC eyes TD=40%), while the rate of FC to the gaze target (FC gaze target ASD= 22%; FC gaze target TD= 21%) was very similar (chi square = 222; df=1; p=0.000). The two groups did not differ in TFF and OL meaning that both groups were able to locate the gaze target.

Conclusions: These findings shed new light on the processing of dyadic and triadic relations in ASD children There were quantitative differences in the way that children with ASD process static eye-gaze direction (see also Klin et al., Spezio et al, 2007). They demonstrated fewer fixations to the eyes region of face compared to controls but equal fixations to the gaze target. These results indicate that children with ASD might be successful in locating relevant objects in the environment due to a compensatory strategy involving over-exploration of the visual-field. Empirical evidences of gaze-direction detection in ASDs might be critical for developing effective treatment approaches aimed to optimized learning outcomes.

116.002 Heterogeneity in Presentation Among Children with Higher Functioning Autism: The Influence of Internalizing/Externalizing Behaviors On Self-Regulatory Behaviors. L. Mohapatra*[1], H. A. Henderson[1], K. E. Ono[1], C. Hileman[1], N. Kojkowski[1], M. Jaime[1] and P. C. Mundy[2], (1)*University of Miami*, (2)*UC Davis*

Background: Typically, cluster analytic approaches used in identifying autism subgroups primarily group individuals based upon social, cognitive, and language impairments. However, many individuals with higher functioning autism (HFA) have elevated internalizing and externalizing symptoms, contributing to their highly heterogeneous presentation. Yet, few studies have specifically examined how internalizing and externalizing symptoms differentiate children with HFA using cluster analysis and how such subgroups differ in self-regulatory styles and social presentation.
Objectives: The purpose of the current study was (1) to use cluster analytic techniques to identify distinct phenotypes in a large sample of children with HFA based upon parent reports of internalizing and externalizing symptoms and (2) to examine how these distinct phenotypes differed on indices of self-regulation and social adjustment.
Methods: Preliminary analyses are reported on 80 children with HFA (71 males, 9 females) between 8-16 years old. Subscales of parent-report measures of social anxiety (SASC-R) and internalizing and externalizing symptoms (BASC-2-PRS) were entered into a hierarchical cluster analysis using Ward's method and Euclidean Squared Distance. One-way ANOVAs were conducted comparing the identified clusters on measures of (a) autism symptoms (SCQ, ASSQ, and SRS), (b) parent and child report of general social adjustment (BASC-2-PRS and BASC-2-SRP), (c) parent report of temperament (EATQ), and a Repeated Measures ANOVA was conducted on (d) performance on a modified

version of the Eriksen Flanker task measuring inhibitory control. Post-hoc analyses were conducted to assess differences between clusters.
Results: Four clusters were identified: (1) *Primary Externalizing, (2) Internalizing/Externalizing,* (3) *Primary Internalizing*, and (4) *No Comorbidity.* The groups did not differ on age, verbal IQ, or perceptual IQ. Regarding autism symptoms, the *No Comorbidity* group was the least symptomatic on the ASSQ, $F(3,78)= 41.8$, $p<.01$, and the SRS, $F(3,78)=3.29$, $p<.01$. The *Primary Externalizing* group displayed the most repetitive and stereotyped behaviors, as reported on the SCQ, $F(3.78)= 3.79$, $p< .05$. In addition, they self-reported the most Social Stress, $F(3,69)=3.52$, $p< .05$, and Anxiety, $F(3,69)= 3.04$, $p< .05$. The *Internalizing/Externalizing* group self-reported marginally greater external Locus of Control, $F(3,69)=2.55$, $p=.06$; however, they did not differ from the other groups on other self-regulatory or social adjustment factors. The *Primary Internalizing* group was rated highest on temperamental Effortful Control, $F(3,76)=5.07$, $p< .01$. In addition, this group demonstrated the highest level of inhibitory control by significantly slowing down on incompatible versus compatible trials on the Flanker task, $t(12)=-2.91$, $p< .05$. The *No Comorbidity* group were rated as low in temperamental Negative Affect, $F(3,76)= 14.17$, $p<.01$ and high in Surgency, $F(3,76)= 9.95$, $p< .01$.
Conclusions: The current study identified four distinct autism subgroups based upon internalizing and externalizing symptoms. These results demonstrate that children with any Internalizing and/or Externalizing comorbidity were rated as having higher ASD symptoms. Differing profiles of regulation were noted between the comorbid groups, with the *Primary Internalizing* group displaying an overcontrolled style whereas those with a *Primary Externalizing* presentation showed greater rigidity, which may negatively impact their social relationships. These findings have implications for creating interventions that target the distinct regulatory styles of these phenotypically different subgroups.

116.003 Leader-Follower Dynamics of Adult-Child Vocal Interaction in Autism Spectrum Disorder. A. S. Warlaumont*[1], D. K. Oller[1], R. Dale[1], J. Gilkerson[2], J. A. Richards[2] and D. Xu[2], (1)*The University of Memphis*, (2)*LENA Foundation*

Background: Children with autism spectrum disorder (ASD) differ from typically developing (TD) children in turn-taking, delayed imitation, behavior initiation, and joint attention. Continued investigation of social interaction in infants and young children with ASD is important both for theories of social behavior in ASD and for developing assessment/treatment approaches. Recent technological advancements now permit continuous day-long audio recording of children's naturalistic audio environments (at home, school, therapy, etc.) with automatic speaker-identification. Using a database established with these new technologies, we report the first application of a statistical method called "cross-recurrence" (CR) analysis to the automated evaluation of adult-child vocal exchanges in ASD and TD groups.

Objectives: The goal is to measure temporal dynamics of vocal adult-child interactions at multiple timescales in day-long recordings of preschool children with and without ASD using new large-scale automated analysis methods. Our hope is that this research will enrich our understanding of how the dynamics of interaction are altered by ASD and add to existing diagnostic and assessment indicators.

Methods: Data were from 438 day-long (12+ hours) longitudinal recordings from 26 children 16-48 months of age diagnosed with ASD and 78 age-, gender-, and SES-matched TD children. Recordings were processed using automatic speaker-labeling software. CR plots were then made for each recording. CR plots were square matrices (child on one axis, adult on the other) wherein each row/column pair represented an event where either the child or an adult vocalized. CR plots indicate temporal ordering between every child vocalization and every adult vocalization. The distribution of values perpendicular to the matrix diagonal (the "diagonal recurrence profile") represents leading-following tendencies at a range of timescales (Richardson et al., 2007).

Amounts of adult-leading and child-leading were compared between ASD and TD recordings.

Results: Multiple regression controlling for child identity (random effect) and for child age, gender, and mother's education (fixed effects) revealed proportionally fewer immediate adult responses to child vocalizations in ASD recordings than in TD recordings ($p < .001$, beta = -.44). Additionally, for the ASD group the ratio of the number of child vocalizations following adult vocalizations within a 30-event lag window to the number of adult vocalizations following child vocalizations within the same size window was smaller than for the TD group ($p < .001$, beta = -.17). Restricting the analysis to child vocalizations that were identified as speech-like (cries and vegetative sounds excluded) or to non-speech-like vocalizations, similar patterns of results were observed.

Conclusions: Throughout the day, ASD and TD groups exhibit differences in dynamics of child-adult interaction. ASD children's vocalizations are less likely to be immediately followed by adult vocalizations, and the balance of child leading vs. following leans more toward the child following. This finding may relate to previous findings that children with ASD initiate interactions less often than TD children. Results also support CR analysis over day-long recordings as a potential method for assessing young children's interaction patterns in ASD.

116.004 Object-Directed Exploratory Behavior in Toddlers with ASD, DD, and TD. S. Macari* and K. Chawarska, *Yale University School of Medicine*

Background: Toddlers with ASD explore their world differently than toddlers with developmental delays (DD) or typical development (TD). Both infant home video studies and prospective studies have documented behavioral differences as early as 12 months of age in infants with ASD compared with DD and TD infants in such domains as visual and manual exploration of objects.
Objectives: While exploration of the social environment has been extensively studied in young children with ASD, less is known about their patterns of object exploration. This area is particularly important considering the amount of time that they devote to exploring their physical environment. Here we examine whether there are specific features of object exploration that differentiate toddlers with ASD from their DD and TD counterparts.
Methods: Object exploration was examined during a standardized 10-minute toy play session in 21 toddlers with ASD (age: M=21 months, SD=3.0), 25 toddlers with TD (age: M=18 months, SD=3.8), and 8 toddlers with DD (age: M=20 months, SD=4.5). The toys afforded a range of sensorimotor exploratory behaviors. ASD and DD groups were matched on nonverbal DQ. Behavior was coded blind to the hypotheses of the study and to group membership.
Results: Compared to toddlers with DD and TD, toddlers with ASD engaged in more manual rotation of objects ($F(2,52)=7.8$, $p<.001$) and prolonged gaze to objects (bouts longer than 10 seconds) ($F(2,52)=6.1$, $p<.01$). Furthermore, they made less eye contact with adults during play ($F(2,52)=13.0$, $p<.001$) than both control groups and showed objects less frequently than TD toddlers ($F(2,52)=5.5$, $p<.01$). Toddlers with DD banged objects more frequently than the other toddlers ($F(2,52)=4.4$, $p<.05$).
A discriminant function analysis was performed to find the most parsimonious profile of object-directed behaviors that best predicted group membership. Two significant functions emerged that differentiated the three groups, _ = .38, _2(16) = 45.6, $p<.001$. The first function separated the ASD group from the other groups with rotating objects and prolonged gaze having the highest loadings. The second function separated the DD group from the other groups with banging objects loading highest. Together, the two functions correctly classified 76% of toddlers with ASD, 75% of toddlers with DD and 80% of TD toddlers.
Simultaneous consideration of spontaneously initiated eye contact and showing in addition to the exploratory behaviors led to correct classification of 95% of toddlers with ASD and 88% of non-ASD toddlers.
Conclusions: In the second year, toddlers with ASD exhibit a profile of object exploration that differentiates them from TD

toddlers and toddlers with DD. They tend to rotate toys more frequently and examine toys visually for prolonged periods of time. Toddlers with DD engaged in banging objects more than toddlers in the other groups. These three behaviors (rotating, prolonged gaze, and banging) classified toddlers into three groups with a relatively high level of accuracy. Consideration of adult-directed social behaviors (eye contact, showing) further improved the fit of the model. These results suggest that characteristics of object exploration during a brief solitary play session can serve as red flags and aid the diagnostic process.

116.005 The MANIFESTATION of CORE Features of ASD in African-American and Latino CHILDREN. A. Hall*[1], R. K. Abramson[2], S. Ravan[2], M. L. Cuccaro[3], J. Gilbert[4], M. Pericak-Vance[4] and H. H. Wright[2], (1)*Univ. S. Carolina Sch. Public Health*, (2)*University of South Carolina School of Medicine*, (3)*University of Miami*, (4)*University of Miami Miller School of Medicine*

Background: Very little has been written on the manifestation of autism spectrum disorder (ASD) in minority populations. Previous studies of autism in African Americans have focused on differences in clinical practices and service utilization (Mandell and Novak, 2005). For instance, Mandell et al. (2002) reported that relative to Caucasian children, African American children are more likely to be diagnosed significantly later. There also has been some research to suggest the prevalence rates ASDs are similar in African-American and Caucasian populations. While the literature has been sparse on ASDs in African-Americans, it has been relatively silent on Latinos. This study examines the symptomatology of Caucasian, African-American and Latino children diagnosed with an ASD as reported on the ADI-R.

Objectives: The purpose of this study is to determine if the core features of ASD are expressed differently in three racial/ethnic groups.

Methods: The sample consisted of 275 participants (African-Americans=40, Latino=22, white = 213). The participants were enrolled in a larger genetic study of ASDs. Parents completed the ADI-R to confirm the diagnosis of ASD.

Results: A MANOVA was performed to determine if the was a significant differences between African-American and Latino children's ADI-R scores. The results indicated there were no main effects of race on any of the ADI-R Social ($F_{(1,62)}$=1.348, p=0.250), Communication($F_{(1,62)}$=2.149, p=0.148), and RSB ($F_{(1,62)}$=1.265, p=0.265) domains. Thus the African-American and Latino groups were collapsed into a single group (non-white). Another MANOVA was performed to determine if the was a significant differences between the non-white group and the Caucasian group. The results indicated there were no main effects of race on the ADI-R Communication and RSB domains. However, there was a significant man effect for race on the Social domain score, $F_{(1,274)}$=4.621, p=0.032. To further clarify this finding, a one way ANOVA was performed on the Social domain subscale scores B1 (use of nonverbals for social regulation), B2 (peer relationships), B3 (shared enjoyment), and B4 (socio-emotional reciprocity). The ANOVA indicate that there are significant differences between the races on the B2 scores ($F_{(1,274)}$=5.548, p=0.019) and the B3 scores ($F_{(1,274)}$= 4.670, p=0.032). African-American and Latino parents reported their children had greater difficulty with developing peer relationships and shared enjoyment than their Caucasian counterparts.
Conclusions: The findings of this study suggest two of the core features of ASD (communication and repetitive behaviors) are manifested similarly in ethnic minority groups and Caucasians. African-American and Latino parents reported greater social deficits in their children than Caucasian parents. This finding raises an interesting question, do African-Americans and Latinos with ASD have greater social deficits than Caucasians or is there something about the culture of these two groups that places a greater importance of social interaction thus the social deficits found in ASD are rated as a greater deficit? More research in this area is needed to further examine this finding.

116.006 Oxytocin Increases Empathic Accuracy in Healthy Adults Who Endorse Traits of Autism. J. Bartz*[1], J. Zaki[2], N.

Ludwig[1], A. Kolevzon[1], N. Bolger[2], E. Hollander[3] and K. Ochsner[2], (1)*Seaver Autism Center for Research and Treatment*, (2)*Columbia University*, (3)*Albert Einstein College of Medicine*

Background: Autism spectrum disorders (ASD) are marked by impairments in social behavior and social cognition. To date, no pharmacological candidates have been identified to specifically target the social domain in ASD. Oxytocin—a neuropeptide implicated in affiliation and aspects of social cognition in animals—is a novel candidate that may hold promise for treating social deficits in ASD. Indeed, intranasal oxytocin (OXT) was shown to facilitate mental state attribution on the Reading the Mind in the Eyes Test in healthy males; although intriguing, it is unclear whether OXT would facilitate more complex, dynamic social cues that people typically encounter in everyday life. Performance on simplified social cognitive tasks does not consistently predict severity of social impairments in ASD, and interventions that produce improvements on these tasks do not necessarily translate to improved social functioning. A critical step in assessing the therapeutic potential of IN-OXT for ASD is employing an ecologically valid proxy for real world social cognition.

Objectives: We aimed to investigate whether intranasal OXT facilitates Empathic Accuracy, a novel, ecologically valid measure of complex social cognition in healthy males. Additionally, we investigated whether individual differences in ASD traits predict response to OXT.

Methods: To date, 27 healthy men completed participation in this double-blind, placebo-controlled, cross-over challenge. Participants received intranasal OXT/placebo; 45-minutes later we administered the EA task in which participants watched and listened to short videos of targets discussing positive or negative autobiographical events, and provided continuous ratings of how positive-negative the target was feeling. These ratings were compared to actual target ratings of target affect. EA was measured as the time-series correlation between perceiver and target ratings. Autism traits were assessed with the Autism Spectrum Quotient (AQ).

Results: Mixed-model analyses showed that participants endorsing few autism traits performed well on the EA task whether on placebo or following OXT. By contrast, participants endorsing many autism traits performed more poorly on placebo than their lower AQ counterparts, but, critically, they showed the greatest improvement from OXT—indeed, on OXT, their performance was indistinguishable from their lower AQ counterparts.

Conclusions: Using an ecologically valid EA task, we found that OXT eliminates deficits in the accuracy of interpersonal judgments in adults endorsing autism traits. This research suggests that 1) the EA task is sensitive to the social cognitive deficits implicated in ASD, and 2) that intranasal OXT may have therapeutic potential for treating complex, more naturalistic social cognition. That OXT selectively improved EA for participants endorsing autism traits highlights the promise OXT holds for treating social deficits in ASD.

116.007 Development of a Method to Study Brain Mechanisms for Emotion Regulation During Social Exclusion and Rule Violation in Autism. D. Bolling*, N. Pitskel, K. A. Pelphrey and M. J. Crowley, *Yale University*

Background: Cyberball, a virtual ball-tossing game, elicits feelings of social exclusion, and requires emotion regulation in typically developing (TD) participants. Few studies have explored the effect of social exclusion on individuals with autism spectrum disorders (ASD), a population marked by impairment in social interaction. Adolescents with ASD playing Cyberball report arousal that is often discordant with resulting mood changes. Considering that autism is characterized by cognitive rigidity and preoccupation with patterns, one might predict that participants with autism would show increased emotional sensitivity and distress to rule violations. No studies have compared brain responses to social exclusion and expectancy violation in participants with ASD.

Objectives: Using a novel adaptation of Cyberball (Cybershape) with a shape-matching rule dictating the correct recipient of the ball, along with the original Cyberball, we aimed to develop a method for examining a

simple social interaction and related emotion regulation. During a functional magnetic resonance imaging (fMRI) scan of children, adolescents, and adults with and without autism, we aim to identify differences in brain responses to social exclusion compared to rule violation within and between participant groups.

Methods: Participants play Cyberball in alternating blocks of fair play and exclusion. In fair play, the participant receives the ball on one-third of the throws; in exclusion the participant does not receive the ball. Each participant also plays Cybershape in alternating blocks of fair play and rule violation. In fair play, the participant receives the shape one-third of the time; the shape rule is never broken. In rule violation, the participant receives the shape one-third of the time; but one of the players consistently violates the shape rule by throwing the shape to the wrong player. After playing, participants are given ten questions addressing emotional reactions to exclusion or rule violation.

Results: Data from 9 TD adults contrasting fair play to either exclusion or rule violation revealed a dorsal-ventral differentiation in medial prefrontal cortex (mPFC). Social exclusion activates ventral mPFC, posterior cingulate, and superior frontal gyrus, often associated with emotion regulation. Alternatively, rule violation activates dorsal mPFC, extensive lateral regions of the prefrontal cortex, and parietal cortex, which are often associated with conditional rule use and task switching. Having established this paradigm in TD adults, we are now running samples of children and adolescents with and without autism. In preliminary analyses, one child (age 12) with ASD had similarly located brain activation to TD adults in both games. Concordant with our hypothesis, this participant showed greater brain activation to rule violation in the aforementioned regions compared to social exclusion. Adolescent ASD and TD participants have shown a negligible difference between brain responses to rule violation versus fair play, suggesting a decreased sensitivity to rule violation in this age group.

Conclusions: The discussed paradigm uses fMRI to study brain regions engaged in emotion regulation during social exclusion or rule violation, and can be used to study participants with and without autism. Furthermore, self-report measures will explore a potential correlation between neural and emotional responses to social exclusion and rule violation.

116.008 Moderating Effect of Temperament On the Relation Between Symptom Severity and Age of First Parental Concern: A Retrospective Study. K. E. Ono*[1], H. A. Henderson[1], L. Mohapatra[1], C. Hileman[1], N. Kojkowski[1], M. Jaime[1] and P. C. Mundy[2], (1)*University of Miami*, (2)*UC Davis*

Background: There is a great deal of variability in the age at which children are formally diagnosed with autism, likely due, in part, to the heterogeneity of ASD presentation. ASD specific behaviors (i.e., symptoms) and non-syndrome specific factors (i.e., temperament) may contribute to the age at which parents first become concerned about their child's development. This study is a retrospective investigation of how symptom severity and temperament relate to age of first concerns. Objectives: To identify the unique and combined effects of syndrome-specific and non-syndrome specific factors on parents' retrospective reports of the age when they first had concerns about their child's development. Methods: Preliminary analyses included 58 higher functioning children with autism (HFA; 8-16 years of age). All children had a community diagnosis of autism, a verbal IQ greater than 70 on the WISC-IV, and met diagnostic criteria on 2 out of 3 diagnostic measures (ASSQ, SCQ, ADOS). Parents completed the Social Communication Questionnaire (SCQ), Autism Spectrum Screening Questionnaire (ASSQ), Early Adolescent Temperament Questionnaire (EATQ), and a subset of items from the Autism Diagnostic Interview-Revised (ADI-R). Three hierarchical regression models were conducted to examine the relations between (1) SCQ total symptom severity, (2) one of the three EATQ factors (Surgency, Effortful Control, or Negative Affect), and (3) the interaction of symptom scores and temperament on parent-reported age of first concern in months on the ADI-R (ADI-R #2).

In each analysis, age of first spoken word (ADI-R #9) was entered in the first step as a control variable. Results: Across all three models, SCQ predicted first concerns in months, in which greater symptom severity related to earlier age of concern, B=-.76, t(56)=-2.13, p=.037. However, Negative Affect was the only temperament variable that significantly contributed, over and above the effects of symptom severity, R2change=.09, F(3,55)=3.48, p=.02. In addition, the interaction of SCQ and Negative Affect significantly predicted age of first concern, R2change=.01, F(4,54)=2.69, p=.04. The significant interaction was probed using guidelines provided by Aiken and West (1991). The regression of Negative Affect on ADI-R was examined at different levels of SCQ (± 1 SD and the mean). Each slope value was tested to determine whether it was significantly different from zero. Results showed that only the slope of the regression at -1 SD of SCQ was significantly different from zero, t(54)=-2.29, p=.026. That is, Negative Affect was particularly important for indicating earlier concerns for children with low levels of symptom severity. Conclusions: The results of this study corroborate recent prospective findings from Garon et al. (2009), which reported that diagnosed ASD-sibs displayed low levels of positive affect, high levels of negative affect, and difficulty controlling attention, compared to a control group and ASD-sibs whom did not receive a diagnosis. Together these findings suggest that high levels of Negative Affect may be an early marker of ASDs, particularly in children showing lower levels of classic ASD symptoms. This emphasizes the importance of examining non-syndrome specific factors, such as temperament, in the study of individual differences in the detection and presentation of ASD.

117 Innovative Technologies Demonstration Session

117.001 1 Male Teens with Asperger's Syndrome and Nonverbal Learning Disorder Learn about Stress and Its Physiological Signs.

D. A. Lucci* and D. S. McLeod, *Massachusetts General Hospital*

Background: It is well documented that stress management is an important life skill for individuals with AS and NLD. Often these individuals have heightened levels of stress and lack an awareness of the causes and the physiological signs. Successful efforts to address these concerns would likely lead to increased self-management of stress and ultimately healthier lifestyles and better emotional functioning.

Objectives: To demonstrate that, through the use of technology (Symtrend/Apple iTouch) and direct instruction about stress, teens with AS and NLD would increase self-awareness in recognizing their personal stressors and physiological signs of stress.

Methods: Nine adolescent males: 8 diagnosed with AS and 1 diagnosed with NLD, ADHD and Sensory Integration; ages 14.6 – 16.6 with a mean age of 15.1, each had average to above average IQs on the WISC-IV. Each participant was enrolled in a therapeutic summer program. They were assigned to one group staffed by two adult counselors. Boys were admitted through an interview and submission of the following documents: school records, psychological reports and completion of our social checklist and the Walker-McConnell Scale of Social Competence and School Adjustment.

Instruction regarding stress took place regularly. Teens had multiple opportunities throughout the day to rate themselves on multiple variables related to stress. They were taught ten physiological signs of stress such as: tension in chest, perspiring etc., fifteen different relaxation techniques (e.g. deep breathing, yoga, etc.) and fourteen different stressors (e.g. change in routine, being teased, etc). They recorded their experience of stress by indicating their stressors and physiological signs by using an Apple iTouch. Staff concurrently recorded their own perspective on each teen for comparison purposes.

Data was collected across 5 settings (Start of Day, Morning, After-Lunch, Afternoon and End of Day) and during specific activities (e.g. Science of Me, Social Thinking Group etc.). Each setting and activity had its own set of data collection questions.

Results: Direct teaching and the use of technology did increase self-awareness on several dimensions of stress. Correlations

were computed to evaluate teen recordings on stressors and physiological signs. The physiological indicators of stress (e.g. stomach pain, tension in back/arms, neck/head/jaw and feeling hot) were positively endorsed where as: shortness of breath, feeling cold, tension in chest, trembling and perspiring were not frequently endorsed. The stressors of perseverative thinking, negative self-thought, black & white thinking, thinking I'm stressed and experiencing something new were positively correlated with these physiological signs. Interpersonal Stressors (e.g. argue with a peer) were negatively or not-significantly correlated with physiological signs.

Conclusions: Direct teaching and technology did enhance teens' understanding and self-awareness of stress. Further analysis will need to be conducted to determine if these physiological signs are representative of individuals with AS or just this group and if being self-reflective about one's signs of stress can be broadened to include interpersonal stressors.

117.002 2 Virtual Reality Based Social Interaction for Children with Autism: Implications for Physiological Response. U. Lahiri*, K. C. Welch, Z. Warren and N. Sarkar, *Vanderbilt University*

Background: Social communication is thought to represent a core domain of impairment in children with Autism Spectrum Disorders (ASD). Utilizing novel technologies for assessment and intervention in this domain is a promising area of new research and may help address current limits of available interventions. In this capacity, physiological cues concerning social anxiety can provide powerful tools in developing specific interventions that promote complex social interactions without necessitating insight into and the ability to accurately report these experiences. Despite technological advances, work on systems that can systematically manipulate specific aspects of social interactions and identify the physiological responses indicative of affective states of this population is still at its infancy.

Objectives: In the present study, we developed a Virtual Reality (VR) based system that systematically manipulated social parameters during interactions and examined affective and physiological variation in response to this manipulation.

Methods: Thirteen pairs of age-matched children with ASD and typically developing (TD) children (age 13-18 years), participated in this study. VR-based social interactions were designed to project virtual human characters (avatars) who displayed different eye-gaze patterns and stood at different distances while telling personal stories to the participants. We measured physiological responses (cardiovascular (ECG) and electrodermal (EDA) signals) via wearable biofeedback sensors and collected a clinical observer's report on the levels of affective state (e.g., anxiety) for each participant who completed two 1.5-hour sessions. The social parameters of interest, eye-gaze and social distance, were examined in a 4x2 design. Four types of eye-gaze (*direct*, *averted*, *normal-while-speaking*, and *flip-of-normal*) dictated the percentage of time an avatar looked at the participant. Two types of social distance, termed *invasive* (1.5ft away) and *decorum* (4.5ft away), characterized the avatar-to-participant distance. Subjective reports and physiological data collected during the task were analyzed to examine the affective and physiological variation in response to social parameter manipulation.

Results: The ASD group's physiological signals showed significant changes to trials rated as eliciting "low anxiety" (LA) versus "high anxiety" (HA). The TD children also showed significant physiological reactions to experimental stimuli for LA and HA trials in similar and different ways than their ASD counterparts. Both ASD and TD groups had significant increases in EDA (e.g., galvanic skin response), with a stronger variation for ASD between LA and HA for Invasive social distance and varying eye gaze. The experiment condition of Averted eye-gaze with distance varying elicited significant increases in ECG (e.g., Pre-Ejection-Period) for ASD but not the TD group.

Conclusions: The results show that the VR system elicits variations in affective ratings and physiological responses to changes in social experimental stimuli for ASD and TD children. This research allows comparative

analysis between ASD and TD groups and may enhance our ability to understand the specific vulnerabilities in social communication of children with ASD. Work incorporating adaptive physiological monitoring into an expanded set of VR-based social interaction utilizing machine-learning mechanisms aimed at exploring specific social communication and sensory vulnerabilities of children with ASD is underway.

117.003 3 Visualizing Multi-Syllabic Speech with Computers for Language Therapy. J. Hailpern*[1], K. Karahalios[2], L. DeThorne[1], J. Halle[1] and J. Lohrens[1], (1)*University of Illinois at Urbana Champaign*, (2)*University of Illinois at Urbana-Champaign*

Background: During the typical development of a child, speech and communication skills appear to unfold effortlessly. For many children with ASD these basic skills remain a lifelong struggle. Without treatment, speech skills, as well as other forms of interpersonal interaction, may be substantially impaired (Lovaas, 1977), leaving individuals with limited means of communicating basic wants and needs. Computer based visualization systems have provided users with new and faster ways to understand large quantities of complex data (Heer 2007). Work on Awareness Displays showed the benefit of abstract representations and their ability to provide continuous streams of data to users about their world. Visualizations have also impacted teaching of complex concepts (Leung 2006) through visual and interactive representations. Our approach to visualizing audio departs from traditional waveform or spectrograp by using a simpler perspective. With perfect speech recognition out of technical reach, much can be learned by looking at the basic vocal parameters: volume, pitch, rate of speech, syllables, and history. Resarch on abstract graphical representation of voice and children with ASD have been promising (Hailpern 2009), though focusing on production not word formation/construction. Objectives: We are developing software that provides real-time visual feedback in response to vocal pitch, loudness, duration, and syllables. Such a re-interpretation of voice will allow for both a new understanding of one's vocalization by audio/visual feedback and will also allow for a tangible comparison to models presented by a clinician. In other words, a child with ASD will be able to both see and hear word models by a clinician, and then use real-time visualization of their own voice to assist in learning to appropriately produce multi-syllabic targets. Our interfaces reward behavior: when children produce an accurate response, they are rewarded with an audio and graphical reward. Methods: We will create software tools to facilitate speech acquisition through implementation of the Task Centered User Interface Design (TCUID) process (Lewis & Rieman, 1994). This process involves working with children with ASD for the full development phase, to emphasize building what the intended users demonstrate they need. In effect, the users become part of the development team. This design will help us design and develop software that accounts for the needs and strengths of 3 groups (speech delays, ASD, and typical children), and determine what aspects of the computer software are most universally understood. Results: This project is currently in progress. The focus of this poster will be upon the fully functional software and it's design. The experiment is slated to begin in January. Conclusions: The aim of this project is to develop, implement, and measure the effectiveness of software tools for facilitating multi-syllabic speech production in children with speech-language disabilities, specifically low and moderate functioning children with autism. In addition to the novel software and empirical data we plan to generate, this cross-disciplinary project will provide an innovative and important approach to developing treatment for children with speech and language disabilities.

117.004 4 Cold Probe Testing Tools for Autism Center. R. Lin*[1], G. D. Abowd[1], R. Arriaga[1] and A. Shillingsburg[2], (1)*Georgia Institute of Technology*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta*

Background: Therapists use a variety of methods to teach skills to children with Autism Spectrum Disorder. Many of these methods require extensive reward protocols. Cold probe testing is a method by which

therapists determine the level a child has mastered a skill without any incentives. At the Language and Learning Clinic of a metropolitan area autism center, the first 15 minutes of therapy are spent assessing the status of every skill that is in treatment using this method. The therapist uses a Cold Probe Sheet to ascertain if a skill is mastered. If a skill is mastered then it is moved into maintenance mode but if it is not then it stays in treatment. Information from this sheet is manually collected and later entered into the computer. The data is then analyzed using a standard spreadsheet program. The current process has a number of limitations. First, it is time consuming for therapists to transfer the data from paper to excel spreadsheet. Second, errors can occur when transferring data from manual to digital format. Finally, the clinical supervisor can not access the patients' results until all of the therapists have input data.

Objectives: The goals of this study were to 1) develop an automated method to process the information collected from the cold probe sheet and 2) automatically transfer the data into spreadsheet.

Methods: We used a human computer interaction perspective to understand the users'needs, this included interviews with therapist and their supervisor. The stake holders were also involved in design cycle. Given their needs we decided to use a digital pen to collect data entered into the cold probe sheet using handwriting recognition technology. Prototype and evaluation cycles were carried out simultaneously. When the system was first deployed, we studied two different groups; one used the new system; the other used the standard manual routine.

Results: The initial handwriting solution had some problems, and the system currently runs a modified version of HWR. This was designed based on semantic context. Our system has a number of strengths. First it maintains treatment practice. The only change is that the therapists must "dock" the pen at least once a day. The new system is quick and automatic. The spreadsheet data easily integrates with other software used in the center (e.g., statistics package). It also provides additional information which may be relevant, such as the time stamp of data input. Initial qualitative data indicates that this system saves hours of time in everyday practice. Another interesting finding is that the system helped to regulate the behavior of the therapists. Therapists are now aware that the system needs discrete symbols and as a result they use better "penmanship" when completing the cold probe sheet.

Conclusions: Overall, the system seems to have helped the therapists in the autism center to reduce their work load and mistake ratio during data entry. In addition the visualization function helps teachers to understand the data they collect. Based on the current system, we will introduce some data mining function in the future.

117.005 5 An Investigation of Parent's Ability to Report Problem Behavior. N. Nazneen[1], Y. Han[1], R. Arriaga[1], G. D. Abowd*[1], N. Call[2] and A. Findley[2], (1)*Georgia Institute of Technology*, (2)*Marcus Autism Center*

Background:

Direct observation is a powerful method for problem behavior assessment. However, it can be costly, intrusive, and it may cause behavior reactivity. An alternative method of observation is video recording, but it can generate a large amount of data which is expensive to manually analyze. A practical approach is selective archiving [Hayes & Abowd, 2008], where a trained observer signals the recording of problem behaviors. For a wider population of observers, for example parents at home, it is initially critical to determine the quality of the data gathered through selective archiving. We report the findings from a study that evaluated the effectiveness of this approach with parents in the home environment. We developed a robust multi-camera system, CRAFT (Continuous Recording and Flagging Technology), which collects several hours of continuous digital video and links it to problem behavior instances identified by parents through a button click on a remote control.

Objectives:

The aims of the study were to validate parent's ability to signal their child's problem behavior and to establish baseline

capabilities of parents as data collectors. We also wanted to investigate the requirements and potential capabilities of CRAFT.
Methods:
In this study, we recruited six families, each with a child diagnosed with a developmental disorder. Participant families either belonged to a clinical intervention program or a home-based treatment program of a severe behavior clinic. A trained observer from the clinic visited each home and installed CRAFT. Before the deployment, the trained observer and the parents had a discussion to determine the target problem behaviors that will be the focus for parent identification. Up to four cameras were mounted based on the parent's ranking of where problem behavior was more likely to happen. A laptop collected the data from the cameras. Parents were instructed to click a button on the remote every time they observed the onset of a problem behavior. After a day, the trained observer went back to collect CRAFT. The observer independently coded the videos in their entirety and identified all instances of target behaviors. Once the ground truth had been established, it was compared to the annotation data obtained from parent "clicks".
Results:
On average, 2 cameras were deployed in each house for approximately 16 hours. Results show that out of 19 verifiable problem behaviors, parents correctly identified 10 and missed 9 instances of problem behaviors. Out of 28 verifiable parent annotations, 18 were false indications. The precision of parent annotation is 0.35 and recall is 0.53.
Conclusions:
Results suggest that parents falsely indicate a high occurrence of target behaviors when it is not present and miss true instances. Future research will address the role of parent education by examining the effect that training has on identifying target behaviors. In addition, given that many severe behaviors occur with high intensity but low frequency, data will be collected over longer periods.

117.006 6 Automatic Classification of Parent-Infant Social Games From Videos. P. Wang*[1], T. L. Westeyn[1], G. D. Abowd[1] and J. Rehg[2], (1)*Georgia Institute of Technology*, (2)*Georgia Tech*

Background: Parent-infant social games, such as peak-a-boo and patty-cake, play important roles in the early detection of autism spectrum disorders. When studying an infant's social ability, psychologists assess his social behaviors by *in situ* observation or behavior analysis in home movies. Current approaches on video-based behavior assessment rely on manual searching of relevant behaviors and manual scoring of the behaviors, such as the frequency of playing peek-a-boo, the diversity of social interactive gestures a child can perform [Colgan et al. 2006]. This procedure is time-consuming and labor-intensive. We aim at developing computer vision techniques to automate video filtering and behavior coding.

Objectives: Develop algorithms that automatically classify social games from unstructured videos. It has the potential to automatically count the types of games a child can play, and their frequencies, and summarize the trajectories a child behaves in the intervention programs.

Methods:

Social games are characterized as repetitions of the dyadic interactions, with a range of permissible variations. In the previous work on automatic retrieval of social games from unstructured videos, social games are modeled as quasi-periodic events in videos and the detection of quasi-periodic patterns indicate the existence of social games. In this work, we use the extracted patterns as training examples, and apply Support Vector Machine (SVM) to recognize different types of games. Each pattern is represented by the histogram of the visual words that belong to its ith occurrence. Our method of collecting examples has two advantages. First, various sequential stages of a game are automatically collected without any human annotations; Second, one video of a social game gives many training examples with class labels, which enables fast collection of a large corpus training/testing data, a essential element in supervised learning methods.

Results:

We have collected two video datasets: 1) about 40 minutes of 5 adult dyads playing toss-the-ball, roll-the-ball and pattycake games in different environments; 2) 85 minutes of 3 parent-child dyads playing freely in a laboratory setting (other games in addition to the above three games are played). 2/3 of dataset 1 is used for training, and the rest 1/3 data is used for testing. Our classifier achieves a recognition rate of 94.44% for 18 pattycake sequences, 81.25% for 16 toss-the-ball sequences, and 92.31% for 13 roll-the-ball sequences. We then apply the learned SVM classifier to dataset 2. It achieves an average recognition rate of 61.41% on the parent-child play examples. Our future work includes expanding our game collection, and refining the representation of the pattern to increase its discriminative power against other games.

Conclusions:

We have presented a method to describe the quasi-periodic patterns that are automatically extracted from social games, and to build a game classifier with the representations. Social games, as the earliest form of social interactions in infancy, constitute a rich source of behavioral data that is not only useful for psychologists, but also amenable for computer vision analysis. Our work continues demonstrating the potential impact that computer vision techniques may impose on behavioral science.

117.007 7 A Mobile Social Compass. M. Tentori*[1], L. Boyd[2] and G. R. Hayes[3], (1)*University of California, Irvine (UCI)*, (2)*North Orange County Special Education Local Plan Area*, (3)*University of California, Irvine*

Background: Social Stories can be tools for teaching social skills to children with autism. They can increase understanding of and suggest appropriate responses to confusing situations. Story-based interventions allow teachers to go beyond teaching basic social skills and include issues related to how the situational context can change in an ongoing social interaction. Social Compass is an intervention package that uses stories and visual cues that, like a compass, serve to "steer the child in the right direction". For instance, in one lesson, children practice how to determine the appropriate distance between them and other people. The visual cue for this lesson is a compass that draws concentric circles to represent the relationship of a child with another person distinguishing from strangers and friends. The success of this therapy lies in how the children might use the newly learned skills outside the classroom. However, there is currently limited support for this kind of mobile, dynamic instruction. Thus, we have designed and developed innovative computing technologies to empower the Social Compass curriculum outside classrooms.

Objectives: Design and implement a mobile social compass to provide through augmented reality technology social cues to help children with autism (CWA) improve social interaction skills.

Methods: For five weeks, we video recorded fourteen CWA to understand the problems they faced when interacting with others. Researchers recorded each child during recess, lunch, or while attending classes for an average of fifteen minutes per day. We also conducted interviews with three of their teachers and a focus group with the immediate social network of the children. Finally, following a user-centered approach, we developed design requirements and scenarios that were later used to iteratively develop the Mobile Social Compass system.

Results: We found out that shared interests of children and how close they are from each other could be used to guide them to maintain appropriate personal space, instant reply and determine to whom interact with. The Mobile Social Compass is a SmartPhone augmented reality application that leverages this relationship to provide children with social cues to help them initiate social interactions, keep them engaged when appropriate, and end interactions smoothly. For example, after learning to use the compass metaphor and symbols in therapy, a child who likes to play chess might consult his Mobile Social Compass and find friends who are currently playing chess. This information is highlighted in the child's application through the compass visual cue. When he approaches the children playing chess, the system gives him social

cues to help him start an interaction. Through this new system, we also enable new ways of keeping records by automatically logging all interactions with the system, which can enable tracking of progress and understanding of the impact of the social compass interventions outside classrooms.

Conclusions: We have designed and developed a mobile system to help CWA improve their social skills outside classrooms. This system augments an existing successful curriculum, called the social compass. We will evaluate this system during summer school to explore its impact on current practices.

117.008 8 Demonstration of a Collaborative Interface to Promote Positive Social Interaction Skills for Children with Autistic Spectrum Disorder (ASD). E. Gal*[1], N. Bauminger[2], M. Zancanaro[3], D. Tomasini[3] and P. L. Weiss[1], (1)*University of Haifa*, (2)*Bar Ilan University*, (3)*Bruno Kessler Foundation*

Background: While various Computer Assisted Instruction tools have been studied, and 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, it has been demonstrated that computer based interventions and virtual environments offer a useful tool for social skills training in children with ASD.
Objectives:

We are investigating a paradigm implemented on the Diamond Touch (DT) table, a Shared Active Surface (SAS), in order to enhance social interaction within children with ASD.

Methods: The DT was originally prototyped by the Mitsubishi Electronic Research Laboratory and is now commercialized by CircleTwelve Inc. 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. 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 to support applications that either completely or partly enforce collaboration.
Results:
In this session we will present two applications of the DT ("StoryTable and "Join in") aimed at enhancing social interaction of children with ASD. In the StoryTable application, pairs of children 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 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 and improve social skills.
More recently we have developed a design framework for applying principles and techniques based on Cognitive Behavioral Therapy (CBT) to implement scenarios that support the development of social skills in children with ASD. One example is "Join In", a game played by two users who must jointly move a basket beneath apple trees by simultaneously touching and dragging on it. The level of difficulty can be graded and complexity can be enhanced. Prior to playing "Join In", the scenario includes clarification of the concept "collaboration"; the children are exposed to a series of solutions to the problem of how to best gather the apples (e.g., call for help from an adult, not gather the apples at all) and are challenged to chose the "best" solution. The children are gradually made aware of the advantages of working together to solve the problem. Once this concept is clarified, the application itself enforces collaboration and further emphasizes its benefits.

Conclusions: We will demonstrate how the "StoryTable", and "Join In" are used to enhance socials skills of children with ASD.

117.009 9 Wireless, in-Situ Measurement of Electrodermal Activity During Occupational Therapy. E. Hedman*[1], M. L. J. Miller[2], M. S. Goodwin[3] and R. W. Picard[3], (1)*Massachusetts Institute of Technology, The Media Laboratory*, (2)*Sensory Processing Disorder Foundation*, (3)*Massachusetts Institute of Technology*

Background: Occupational therapists strive to help children and adults better understand and regulate their physiological arousal. Physiological arousal is often assessed by electrodermal activity (EDA), a peripheral measure of the sympathetic nervous system. Traditionally, EDA is measured on the finger tips via electrodes wired to a computer. This equipment constraint can make measuring physiological arousal during active therapy sessions very difficult, if not impossible.

Objectives: iCalm – a wireless, comfortable sensor worn like a sweatband on the wrist or ankle – can measure EDA and physical activity responses over long periods of time in natural settings. The current study asked children to wear iCalm during Occupational Therapy (OT) to explore: (1) how usable iCalm is for children with sensory challenges while they participate in active therapy sessions, and (2) what relationships exist between EDA and specific OT interventions.

Methods: 22 children, ages 3-12, with a diagnosis of ASD, ADHD, and/or Sensory Processing Disorder wore iCalm for one-hour OT sessions (n=85 sessions). Repeated measurements (2 to 6 times for each child) provided internal reliability. EDA was synced with a video feed for post-event annotation. Parents and therapists were also repeatedly asked about iCalm's comfort, feasibility, and utility.

Results: All children in the study tolerated wearing iCalm for the duration of their OT sessions. Detailed visual analyses of the EDA data revealed that specific OT activities consistently increased or decreased children's physiological arousal. For example, a child gently rocked in a lycra swing repeatedly showed a sharp decrease in his EDA. An activity where a child listened to herself speak on a microphone that amplified her voice into earphones tended to increase her EDA. Temporal variation in EDA was also found across participants, with generally lower EDA in the morning than afternoon sessions.

Conclusions: Assessing physiological arousal during active OT sessions appears to have a number of benefits. First, we were able to identify when and how specific interventions impacted a child's physiological arousal, suggesting that EDA may be a useful measure of treatment effectiveness. Second, repeated measurements across participants at various times in the day suggest there may be optimal and suboptimal times to deliver OT, depending on whether the intent is to increase or decrease arousal. Finally, our qualitative results suggest that giving children, therapists, and parents live feedback from iCalm may also provide new methods to learn how a child with ASD's environment and internal state interact.

117.010 10 Enhancing Motivation through Computer-Assisted Instructional Practices. C. Whalen*, *TeachTown*

Background: Enhanced motivation has been demonstrated to improve skill acquisition, language, social behaviors, generalization, and decrease problem behaviors (e.g. Koegel, Koegel, and McNerney, 2001). This effect has been shown in numerous computer-assisted instruction interventions (e.g. Moore & Calvert, 2000). With increasing numbers of students with ASD, decreasing funding and resources, and increasing numbers of studies supporting its efficacy, CAI is becoming a viable option for schools and families to educate children with ASD. *TeachTown: Basics* is a CAI program that has demonstrated efficacy with parent (Whalen, et al., 2006) and teacher implementation (Whalen, et al., 2010). This program teaches language, academic-cognitive, adaptive, and social skills through computerized ABA (Applied Behavior Analysis), and includes a comprehensive curriculum of supplementary activities for the natural environment using *TeachTown Connection Activities*, based on naturalistic teaching strategies such as Pivotal Response Training (PRT).

Objectives: In this study, student motivation while using the computer was assessed using the *TeachTown: Basics* program.

Methods: Videotapes of 47 preschool and K-1 students with ASD were assessed by graduate student blind raters to measure motivation using the following behaviors: attention to task, positive affect, spontaneous language, joint attention, social initiations, and problem behaviors while using the *TeachTown: Basics* computer program and while interacting in a 1:1 teaching situation (either regular classroom activity or *TeachTown Connection Activities* with a teacher or other classroom staff. One half of the students were assessed at 3 months and again at 6 months to assess changes in behavior over time.

Results: Overall, students demonstrated increased motivation (based on increases in behaviors listed above) on the computer vs. other 1:1 teaching situations. This increased motivation did not significantly decrease at 6 months vs. 3 months.

Conclusions: This study supports previous research indicating that children with ASD may demonstrate increased motivation on the computer compared to other teaching situations. It also shows evidence for potential positive collateral effects using CAI, including enhanced positive affect and socialization with adults. Further research in this area will assess how motivation can be further enhanced using the computer and other types of media, and how enhanced motivation may lead to stronger intervention outcomes in the school environment.

117.011 11 Investigating the Role of Lateral Gaze and Peripheral Vision in Atypical Gaze at Human Faces with Children with ASD During Naturalistic Social Interactions. A. G. Billard*[1], B. Noris[1], F. Ansermet[2] and J. Nadel[3], (1)*EPFL, Ecole Polytechnique Federale de Lausanne*, (2)*University Hospital of Geneva*, (3)*CNRS and the University Pierre & Marie Curie, Pitie-Salpetriere*

Background:
Marked impairment in the use of eye-to-eye contact and attention to human faces (Trepagnier & Sebrechts, 2002) typical of Autism Spectrum Disorders (ASD) was reported to appear early in development (Osterling & G.Dawson, 1994). Recent efforts have thus been directed to document these atypicalities in very young children so as to gather information on the origins of deficits in social communication in the ASD.

Eye-tracking systems have proved particularly useful for systematically assessing gaze behavior of children with ASD in the above contexts. While the majority of these studies focused on foveal vision, recent evidence suggests that eccentric vision is used actively by children with ASD to optimize what is perceived with difficulty (Mottron_et_al., 2007).

Objectives:

To decipher the complementary role that foveal and excentric vision play when looking at faces, we explored eye-gaze peculiarities in children with ASD using a novel eye-tracking device that allows monitoring in conjunction foveal and peripheral vision and this in *naturalistic settings,* (in contrast to most eye-trackers that oblige the child to watch a computer screen). Studying eye-gaze behavior in a naturalistic social interaction was thought to be crucial, as social deficits of children with ASD are more pronounced in everyday settings than in experimental tasks (Klin_et_al., 2002a ; Nadel & Butterworth, 1999).

Methods:

A group of 13 ASD children (4 female, 9 male, age 3-10) diagnosed with DSMIV-R (APA, 2000) and ADI-R (Lord_et_al, 1994) and presenting mild to severe autism (M=40.4- 6.9, range=29-47) was compared to a group of 13 typically developing (TD) children, matched on developmental age (1.6–4.3 dev. Age), as measured by Vineland Adaptive Behavior Scales (Sparrow, Balla, & Cicchetti, 1984).

For the two groups of children, the task consisted of a 20-30 minutes play session with the child's caretaker (blowing soap bubbles and creating forms with play-doh) .

The child's gaze was monitored via a novel eye-tracking device consisting of a camera-on hat that records what the child can see and what (s)he actually looks at. Eye-gaze peculiarities were quantified by measuring the number, duration and frequency of gaze

fixations at the other person in both foveal and eccentric vision. For each of these measurements, the effect of group diagnosis (ASD/ control), gender, chronological age and developmental age was assessed through a four-way anova.

Results:

Children with ASD dramatically differed in their gaze strategy from the TD children. The ASD group looked less frequently ($p<0.000001$), less longer ($p<0.0002$) at the other and, when they did, they looked often through lateral glances, i.e. the face of the adult tended to appear on the periphery of their broad field of view. The differences were found to be independent from the severity of the disorder, chronological and developmental age and gender.

Conclusions:

These findings suggest that precise measurement of the frequency, duration and directionality of gaze towards faces are robust indicators of ASD and, as such, may provide quantified information to complement clinical observations and confirm the prevalent use of eccentric vision from fovea in children with ASD (Ritvo et al., 2009).

117.012 12 The Use of Ipod Technology as An Alternative and Augmentation Communication Device for Children with Autism. G. R. Mancil*, *University of Louisville*

Background: There is concern about the socially appropriate AAC devices for individuals with autism. Objectives: The purpose of the study was to determine the effectiveness and efficiency of the use of an iPod as an AAC device on increasing communication initiation and responses, decreasing aberrant behavior, and increasing spontaneous communication with children with autism. Methods: The subjects were referred by a local autism center that provides services for children with autism, their parents, and teachers. The subjects' diagnosis of autism 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 to use the iPod as an AAC device using milieu therapy procedures during routines in their respective schools. The researcher trained the teachers who then provided training to their respective students. Sessions were videotaped, coded, and then graphed using a multiple probe format. Results: The subjects obtained efficient use of the iPod AAC device within a 12-week period. Communication initiations and responses increased for all participants. Aberrant behavior concurrently decreased and latency to respond to a communication opportunity averaged between 2 and 3 seconds, which is consistent with neurotypical peers. Spontaneous communication also increased as evidenced by generalization to untrained settings occurred. Conclusions: Findings of this study show the utility of an iPod as an AAC device to simultaneously increase communication initiations and responses, decrease aberrant behaviors, and increase generalization to untrained settings and persons.

117.013 13 Using Social Mirrors to Teach Conversation Skills to People with Social Skill Deficits. T. Bergstrom*[1], K. Karahalios[1], M. Dixon[2] and S. Wayland[2], (1)*University of Illinois at Urbana-Champaign*, (2)*University of Maryland*

Background:

Many people with developmental disorders like Asperger's Syndrome (AS), high functioning autism (HFA), non-verbal learning disorder (NVLD), and pervasive developmental delay – not otherwise specified (PDD-NOS) have difficulty with conversational interaction: turn-taking, interrupting, conversational dominance, turn length and emphasis with vocal volume. Conventional intervention has focused on remediation by teaching, practicing, and then observing social skills. Few interventions occur *during* conversation. We use the Conversation Clock, a visual computer interface, to provide immediate conversational feedback.

The Conversation Clock creates a constant visual depiction of conversation based on personal microphone input: representing current volume as a bar, minutes as concentric rings, and speakers by color. This visualization is projected onto an easily visible circular table. The persisting

visualization of speech, silence, turns, and overlapping speech make concepts like interruptions and conversational dominance more salient in conversation. From this feedback, people can evaluate and change their behavior.

Objectives:

This study will analyze the effectiveness of the Conversation Clock, alongside conventional interventions, in modifying conversational skills of children with social skills deficits. A secondary goal is to accurately define who benefits most from this type of intervention by carefully characterizing our participants – their strengths, weaknesses, preferences and temperaments. We hope to move beyond diagnosis to a more comprehensive understanding of our participants.

Methods:

Participants are children and adults over the age of 14, diagnosed with AS, HFA, NVLD, or PDD-NOS. We assess participants using standardized tests: Test of Language Competence-Expanded; Detroit Test of Learning Aptitudes; Behavioral Assessment of Dysexecutive Syndrome; Kaufman Brief Intelligence Test and the Perceptual Learning-Style Preference Questionnaire. Nonstandardized assessments include: The Quick Scan (of Abilities and Challenges); Social Communication Skills Rating Form; an Interest Survey; and a Case History.

Each participant is paired with a typically-developing peer of similar age with similar interests. In our control condition, clinicians teach participants the rules of social interaction, give them a chance to practice those skills, and then analyze a video recording with the participant via a social autopsy. The experimental condition adds the Conversation Clock to provide immediate feedback.

During conversation sessions, pairs read and hear the beginning of a story and work to create three endings. Participants rank the endings from least to most favorite before describing them to the clinician.

Sessions follow the schedule:

- Assessments Familiarization (game)
- Pre-Intervention (no autopsy)
- Pre-Intervention (no autopsy)
- Pre-Intervention (no autopsy)
- Intervention (Half Control: Half Experimental)
- Intervention
- Intervention
- Intervention
- Intervention
- Post-Intervention (no Conversation Clock, no autopsy)

Results:

We will code participants on all the acoustic measurements collected to determine whether conversation more closely tracks normal dialog after the intervention.

We will show whether participants benefit from the Conversation Clock more than they do with conventional therapy. In addition, we hope to learn whether we can predict and/or characterize subgroups that will benefit most based on our pre-test assessments.

Conclusions:

Results of the study will add to the body of data concerning the conversational characteristics of children with social skills deficits and guide in the development of effective computer-interface interventions in treatment.

117.014 14 Comparison of Child-Human and Child-Computer Interactions for Children with ASD. M. P. Black*[1], E. Flores[2], E. Mower[1], S. Narayanan[1] and M. E. Williams[3], (1)*University of Southern California*, (2)*USC University Center for Excellence in Developmental Disabilities at Childrens Hospital Los Angeles*, (3)*Keck School of Medicine, University of Southern California*

Background: Children with autism spectrum disorders (ASD) exhibit qualitative and

quantitative differences in social communication. Interventions targeting such differences require intensive professional time and are often expensive. Interactive computer technology has the potential to provide a consistent and affordable way to elicit verbal and nonverbal social interaction in children with ASD. Animated computer characters when acting as social partners are referred to as embodied conversational agents (ECA). By adapting the design of the ECA to the specific needs of a child, ECAs could become a powerful tool for clinicians, therapists and teachers. The ECA platform allows for detailed analysis of behavioral patterns within a standardized situation, enabling researchers to study communication approaches and changes over time.

Objectives: In this pilot study, seven children diagnosed with autism interacted with a psychologist and an ECA. Our goal is to compare the children's verbal and nonverbal behavior between the two conditions (child-human and child-ECA) using our proposed multimodal audio-visual coding scheme. Our planned analyses will determine whether ECAs provide an engaging and socially stimulating interaction platform for children with ASD, and will help identify appropriate modifications to apply in future intervention studies.

Methods: Participants in the study were 7 children (6 boys and 1 girl), ranging in age from 5 to 9 years (mean age = 6.9 years). All were recruited from the Autism Genetic Resource Exchange (AGRE) database, and had been diagnosed with autism by AGRE researchers using the ADOS and ADI-R measures. The children each had short conversations (1-5 minutes) with both a psychologist and an ECA (separately). Their parent remained in the room throughout. The ECA, a teenage-looking boy named "Josh," moved his mouth and head while speaking pre-recorded utterances. The human and computer sessions were both scripted, and the ECA's responses were controlled by an engineer from an adjoining room. We recorded all interactions with multiple audio-video sensors. We developed a coding scheme to mark relevant social communicative cues of the children (e.g., prosody of speech, turn-taking in conversation, head orientation, use of pointing and other gestures, initiation of joint attention with their parent). These codes, as well as direct quantitative measures derived from the audio and video characterizing spoken and gestural behavior, are used to compare communicative behaviors for the child-human vs. child-ECA conditions.

Results: Six of the seven subjects were verbally fluent and engaged in interactions with both the psychologist and the ECA according to the study design. Therefore, we found that the ECA we developed was effective in eliciting natural communication with verbally fluent children with ASD. One of the subjects rarely used verbal language to communicate with the psychologist, parent, or ECA. We are currently coding and analyzing the multimodal data and will report differences between the two dyadic conditions at the conference.

Conclusions: We will discuss our hypotheses regarding modifications in the ECA to elicit social communication from children at varying levels of functioning within the autism spectrum, and conclude with future planned experiments. Work supported by Autism Speaks and NSF.

117.015 15 Training Social Problem Solving Skills in Adolescents with High Functioning Autism Spectrum Disorders (HFASD).

F. A. Boujarwah*[1], H. Hong[1], J. Isbell[2], R. Arriaga[1], G. D. Abowd[1] and L. J. Heflin[2], (1)*Georgia Institute of Technology*, (2)*Georgia State University*

Background:

Individuals with high-functioning autism spectrum disorders (HFASD) typically have deficits in socialization that interfere with their educational experience and quality of life. They require explicit instruction to acquire age-appropriate social skills. There is a paucity of research that includes adolescents with HFASD, but there are indications that they respond well to computer-assisted instruction.

Objectives:

To develop technology that can be used to teach effective problem solving by allowing

an individual to experience social situations and choose appropriate responses to unexpected events. Technology can also assist and support reflecting on those experiences, providing the individual with an opportunity to process information that can be recalled for later use. Finally, it can gather data to assess the individual's skill level and determine the difficulty of subsequently presented scenarios.

Methods:

A prototype made up of three scenarios was created. Each scenario involves the presentation of a social situation in which some obstacle arises (e.g. Your family is going to a new restaurant). The software then guides participants as they navigate the social situation and find an acceptable solution. Each step in the situation is presented with audio narration, text, and a picture. The scenarios differ in level of difficulty, and within each scenario the possible solutions vary in complexity. Once the student has found a solution they are asked to reflect on their decisions by recreating the social story using puzzle pieces that are placed in order on a timeline. Finally the story is played back to them. The users path through the software was logged by the system.

An exploratory study was conducted in a large metropolitan city with 8 males (age: 13-19 with HFASD). On the first day problem solving tests were administered (Test of Problem Solving 2-A (TOPS 2A) and the Social Problem Solving Inventory (SPSI)) to determine the participants' social problem solving competence. The following week the participants were asked to interact with the software and complete one scenario each day for three consecutive days. After completing each scenario the participants were allowed to play a computer game.

Results:

Only 2 participants were able to complete the standardized assessments. Despite this difficulty, all the participants were able to successfully complete both the experience and reflection components of all 3 scenarios in our system. Log data indicated that the choices the participants made lead for multiple paths to a successful solution to be explored. In addition, 3 of the 8 participants chose solutions that were considered to be more complex in each of the three scenarios, and all the participants chose a complex path in at least one scenario. Overall, all the participants responded positively to the system.

Conclusions:

The system enables adolescents with HFASD to practice an effective problem solving process. Participants in our study that were unable to complete standardized assessments of social competence were able to use our software with ease. In the future additional scenarios will be developed based on the observed and expressed needs of both educators and adolescents on the spectrum.

117.016 16 A Demonstration Measurement System Relevant to Autism Risk and Symptomatology: Continuous Non-Expert Ratings of Infant and Parent Emotion. D. S. Messinger*[1], J. K. Baker[2], S. M. Chow[3] and J. D. Haltigan[1], (1)*University of Miami*, (2)*University of Wisconsin-Madison*, (3)*University of North Carolina*

Background:

Studies of infant siblings of children with an Autism Spectrum Disorder (Autism Siblings) are concerned with early deficits relevant to autistic symptomatology. These deficits are typically subtle, suggesting the need for sensitive tools with strong face validity. Here we report on such a tool. The Continuous Measurement System allows non-experts to rate video records of behavior in time. The System can also be used for expert coding and is available for free download at http://measurement.psy.miami.edu/.

Objectives:

Examine the utility of continuous non-expert measurements in detecting differences in autism-related behavior.

Methods:

In the current study, 181 students with no specialized training continuously rated

negative-to-positive emotional valence using a joystick interface. They rated 20 Autism Siblings and 18 comparison siblings (six-month-olds) participating in the face-to-face/still-face protocol with their parents. Between 16 – 20 individuals rated each infant and each parent.

Results:

There was high concordance between mean ratings of affective valence and expert coding of infant and parent negative and positive facial expressions. During the still-face episode of the FFSF when parents are instructed to be non-responsive, Autism Siblings were rated significantly less positively that were comparison siblings, $t(25.94) = 2.62$, $p = .01$, Cohen's $d = .86$ (Baker et al., in press). During the still-face, Autism Siblings also exhibited reduced group variance in positive affect but greater variance in negative affect than comparison infant siblings.

Time-series analyses were used to explore infant-parent influence and self-regulation (auto-regression) during interaction (Chow et al., in press). There were no group differences in interactive influence. Instead, individual Autism Siblings exhibited higher levels of self-regulation than comparison infants. The effect was only evident the still-face and reunion episodes, i.e., during and after the perturbation introduced by asking the parent to be non-responsive (ps $< .05$). In other words, Autism Siblings were, on average, less emotionally perturbed by the FFSF procedure than other infants.

Conclusions:

Multiple, independent assessments by untrained raters can be used to efficiently measure key constructs relevant to autism risk. Findings replicated the well-established still-face effect and identified subtle risk associations consonant with results from previous investigations. Subtle differences including reduced mean levels of positive affective valence, and reduced variability of affective valence over time were evident among infants at risk for autism. These findings suggest that infant siblings of children with ASDs show relatively depressed but relatively invariant affect when they are not being engaged by their parents. The measurements have high face validity because they capitalize on the ability of human beings to respond to subtleties of behavior in a continuous fashion. The unique information offered by intuitive non-expert ratings is a potential alternative to complex and costly behavioral coding systems in studies of Autism siblings and, potentially, in studies of children and adults with ASDs.

117.017 17 Embedding Focused Interests Into Computer-Mediated Autism Interventions. R. R. Morris*, C. R. Kirschbaum and R. W. Picard, *Massachusetts Institute of Technology*

Background: Individuals diagnosed with autism spectrum disorder (ASD) often have intense, focused interests. These interests, when harnessed properly, can help motivate an individual to persist in a task that might otherwise be too challenging or bothersome. For example, past research has shown that embedding focused interests into educational curricula can increase task adherence and task performance in individuals with ASD. However, providing this degree of customization is often time-consuming and costly and, in the case of computer-mediated interventions, high-level computer-programming skills are often required. New technologies that automatically embed focused interests into interventions are sorely needed.

Objectives: Our goal is to create an open-source algorithm that automatically uploads user-specified content into an online intervention for individuals with ASD. To explore this approach in a natural setting, we evaluated components of our technology in a user study with six adolescents on the autism spectrum.

Methods: In our algorithm, users enter a description of a focused interest into a query box, and the results of a Google image search are returned. Our search method filters the images, eliminating pictures that are too small, large, or oblong to be resized properly. The remaining images are automatically resized and presented to the user as tiles in a new window. The user can

then select which images s/he would like to see incorporated into the software. Additionally, our method removes the background of some of the returned images, so that they can be more elegantly embedded into certain computer programs. Two females and four males on the autism spectrum participated in game-play sessions to test this technology. Two different games were created, and two versions of each game were presented (one with customizable content, and one without). After playing each game for two minutes, each child was given a choice to play any of the four games. They were shown tiled depictions of the four games and were told to point to the game they wanted to play next. All of the game content was selected before the experiment, and was based on the suggestions of each child's teacher. This was done because some of the children had limited verbal abilities and might not have been able to tell us about their preferred interests, and because we wanted to prepare our tiled depictions of the games in advance.

Results: Five of the six children chose to play one of the customizable games during the free-choice session. The child who did not choose one of the customizable games kept requesting another cartoon character instead. Without our prompting, she navigated to the query box in our game and began to type in the name of this character. We helped her update the game according to her preference, and then she played it quite happily.

Conclusions: Our algorithm was robust and was able to embed customizable content into each game. The study also highlights the value of customizable content that can be updated and altered at any time, especially at the request of the user.

117.018 18 Eyes up: Interactive Tangible-Digital Puzzles for Learning about Eyes. M. Eckhardt*, M. S. Goodwin and R. W. Picard, *Massachusetts Institute of Technology*

Background: Autism is a complex and heterogeneous condition that is typified by difficulty with social and emotional cue recognition and expression. These social-emotional processing differences make recognizing subtle social-emotional cues difficult for persons diagnosed with Autism Spectrum Disorder (ASD). In particular, people diagnosed with an ASD typically perform worse then neurotypical (NT) individuals in recognizing facial expressions, especially when recognition is dependent solely on information surrounding the eyes. This may be due, in part, to an aversion to eye contact and/or atypical scanning behavior of the face region by those with ASD. However, eyes provide a valuable source of social-emotional information during interaction. Therefore, it is important that we address these difficulties in recognizing these valuable signals by developing methods and tools to help people better recognize and understand these social-emotional cues.

Objectives: Our goal is to develop a physical, tangible-digital puzzle game, *Frame It*, that can be used by any child, with the purpose of facilitating teaching or therapy through playful interaction while recording play characteristics. In particular, we seek to develop a game that will be able to affect the visual-scanning behavior and expression recognition ability of children diagnosed with ASD. *Frame It* requires the player to construct a puzzle of a person's eye region and then assign an expression label to that region.

Methods: The development of *Frame It* was approached using a user-centered design methodology that included consulting with users, teachers, therapists and educational experts. Design and testing sessions were conducted with both ASD and NT children. We additionally conducted usability sessions with eight ASD and eight NT children, measuring several aspects of their experience with the novel game.

Results: Usability tests showed that *Frame It* was accessible by both groups, and interaction was enjoyable. Because of the game's ability to record play interaction, we were also able to gain quantitative insight. We found a significant difference in the number of pieces used while attempting to construct the correct puzzle from a set of multiple puzzles. We also found a significant difference in the spatial ordering of pieces during construction. In addition, we were able

to see a significant difference in correct expression labeling of the eye region, with the ASD group having more mislabels. Another interesting result found was that the ASD group completed more puzzles and had a lower average puzzle construction time than the NT group, despite manipulating more pieces during construction. This may suggest that the two groups used different strategies for solving the puzzles.

Conclusions: The user-centered design approach allowed for the development of a system accessible by a wide range of users, with varying physical and cognitive abilities. In addition, the designed system allowed for, and recorded, playful interaction. The recorded data set was used to reveal significant differences between groups, and highlights the usefulness of physically embedded computational devices. Future studies will explore the use of *Frame It* as a tool to affect the visual-scanning behavior and expression recognition ability of children with respect to other people's eye region.

117.019 19 Results From An RCT of FaceSay Software Games. C. Wimsatt*, *Symbionica, LLC*

Background: In vitro generalization of social skills - i.e. to another in vitro setting - have been reported in a number of RCTs of promising technology interventions. Generalization of social skills to everday life, however, has been limited to anecdotal reports. Even the often cited Bernard-Opitz study asks at the conclusion "whether behavior learned in the computer setting generalizes to the real setting...". In this RCT, the FaceSay HFA and LFA groups showed improvements in social interactions with peers in blinded playground observations (Hauck, 1995).

Objectives:
Aim 1: The primary aim of the study was to examine the effect of FaceSay on emotion and facial recognition skill development in children with an ASD. It was predicted that the intervention groups would improve both emotion recognition (Hypothesis 1) and facial recognition (Hypothesis 2) skills after the intervention.
Aim 2: The secondary aim of the study was to examine the impact of FaceSay on social behaviors in the natural environment. It was predicted that the intervention groups would improve in observed and reported social skills after the intervention.

Methods: Forty-nine children met the inclusion criteria of a prior diagnosis of ASD (DSM IV) and confirmation of the diagnosis using the CARS scale. Participants were grouped into High Functioning Autism (HFA, N=24; KBIT > 70) and Low Functioning Autism (LFA, N=25; KBIT < 70). Participants were randomized to either treatment (FaceSay) or control (Tuxe Paint). Participants attended 12 sessions over approximately 6 weeks at their school.

Outcome Measures:
Emotion Recognition: Ekman and Friesen static photos and schematic drawings of emotions
Facial Recognition: Benton
Social Validity: Parent SSRS
Playground Observation: Blinded research assistants observed each child interacting on their normal playground during recess for five minutes twice on two separate days at baseline and twice again after the intervention using the Social Skills Observation (Hauck, 1995).

Results: For all of the Hypotheses, separate ANCOVAs were run for the LFA group and the HFA group. For these analyses the independent variable was the group (training or control). The dependent variable was the post-test score, and the covariates were the pre-test score and KBIT score.
Hypothesis 1 - Improved Emotion Recognition LFA Results: $F(1, 21) = 4.52$, $p < 0.05$. HFA Results: $F(1, 20) = 29.31$, $p < 0.001$
Hypothesis 2 - Improved Facial Recognition. LFA Results: Not significant. HFA Results: Benton-Short form $F(1, 20) = 10.86$, $p < 0.01$, Benton-Long form $F(1, 20) = 4.67$, $p < 0.05$
Hypothesis 3 - Improved social interaction in natural environment: LFA Results for SSRS $F(1, 21) = 14.42$, $p < 0.01$ and Social Skills Observation, $F(1, 21) = 5.05$, $p < 0.05$. HFA results for SSRS $F(1, 20) = 4.36$, $p = 0.05$ and Social Skills Observation, $F(1, 20) = 13.61$, $p < 0.001$.

Conclusions: The HFA group improved more than the LFA group, but both FaceSay groups showed significant improvment in playground social interactions with their peers, where it counts, an important breakthrough for the students and the field.

117.020 20 Eliciting Social-Cognitive Behaviors in Children with ASD Using a Novel Interactive Animated Character. C. Samango-Sprouse*[1], C. Lathan[2], K. Boser[3], L. Georganna[4] and J. Hodgins[5], (1)*George Washington University*, (2)*AnthroTronix, Inc.*, (3)*Individual Differences in Learning, Inc*, (4)*WALT DISNEY PARKS & RESORTS*, (5)*Carnegie Mellon University*

Background: This study is the first attempt to quantify anecdotal reports by parents of children with ASD that the character "Crush," a part of the 'Turtle Talk with Crush' theme park attraction, elicits social-cognitive behaviors in ASD. The interactive animation approach builds on the Crush character as a co-participant in the human interactions, which has been shown in previous research to allow for the more immediate transfer of social behaviors to natural 'human' contexts.

Objectives: We investigated the hypothesis that interacting with Crush elicits social-cognitive behaviors and we studied key aspects of the Crush attraction that facilitate interactive behavior for social skills therapy in children with ASD.

Methods: All six participants (mean age- 4 yrs and 7 mos) had a clinical diagnosis of ASD and had no prior experience with the attraction. All children had less than 85 spoken words on the CDI and a mean T-score of 117 and 101 on the SRS and GARS-2 respectively. Children participated in one 12 minute show and one 3-5 minute "meet and greet" with the Crush character. The Crush actor, who operates the character remotely, receives extensive training on how to slow "pacing" for optimal audience responses and how to contrast voice modulation to create an engaging social atmosphere. The animation was shown on a 9 ft by 16 ft screen in a 200 person theatre.

Results: The results confirm that "Crush" can elicit social-cognitive behaviors in children with ASD including increased consistency of social greetings and referencing, joint attention, verbal and motor imitation, and initiation of motor planning and sequencing. Some examples include social smile, repetition of Crush's words or peers' responses, initiating response, pointing and tracking objects in Crush's tank, clapping/laughing, and imitating gestures. In particular, we found that two out of six subjects demonstrated a dramatic increase, over baseline reports, in social-cognitive behaviors such as motor or verbal imitation. We also found indications that the subjects may respond best in the group 'show' where they benefit from the heightened group arousal to the character and subsequently profited from observing and imitating their peers.

Conclusions: The initial results point to a method that combines interactive, engaging animation with the advantages of a group setting. The advantages of Crush over previous attempts which use (video) 'modeling' alone is that the skills are learned in a more naturalistic, fun, high-energy environment that increases arousal level for greater sustained attention and learning. These preliminary results suggest an alternative and creative mechanism to develop social-cognitive and motor learning opportunities for children with ASD.

117.021 21 Interactive Autism Network (IAN): Towards An Efficient and Responsive Online Research Infrastructure. P. Law*, C. A. Cohen and J. K. Law, *Kennedy Krieger Institute*

Background: Lack of efficiency in subject recruitment and data collection, and lack of public trust in the medical and research establishments, have historically compromised the pace of autism spectrum disorder (ASD) research, especially genetic/etiologic, therapeutic, and health services studies. Given the increasing prevalence of ASD and resulting societal burden, governments and non-governmental organizations have begun to invest in optimizing research efforts by enhancing research infrastructure and emphasizing collaboration among scientists, the community, providers and policy-makers.

Objectives: To demonstrate the potential and viability of an online system to collect extensive longitudinal information about

individuals with ASD and their families, provide the research community with a valid scientific dataset, link the dataset to other sources including clinical databases, recruit subjects for a vast array of research projects, involve the public in research priority setting, and educate the public about the importance of research.

Methods: IAN developed an online system consisting of a longitudinal research study and a community that fosters bi-directional exchange between families and researchers. The IAN study uses the Health Research Management Platform (HRMS) developed by Medical Decision Logic, Inc. Parents or guardians of individuals with ASD and independent adults with ASD use this platform to answer questions about themselves and their families, including the completion of standardized autism-related assessment instruments. The extensive data collected, along with appropriate subject consent, enables the project to provide recruitment assistance for U.S. research projects and a large longitudinal dataset internationally. A web-based authoring environment supports ongoing development based on the information needs and collaborative efforts of families and individuals with ASD, researchers, policy makers, and the therapeutic community. IAN hosts a website with interactive and community features that provides opportunities for the public to discuss and learn about ASDs and ASD research, fostering subject participation, community involvement, and researcher/community trust.
Results: From April 2007 to November 2009, the study consented 31,689 individuals with ASD and their families: 11,749 are children and 516 are adults diagnosed with an ASD. More than 230 research projects have applied for or are using IAN subject recruitment services or data. The IAN Community has over 14,000 members and is visited by approximately 1,000 people per day. Over 15,000,000 pages have been viewed. An information dashboard that supports policy decisions at a state level was developed in collaboration with the Missouri government. IAN has been funded by the National Institutes of Health to integrate its data with the National Database for Autism Research (NDAR), which will, in turn, link to other important research datasets. Two ongoing data validation studies of parent-reported data will be completed by the May 2010 meeting. IAN is currently funded to assist in the collection of biomaterials from 2400 families, doubling the number of available ASD individual samples worldwide.

Conclusions: IAN demonstrates that online research environments are feasible, and can have a powerful impact in facilitating disease-specific research and public knowledge in a short period.

117.022 22 Enhancing Social Interaction through Story-Telling Among High-Functioning Children with Autism. E. Gal*[1], P. L. Weiss[1], L. Lamash[1] and N. Bauminger[2], (1)*University of Haifa*, (2)*Bar-Ilan University*

Background: A deficit in social interaction is considered to be a major characteristic of children with Autism Spectrum Disorder (ASD). Recently a number of computer-based approaches have been used to facilitate social interaction in these children. In the present presentation we describe an intervention study aimed at enhancing social skills in children with HFASD based on an "enforced collaboration" paradigm.

Objectives: To examine whether an "enforced collaboration" paradigm enhances the ability of children with High Functioning (HF) ASD to interact in social situations. Specifically, we investigated whether this paradigm improved the children's cooperative skills, play behavior, pro-social behaviors, non-verbal communicative behaviors, play skills and decreased their repetitive behaviors.

Methods: *Instrumentation*. Circle Twelve's "Diamond Touch" table, a touch-and-gesture-activated device designed to support small-group collaboration, was used to implement the "enforced collaboration" paradigm. This technology is unique in its ability to identify simultaneous inputs from multiple users. The StoryTable, an application run on the Diamond Touch, was designed to require that some of the tasks be performed simultaneously by the children. *Participants* included 14 children with HFASD, aged 8-12 years, and with a verbal IQ above 80.

Procedures. The children were divided into seven pairs according their level of language as the major criterion. The intervention consisted of 12 30-minute sessions given over 4 weeks. Children participated in pairs to select a story background from a multimedia repository and composed a narrative while taking turns recording it via the StoryTable audio recorder. The "enforced collaboration" paradigm was implemented through the need to perform specific simultaneous functions (e.g., selecting a mutually acceptable background, playing back the recorded story). A moderator used Cognitive Behavioral Therapy techniques to teach basic collaboration concepts prior to each session.

All interactions and the pre and post tests described below were videotaped and behaviors were coded using the Social Interaction Observation which assessed cooperative skills and social interactions including social conversation and play as well as autistic behaviors.

The children were assessed prior to and following the intervention using one high technology task: (1) the collaborative puzzle game, a non-narrative, "enforced collaboration" task also implemented via the DiamondTouch table, and three non-technology tasks including (2) a board game version of the StoryTable task, (3) a collaborative construction game (MarbleWorks) and (4) a collaborative collage.

Results: There was improvement in three areas of social behaviors: (1) more initiations of positive social interaction with peers; (2) higher levels of shared play; and (3) lower frequency of autistic behaviors while using the StoryTable in comparison to the free construction game activity.

Conclusions: The results suggest that the "enforced cooperation" paradigm may: (1) serve as an environment that potentially meets the needs of children with HFASD, (2) have considerable potential for enhancing several key social behaviors, (3) help control the need that these children have to exhibit autistic behaviors, and (4) generalize to other tasks that require collaboration. This study provides a base for developing further technologies to enhance social interaction among children with ASD.

117.023 23 Randomized Study of Web-Based Teacher Coaching. R. A. Johnson*[1], L. A. Ruble[1], J. H. McGrew[2] and L. A. Jung[1], (1)*University of Kentucky*, (2)*Indiana University - Purdue University Indianapolis*

Background:

Research that provides scientific decision making in the selection and use of professional development models has the potential for major impact in both urban and rural areas of the U.S (Pianta, 2006). Access to specialists in ASD is problematic for rural communities, and this difficulty is exacerbated in rural communities that are geographically isolated and impoverished such as those in Appalachian Kentucky. The costs associated with professional development, consultation, and travel far exceed available resources.

Objectives:

The primary goal is twofold: (a) to test the preliminary effectiveness of a web-based teacher coaching or face-to-face teacher coaching intervention on child educational outcomes and (b) to examine teacher use and attitudes towards technology as a possible moderator of child outcome.

Methods:

Twenty special education teachers were recruited from South Central and Eastern Kentucky Participants were randomized into one of three groups: (a) placebo control, n = 7; (b) face-to-face coaching, n = 7; or (c) web coaching, n = 6. The participants in the two experimental groups will receive a manualized consultation intervention called COMPASS (Ruble & Dalrymple, 2002). Following the consultation phase that occurs at the beginning of the school year, teachers in the experimental groups will receive four coaching sessions. During the coaching phase, video recording will be conducted of the teacher instructing the child with ASD using the teaching plan developed as a result of the consultation. Coaching sessions will consist of a manualized structured interview using a problem solving approach. The two

experimental groups differ in that the face-to-face coaching will occur in the classroom whereas the web-based coaching will occur via internet technology using Adobe® Connect™ video conferencing. The placebo control group will receive online autism training only. Child outcomes will be measured at the end of the school year using an observational coding approach and goal attainment scaling conducted by a member of the research team who is blind to group assignment. Between group analysis on child goal attainment will be conducted at Time 1 and Time 2. Web-based participants will complete an attitude towards technology questionnaire adapted from the Computer Attitude Scale (Loyd & Gressard, 1984) and a frequency of computer use questionnaire.

Results:

The study is currently underway. Preliminary data will be presented. We do not expect to see any difference between the web-based experimental group and the face-to-face experimental group. We do however predict that any variability between these two groups can be explained by their attitude toward technology and their frequency of use of computers. These variables will act as a moderator of web-based intervention effectiveness.

Conclusions:

Preliminary conclusions will be presented. If the results are as predicted, it will be possible to predict which rural teachers are the best targets for intervention.

117.024 24 Understanding the Context of Stereotypical Behaviors. N. Nazneen*, F. A. Boujarwah, A. Mogus, S. Sadler, M. Habibulla, G. D. Abowd and R. Arriaga, *Georgia Institute of Technology*

Background:

A vast literature exists related to the incidence and impact of stereotypical behaviors in individuals with Autism Spectrum Disorder (ASD). These behaviors may significantly interfere with the individual's ability to perform regular tasks, acquire new skills and integrate socially. Being aware of the individual's external environment as well as physical and physiological characteristics will allow the caregiver to understand causes of stereotypical behaviors. There has also been a significant amount of work done on the recognition of repetitive behaviors and their relation to physiological change. To date, however, there is no technology that enables the stakeholders to derive better inferences about the inducers of repetitive behaviors or to determine if interventions have been successful in reducing their numbers.

Objectives:

To empower caregiver with the ability to infer causes of stereotypical behaviors and determine if interventions are effective in reducing them.

Methods:

We have developed a system called *iExpress*, to contextualize stereotypical behavior by mapping occurrences, identified by analyzing data from on-body accelerometers, to heart-rate data and audio-visual information obtained from the environment. iExpress tacitly captures important events of interest, stores data over a period of time and provides a visualization tool to perform analysis. A formative study has been conducted with 12 participants involving 4 parents, 3 children with ASD and five caregivers. Children were asked to use wearable wrist mounted accelerometers and a heart rate monitor in order to determine their comfort level. Parents were introduced to the iExpress prototype with synthesized data. After they interacted with the system they filled a short questionnaire. This was followed by a focus group discussion on the feasibility, usefulness and usability of iExpress. In another setting five caregivers of children with ASD were asked to fill out a questionnaire and participate in a focus group. The caregivers included 4 teachers one of whom was also a therapist and one consultant.

Results:

All the participants provided positive feedback on the iExpress prototype. None of the participants including child participants

indicated any opposition or signs of discomfort to the on-body sensors. All participants indicated willingness and a desire to share the data with other stakeholders. They suggested integrating iExpress with the child's schedule so that correlations could be made between what the child was doing at that time, and the events of interest. This would be most useful at school, where the child follows a more structured schedule. The participants also suggested augmenting the system to turn it into a diary of events by allowing note taking. Parents showed a high interest in using iExpress on a daily basis and the caregivers were keen to use it at least once a week.

Conclusions:

Feedback received from study participants indicated that the iExpress system could be very useful to parents and other caregivers in determining causes of stereotypical behaviors. Our initial apprehensions about children having a reaction to the on-body sensors turned out to be unwarranted. We were pleasantly surprised that both parents and caregivers wanted to use iExpress more frequently than our initial expectations.

117.025 25 Self-Monitoring with Handheld Computers by Teens with High Functioning Autism/Asperger's Syndrome in Mainstream Settings. M. Levine*[1], K. Hearsey[2], G. Mesibov[2] and R. J. Calvanio[3], (1)*SymTrend, Inc.*, (2)*University of North Carolina at Chapel Hill*, (3)*Massachusetts General Hospital*

Background: Recent studies have shown that skill acquisition is improved in intense programs in which HFA/AS students (in a ASD-only school or camp setting) self-record their skill execution on a handheld computer and receive supervisor feedback about their recordings. Intensive use means that frequent recordings followed by feedback are 1) done under professional supervision and occur 2) on the same day, 3) every day, 4) throughout the day.

Objectives: To determine under what less intense program conditions the computer self-recording with feedback paradigm would prove successful. In particular, we tested to see if the paradigm would be successful under less ideal conditions in mainstream settings, where the training and feedback 1) was provided by non-professional strangers, 2) was less frequent, and 3) occurred only during part of the day.

Methods: Sample: Forty-two students identified as having HFA/AS by special education staff at 11 middle and high schools in Massachusetts and North Carolina participated; 30 Intervention Group students (IG's) and 9 Wait List Control Group students (WL's) provided data for this report. Parents and students provided consent for participation. Parents and teachers completed standardized tests prior to data collection. The students spent all or nearly all of their day in mainstream classrooms. Procedure: Baseline: Trained adults observed the students for four weeks 3x/week in three classes, using Palm handheld computers with software from SymTrend, Inc. (software is now on the iPod touch). Observers recorded data using six classroom behavior scales, checklists of positive and negative social pragmatic behaviors, and seven mood/arousal rating scales. Training: IG's were then trained on self-recording with a similar protocol; training typically started with visual images on paper; the students were then taught to translate the content to responses on the handheld. Intervention: IG's then self-recorded during two classes daily for up to 10 weeks, while the adult observers monitored them simultaneously. Adults met with the students twice/week to show charts displaying both data sets together. They discussed strategies for coping with problems uncovered during the observations. WL did not use handheld computers.
Results: For the WL's, substantial feelings improvement occurred spontaneously for nearly half the students (44%). This feelings improvement was not accompanied by a behavioral improvement. Indeed, in 22% of WL's with feelings improvement, there was a substantial behavioral worsening. The IG's showed a quite different profile of improvement and worsening. The IG's produced a greater incidence of substantial behavioral improvement: 27% (vs. 11%). More than half of this 27% (i.e., 17%) also showed feelings improvement compared to none in the WL's. The primary areas of improvement in the IG's were in feeling more

calm and confident and improving self-control and self-expression.

Conclusions: WL's showed considerable spontaneous feelings improvement with little behavioral improvement. The intervention produced considerably more instances of substantial behavioral improvement, and did so with feelings improvement half the time. Despite a much more limited protocol implementation in mainstream settings, the recording-feedback paradigm shows promise for improving classroom social behavior.

117.026 26 Rachel: An Embodied Conversational Agent for Eliciting and Analyzing Emotional Interactions in Children with Autism. E. Mower*[1], E. Flores[2], M. P. Black[1], M. E. Williams[3] and S. Narayanan[1], (1)*University of Southern California*, (2)*USC University Center for Excellence in Developmental Disabilities at Childrens Hospital Los Angeles*, (3)*Keck School of Medicine, University of Southern California*

Background:

Emotion production and perception are a crucial part of human interaction. Emotions modulate vocal, facial, and physical expressions in natural communication. Previous research has demonstrated that children with autism have difficulty recognizing and understanding emotions. Quantitative evaluations can aid in identifying child-specific social deficits, potentially producing, in the long-term, more effective and targeted interventions. Embodied Conversational Agents (ECA) provide an important platform for analyzing a child's communicative patterns. ECAs produce consistent and modifiable scenarios permitting a controlled evaluation of a child's communication abilities. The goal of the current work is to determine how a suite of ECA technologies can be used to elicit and evaluate natural affective child communication patterns.

Objectives:

The ECA employed in this work is designed to elicit, and analyze, complex, but phased, structured, and naturalistic interactions. The tool is intended to encourage affective and social behavior through the design of the accompanying scenarios.

Methods:

The tool is adapted from earlier studies at the USC. These studies suggested that an ECA could elicit natural communication patterns in typically-developing children and children with autism. In the updated design, the interaction scenarios are emotion problem-solving tasks. In these tasks, children are presented with emotional imagery. They are asked to identify emotional inconsistencies (e.g., missing faces, mismatched faces) and explain why these inconsistencies were identified.

The ECA serves as an emotional coach. It introduces the scenario and produces queries whose difficulties are dependent on the child's ability. If the child easily identifies the emotions in the images, the ECA coaches him through low-level points, asking him to determine the emotional causes. If the child is unable, or unwilling, to identify the emotions present, the ECA coaches him through empathetic exercises, relating the child's preferences to the presented scenarios.

The tool is designed to elicit affective and social behavior for analysis. The child's behaviors are recorded using audio-visual sensors and the ECA's prompts are logged for post-hoc analysis. The interaction follows the Wizard-of-Oz paradigm, permitting the creation of a structured interaction simulating a discourse between a child and machine while avoiding the technological difficulties inherent in speech understanding.

Results:

The ECA technologies discussed in this abstract have been designed, implemented, and tested on typically developing children. Previous studies demonstrated the usability of this type of technology on typically developing children and children with autism. We are currently recruiting children with autism to study affective child-machine interaction patterns. The presentation at the conference will include a demonstration of the technology.

Conclusions:

ECA technologies provide an effective platform for eliciting and analyzing children's communicative abilities. This tool is a modular system; scenarios can be interchanged or even created based on the needs of the experimental protocol. It also records time-stamps of the ECA behavior. The combination of the modularity and detailed record facilitates detailed and quantitative post-hoc analyses for the identification of social affective deficits in children with autism. This work is supported by the National Science Foundation and Autism Speaks.

117.027 27 Design and Evaluation of Interactive, Customizable and Extensible Speech Enabled Games as Speech Therapy for Kids with Autism. M. E. Hoque*, M. S. Goodwin, R. E. Kaliouby and R. W. Picard, *Massachusetts Institute of Technology*

Background: Approximately one third to one half of individuals diagnosed with an ASD have significant difficulty using speech and language as an effective means of communication. While conventional speech-language therapy can help address these issues, it can be tedious, time consuming, and minimally engaging. Objectives: We aimed to create and evaluate a suite of engaging, customized, interactive computer games to help children improve speech difficulties relating to loudness and speech rate (both of which have direct impact on intelligibility). The games were easily customizable to suit the needs and interests of individuals with diverse levels of ability and free and open-source, making them accessible to all with an Internet connection. Our objective was to supplement regular speech therapy with entertaining and customizable tools that a speech-language therapist can use when working with individuals on the autism spectrum. Methods: Eight children (two females, six males) on the autism spectrum (ranging in age from 7_20yr) who had difficulties with loudness and/or speech rate participated in this study. Participants were matched and assigned to two groups of four (A and B) based on their speech difficulties, age, and gender. After an initial baseline assessment of loudness and speech rate, Group A engaged in two weeks of computerized speech therapy while Group B engaged in two weeks of conventional speech therapy. In the following two weeks interventions were switched and Group A received conventional speech therapy while Group B received computerized speech therapy. Speech was recorded during all sessions and loudness and speech rate were calculated and summarized at the end of each intervention period. Results: Out of our eight participants, six had "speaking louder" as a target. Five of the six showed a statistically significant increase in loudness at the end of the study compared to baseline. Three of those five showed either comparable or significantly greater improvement following the computerized speech therapy compared to conventional speech therapy. Only one participant showed a significant decrease in loudness following the computerized sessions compared to conventional therapy. Five participants had "speaking slower" and two had "speaking faster" as targets. Two participants showed a statistically significant desirable change in speech rate after intervention compared to baseline. One spoke more slowly after conventional therapy and the other spoke more slowly after the computerized therapy. Conclusions: Our computerized intervention appeared engaging and effective for the majority of our participants. Some participants demonstrated statistically significant changes in speech following the computerized therapy relative to conventional therapy, suggesting that a subset of individuals on the autism spectrum may especially benefit from our intervention. The finding that some participants had statistically significant gains in both the computer as well as the conventional therapy sessions is also promising since computer therapy may be a useful option for individuals who cannot afford, or do not otherwise have regular access to or interest in, speech_language therapy.

117.028 28 National Database for Autism Research (NDAR): From Database to Network. G. Navidi*, D. Hall, M. F. Huerta, K. Mead and E. Stanton, *National Institute of Mental Health, National Institutes of Health*

Background: The Autism Spectrum Disorder (ASD) research enterprise is characterized by the significant heterogeneity of the disorder, small research sample sizes, and a strong sense of urgency. The National Database for

Autism Research (NDAR) is designed and implemented to facilitate progress in this particular environment. Beyond providing investigators with significant technical capabilities for their data, NDAR has developed strategies to assure protection of research subjects, ensure data quality, and harmonize compatibility across other ASD research data sources.

Objectives: Funded by the National Institutes of Health (NIH), NDAR is a bioinformatics platform with objectives to: 1) facilitate data sharing and scientific collaboration, 2) provide bioinformatics solutions to address community-wide needs and 3) enable the effective communication of detailed research data, tools and information.

Methods: NDAR is a collaborative effort with the ASD research community resulting from engagement with privately and publically funded researchers through special interest groups, workshops, and other meetings. NDAR's Global Unique Identifier (GUID) protects the identity of a research subject while allowing for the collection and analysis of data across time and projects. NDAR's Data Dictionary Tool currently defines 15,000+ data variables for clinical assessments, imaging, and genomics; allows researchers to define their own data structures; and works with the NDAR Validation Tool to ensure the quality and standardization of data. NDAR's policies and procedures ensure that data are shared at appropriate times without compromising research, allow NDAR to be used as a private collaborative space, and control the submission and access of research data. NDAR's federation capability allows for the deep linking into other ASD and ASD relevant data sources, providing direct access to data while allowing the data to reside under the control of the originating organization.

Results: NDAR receives data from the NIH Autism Centers of Excellence (ACE) grantees and will soon receive data from 43 autism research grants funded under the American Recovery and Reinvestment Act (ARRA). The submission of both descriptive and experimental data from the combined targeted enrollment for these projects will result in data from tens of thousands of subjects. And, all investigators conducting human ASD research, regardless of funding source, are strongly encouraged to share data via NDAR. NDAR is now deeply linking with major public and private informatics platforms relevant to ASD research. The Interagency Autism Coordinating Committee has recognized the value of NDAR by adding NDAR to specific objectives in its 2010 Strategic Plan.

Conclusions: NDAR not only continues to develop its capabilities, but is also working closely with other major public and private informatics efforts to form a rich global network of data and tools. This network will add value to ASD research beyond the sum of the contributions of the individual platforms, giving researchers access to more data than any one researcher could collect, and giving access to a broad range of robust analytic tools. This network will give autism research a bigger – and better – bang for the buck, and will accelerate progress in this pressing area of public health.

Brain Imaging Program

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118.100 100 Alterations in Brain Volume and White Matter Microstructure Predict Symptoms of Autism in Angelman Syndrome. S. U. Peters*[1], C. A. Bacino[2], T. L. Merkley[3], Z. Chu[2], R. Yallampalli[2], P. Adapa[2], E. Traipe[2], J. V. Hunter[2] and E. A. Wilde[2], (1)*Vanderbilt University*, (2)*Baylor College of Medicine*, (3)*Brigham Young University*

Background: Angelman syndrome (AS) is a neurogenetic disorder that is characterized by severe mental retardation, lack of speech, ataxia, seizures, and frequent outbursts of laughter. Previous studies have indicated overlap of autism and AS. Objectives: To examine the neuroanatomical correlates and the disruptions in white matter pathways that contribute to symptoms of autism in AS. Methods: We utilized diffusion tensor imaging (DTI) and quantitative magnetic resonance imaging (MRI) to characterize all patients. Fourteen deletion positive patients with AS between the ages of 8-17 were enrolled; and 13 typically-developing controls with comparable age and gender were enrolled. Patients with AS received the Bayley Scales of Infant Development-III, Vineland Adaptive Behavior Scales-II, Autism Diagnostic Observation Schedule, and the

Aberrant Behavior Checklist. Results: The results of quantitative MRI indicated that after controlling for total intracranial volume and age, AS patients have reduced volumes compared to controls in the cerebellum ($p<.01$), caudate ($p<.001$), globus pallidus ($p=.013$), amygdala ($p<.01$), and corpus callosum ($p<.05$). Reduced volume in the corpus callosum was associated with more impairments in socialization ($p<.05$), play ($p<.05$), and higher levels of stereotypic behaviors ($p<.05$). Reduced volume in the amygdala was associated with more stereotyped behaviors ($p<.05$), and greater impairment in social communication ($p<.05$) and social interaction ($p<.05$). Reduced volume in the globus pallidus was associated with more impairment in social communication ($p<.05$) and play skills ($p<.05$). On DTI studies, we observed reduced fractional anisotropy (FA), higher radial diffusivity (RD), and higher apparent diffusion coefficient (ADC) values in the arcuate fasciculus (AF) and the uncinate fasciculus (UF) (a pathway related to social engagement/affect) in individuals with AS compared to controls. High RD and reduced FA in the AF in children with AS correlated with lower expressive and receptive language, deferred imitation, and more impaired socialization and play skills. Higher RD, higher ADC, and reduced FA in the UF corresponded to increased social withdrawal. Within this study, seven patients with AS exceeded ADOS cutoff scores for the criteria of autism, while seven patients did not exceed these cutoffs. When examining volumetric differences, we found that children with AS and autism had reduced volumes in the amygdala ($p<.05$) compared to children with AS alone. On DTI, patients with AS and autism exhibited lower FA and higher RD in the UF and the AF compared to those with AS alone ($p<.05$). Conclusions: Compared to controls, patients with AS exhibit changes to brain structure and white matter pathways that are related to social engagement, stereoptyped behaviors, and play skills. Although prior studies have demonstrated some overlap with AS and autism, this study also demonstrates within-group differences in brain structure and white matter pathways such that patients with autism and AS show even more brain-based alterations as compared to their peers with AS alone. Taken together, our findings seem to suggest that the AS gene, UBE3A, is expressed throughout the brain and that disruptions in UBE3A lead to disruptions in cortical and subcortical regions as well as white matter pathways that contribute to core deficits of autism.

118.101 101 Amygdala, Hippocampus, and Delayed Memory Impairments in Autism. J. S. Southwick*[1], E. D. Bigler[1], M. B. DuBray[2], A. Froelich[2], A. L. Alexander[3], N. Lange[4] and J. E. Lainhart[2], (1)*Brigham Young University*, (2)*University of Utah*, (3)*University of Wisconsin*, (4)*Harvard University*

Background: Impaired cognitive functioning including memory is frequently associated with autism spectrum disorder. Little is known about potential anatomical differences that may be associated with the cognitive deficits observed in autism as compared to typical developing individuals. Several studies have demonstrated that individuals with autism exhibit particular memory deficits, especially delayed retention, for tasks involving complex information, such as the memorization of stories or pictures that they are not intrinsically interested in. Because of the purported role of the hippocampus and amygdala in both memory and autism it is hypothesized that differences in the relationship of these medial temporal lobe structures to memory exists between autism and typical developing controls.
Objectives: Determine the relationship between amygdala and hippocampus volume and delayed memory performance in autism and typical development.
Methods: High functioning, all male participants with autism (n = 46) and typically developing controls (n = 28) ages 5 to 19 completed a delayed verbal recall task, Memory for Stories, and a delayed nonverbal recognition task, Facial Memory, from the Test of Memory and Learning (TOMAL). Memory tests were individually administered as part of a larger battery of neuropsychological measures, including assessment of intellectual ability. To maximize on the potential for the greatest differences in memory performance, only the 30 minute delayed recall component was examined. All subjects underwent magnetic resonance imaging (MRI) with image quantification being performed by the FreeSurfer automated image analysis

program.
Results: Groups were matched for Performance IQ (autism, 106.15; controls 111.71) and age (autism, 11.6 yrs.; controls, 11.9 yrs.), and did not differ in head size, handedness, or hippocampal or amygdala volumes. As expected, significant differences were found for Verbal IQ (autism, 93.15; controls, 111.71; p <.001), Memory for Stories-Delayed (autism, 6.93; controls, 11.32; p <.001), and Facial Memory-Delayed (autism, 7.83; controls, 10.04; p <.001). Partial correlations, controlling for intracranial volume, revealed group differences in amygdalo-hippocampal memory relationships. All correlations for controls were significant for Memory for Stories-Delayed (.40 to .45; p < .05 to .02); both left (.42, p < .04) and total hippocampal volumes (.35; p <.09) related to Facial Memory. Amygdala volume did not significantly correlate with Facial Memory. No significant correlations were found for participants with autism for either memory variable or amygdalo-hippocampal measurement (-.11 to .20; all p values >.20).
Conclusions: The volume of medial temporal lobe structures was found to relate to complex, delayed memory performance in typically developing controls but not individuals with autism. Although participants with autism were equated to controls in terms of non-verbal IQ and there were no differences in age, intracranial volume nor amygdala and hippocampal volumes, distinct differences were observed in memory performance for delayed retention of content information for stories and recollection of observed faces. The absence of significant correlations in the autism group suggests a disconnection in the typical associations observed with medial temporal lobe structures and memory function. This likely has implications for atypical medial temporal lobe connectivity that may be related to the expression of autism and associated cognitive deficits.

118.102 102 Anatomical Phenotyping in a Neuroligin3 Mouse Model of Autism Using Magnetic Resonance Imaging. J. Ellegood*, J. P. Lerch and R. M. Henkelman, *The Hospital for Sick Children*

Background: The Neuroligins and Neurexins are synaptic cell adhesion genes, and disruptions in these genes have shown up in a wide array of Autism association studies (Jamain et al. 2003; Laumonnier et al. 2004). Mouse models with a Neuroligin3 knockout show reduced communication skills (ultrasonic vocalizations) and a lack of social novelty preference (Radyushkin et al. 2009). A Neuroligin3 knockdown model, which displays an approximate 90% loss of Neuroligin3, has also displayed abnormal social interaction (Tabuchi et al., 2007).

Objectives: The purpose of this study was to assess differences in neuroanatomy and white matter microstructure between the Neuroligin3 mutant and wild-type mice.

Methods: Eight male Neuroligin3 mutant (Jackson Labs #008475) fixed mouse brains and 8 male wild type (B6/129 - Jackson Labs #101045) fixed mouse brains, all 108 days old, were examined.

MRI Acquisition - A 7.0 Tesla MRI scanner (Varian Inc., Palo Alto, CA) 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 for a set of 3 brains imaged in parallel was ~11 h and 16 h for the two methods, respectively.
Data Analysis – We use image registration to align a neuroanatomical atlas defining 62 separate brain regions towards each scan. Volumes of individual structures for each mouse were calculated as percentage brain volume. Changes in white matter were determined by registering fractional anisotropy (FA) maps to the same atlas and computing average FA values per structure. Group differences in volume or FA were calculated using t-tests, multiple comparisons controlled using the False Discovery Rate (FDR).

Results: Significant proportional volume changes were found 19 different regions, with FDRs of < 7.5%. Some of the notable regional changes were decreases in the corpus callosum (6.5%), fornix (6.5%), dentate gyrus of the hippocampus (9.9%), stratum granulosum of the hippocampus (12.9%), internal capsule (7.3%), striatum (3.6%), and thalamus (6.8%). Furthermore, increases were found in the medulla (6.1%),

interpeduncular nucleus (13.2%), inferior cerebellar peduncle (5.9%), and forth ventricle (21.9%). Despite the volume changes found in many white matter structures, such as the corpus callosum, internal capsule, and fornix, there were no significant FA differences detectable in the white matter of the Neuroligin3 mouse.

Conclusions: This study highlights volumetric changes in 19 different regions in the brain of the Neuroligin3 mouse. Furthermore, volume decreases are found in major white matter structures, such as the corpus callosum (the most significant volume difference, p-value < 0.0001, FDR < 1%), and these changes may be related to those seen previously in human autism (Alexander et al. 2007), although in that study FA decreases were also found. A change in volume without a decrease in FA seems to indicate that while there may be a loss in size of the white matter bundles, the myelination and integrity of white matter tracts seem intact.

118.103 103 Association of Primary Sensorimotor White Matter Abnormalities with Anomalous Patterns of Motor Learning in Children with Autism. D. Crocetti*[1], P. Srinivasan[1], J. Izawa[2], R. Shadmehr[2] and S. H. Mostofsky[3], (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins University*, (3)*Kennedy Krieger Institute, Johns Hopkins University School of Medicine*

Background:

There is increasing evidence suggesting that autism is associated with impairments in motor skill development (e.g., Jansiweicz et al., 2006; Mostofsky et al., 2006; Dzuik et al., 2007; Dowell et al., 2009). When learning motor skills, internal models of action are formed whereby associations are built between motor commands (mediated by motor and premotor cortices) and sensory feedback (mediated by somatosensory and posterior parietal cortices). Production of motor commands is based on the brain's ability to interpret this sensory (visual and proprioceptive) input. Recent findings (Haswell et al., 2009) suggest that during motor learning, children with autism spectrum disorder (ASD) build a stronger than normal association between motor commands and proprioceptive feedback and a weaker than normal association between the same commands and visual feedback. This is consistent with imaging and postmortem studies (Casanova et al., 2006; Herbert et al., 2004) revealing an over-expression of short-range axons in children with autism including axons connecting the primary motor and somatosensory cortices (i.e. primary sensorimotor cortex), where activity fields of neurons are in the intrinsic coordinates of proprioception (Scott et al., 1997).

Objectives:

To examine the association between white matter connections localized within the primary sensorimotor cortex (SM1) and autism-associated differences in skill performance and learning.

Methods:

Diffusion tensor imaging was acquired in 17 children with ASD and 18 typically-developing (TD) children. A white matter parcellation atlas within MRIStudio (Mori et al., 2008) was used to measure mean fractional anisotropy (mFA) within primary somatosensory (postcentral gyrus) and primary motor (precentral gyrus) regions. For a subset of these subjects (9 ASD, 6 TD) motor learning was assessed using a reaching task that involved learning an internal model of a novel tool, a robotic arm. The objective of the task was to move the arm to a video-displayed target within a set time-window. The task was comprised of three targets: Target 1 assessed task learning, Target 2 assessed generalization to extrinsic visual coordinates, and Target 3 assessed generalization to intrinsic proprioceptive coordinates.

Results:

Group analysis revealed a trend ($p=0.09$) for decreased FA in right + left somatosensory cortices (S1). Analysis revealed that for children with ASD, mFA in left + right SM1 correlated with increased force for Target 3 ($R=-0.70$, $p=0.03$), such that lower SM1 FA predicted the autism-associated tendency to rely on proprioceptive feedback during motor learning. No significant correlation was observed in TD controls.

Conclusions:

The findings reveal that for children with ASD, their tendency to excessively rely on proprioceptive, rather than visual, feedback during motor learning is associated with lower FA in primary sensorimotor white matter. The findings suggest that disorganized patterns of localized white matter connections within SM1 may contribute to abnormal formation of action models in autism. We have reported (Dziuk et al., 2007; Haswell et al., 2009) that autism-associated abnormalities in motor skill learning and skill performance strongly correlate with measures of the core social deficits that define autism. Our findings here therefore support proposed models suggesting that the behavioral impairments of autism are associated with disorganized patterns of white matter connectivity.

118.104 104 Behavioral Correlation with Hemispheric Structural Connectivity in Autism. N. Adluru*[1], K. M. Dalton[2], T. Graupner[2], A. L. Alexander[2] and R. J. Davidson[2], (1)*University of Wisconsin-Madison*, (2)*University of Wisconsin*

Background: While there have been studies correlating functional connectivity and behavior, structural connectivity analysis for autism has not been widely investigated. Diffusion Tensor Imaging (DTI) provides unique information about the underlying tissue structure of brain white matter in vivo, including both the geometry of fiber bundles as well as quantitative information about tissue properties as characterized by measures such as tensor orientation, anisotropy, and size.

Objectives: The aim of this study is to investigate group differences between correlations of hemispheric structural connectivity (preliminary characterization) in the brain with heart rate variability (HRV) & gaze fixation (GF) for individuals with a diagnosis of high functioning autism spectrum disorder (ASD) and typically developing (TD) individuals.

Methods: The behavioral data was acquired while participants performed an event related facial emotion discrimination task. Happy and fearful faces were presented with a combination of happy and fearful voices. The HRV and GF data was averaged over all the degrees of freedom. Diffusion Tensor Images (with 12 gradient directions) were acquired and spatially normalized using diffeomorphic normalization of tensors into a population specific template. Hemispheric connectivity (h) is characterized as the ratio between the number of fiber tracts crossing mid-sagittal plane and the number of ipsilateral tracts. h=(# intra-hemispheric fiber tracts)/(# inter-hemispheric fiber tracts). The heuristic behind such a characterization is to capture long-range vs. short-range structural connections in the individuals. We used Pearson's correlation coefficients (r) to investigate support for the alternative hypothesis (r_h^{ASD} != r_h^{TD}) of finding group differences in the hemispheric ``wiring`` of the brains.

Results: The mean (m) and standard deviations (s) of the hemispheric connectivity for the two groups are: m_h^{TD}=9.5944, m_h^{ASD}=9.9749 and s_h^{TD}=0.9840,s_h^{ASD}=1.1824. We also performed two-sample t-tests assuming unknown variances (Behrens-Fisher problem) (result, p=0.3363) as well as assuming equal variance (result, p=0.3449). The sample correlations and corresponding p-values for two-tailed distributions for the two measures are presented below:

	Heart Rate Variability (HRV)
r_h^{TD}	0.225187
r_h^{ASD}	-0.190279
z	0.97
n^{TD}	14
n^{ASD}	13
p	**0.332**

Conclusions: Although correlation with HRV shows more group difference than that with GF, the difference is statistically insignificant (since p >> 0.05) to support the alternative hypothesis. Although the standard deviation of the hemispheric connecitivity is higher for the ASD group (s_h^{ASD}>s_h^{TD}) *and* null-hypthesis could not be rejected at the 5% significance level, the statistical support for the alternative hypothesis (m_h^{ASD} != m_h^{TD}) is not significant. Preliminary characterization of

hemispheric structural connectivity (h) does not reveal any significant structural connectivity differences between ASD and TD individuals. A finer characterization using High Angular Diffusion Imaging (HARDI) might reveal subtle differences between the groups.

118.105 105 Construction of a Stereotaxic DTI Atlas with Full Diffusion Tensor Information for Studying White Matter Maturation From Childhood to Adolescence Using Tractography-Based Segmentations. J. S. Verhoeven*[1], C. A. Sage[1], A. Leemans[2], W. Van Hecke[1], D. Callaert[1], R. Peeters[1], P. De Cock[1], L. Lagae[1] and S. Sunaert[1], (1)*University Hospitals of the Catholic University of Leuven*, (2)*University Medical Center Utrecht*

Background:

Altered brain growth dynamics causing excessive white matter (WM) connections in some portions of the brain and underconnectivity in others, is a recently proposed etiological model for autism spectrum disorders (Courchesne et al, 2007). WM maturation and WM connectivity can be studied with diffusion tensor imaging (DTI), which allows reconstruction of WM fiber tracts (fiber tractography, FT). However, FT results highly depend on the manual delineation of regions-of-interest (ROI) and the algorithm settings, often rendering the reproducibility and reliability questionable. Predefining these ROI on a fractional anisotropy (FA) atlas in standard space has already been shown to improve the reliability of FTresults (Wakana et al, 2008).
When studying neurodevelopmental diseases, the availability of reliable data processing techniques and normative data from healthy controls is essential for the interpretation of pathological findings.

Objectives:

The aim of our study was to obtain normative DTI data by studying laterality and age-related maturational WM changes in 42 normal subjects aged 0 to 18 years using tractography-derived tract segmentations in a standard DTI atlas space.

Methods:

DTI data were acquired at 3T using a SE-EPI sequence with 45 directions of diffusion (b = 800 s/mm2). First, a DTI atlas containing full diffusion information was generated using DTI data of 36 healthy volunteers (age range = 19-24 years) and both affine and non-rigid coregistration of the DTI data (Van Hecke et al, 2007). On the resulting DTI atlas, we performed deterministic FT of 11 bilateral and 4 unilateral WM tracts using robust ROI definition protocols (Wakana et al, 2008; Stieltjes et al,2003). Tract masks were derived from the tract reconstructions and were used to extract mean FA- and MD-values for each tract in 42 individual DTI datasets of children aged 4 months-18 years. WM maturation was assessed by evaluating the effect of age on FA or mean diffusivity (MD) using Pearson correlation tests. WM asymmetry was evaluated by performing paired t-tests on the left and right mean FA- or MD-values obtained in the bilateral WM tracts after correction for age. Statistical threshold for significance was set at $p<0.05$ and Bonferroni correction was applied to account for multiple testing.

Results:

Significant increase of FA and decrease of MD with age was found in all of the 26 tract masks. The decrease of FA was shown to be mainly due to the decrease of perpendicular diffusivity with age. In 6 out of 11 bilateral tracts, significant asymmetry of FA and MD was demonstrated.

Conclusions:

We have generated a DTI atlas containing the full diffusion information in standard coordinate space, from which tract masks can be derived. Using these tract masks, we observed maturational changes in most of the major WM tracts in healthy children, providing normative data for the study of neurodevelopmental disorders. Furthermore, major functional pathways in the language, motor, and limbic system, showed significant asymmetry in terms of the observed diffusion metrics. Tract masks may thus be helpful in delineating how typical developmental trajectories are altered in individuals with developmental disorders, such as autism

spectrum disorders.

118.106 106 Corticocortical and Thalamocortical Resting State Sensory Area Correlations Are Atypical in Autism. I. Soulières*[1], E. B. Barbeau[1], S. Whitfield-Gabrieli[2], L. Mottron[1] and T. A. Zeffiro[3], (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*Massachusetts Institute of Technology*, (3)*Neural Systems Group, Massachussetts General Hospital*

Background: Autism is characterized by a broad range of atypicalities in perceptual processing, notably including advantages in visual search, figure/ground discrimination, block design and pitch discrimination. It has been suggested that these differences may arise from variations in the local influences governing the interactions among collections of neighboring, functionally related sensory regions responsible for the early stages of perception. The examination of resting state correlations allows exploration of inter-regional interactions occurring in a part of the frequency spectrum lower than that usually thought to support the flow of information associated with task-related activity. As such, the strength and spatial pattern of these correlations may provide complementary information concerning the anatomical and functional infrastructure supporting perceptual system operation in autistics.

Objectives: To compare the patterns of functional correlations in perceptual brain regions between autistic and non-autistic individuals, during rest.

Methods: Our sample included 19 autistic and 21 non-autistic participants, matched for age, sex, manual preference and IQ. Using a 3T MRI system, we examined interregional BOLD-contrast cortico-cortical and thalamocortical bivariate correlations in time series collected over a 10 min period while participants were instructed to remain still with eyes closed. We examined a collection of cortical and subcortical seed regions involved in early sensory processing, including the thalami and primary cortical areas in visual, auditory, olfactory and somatosensory systems. Coordinates for the seed regions were selected with masks obtained from the AAL atlas.

Results: Restricting the analysis to those target cortical regions which exhibited positive correlations with the specified seed regions, we observed a strikingly consistent pattern of results revealing that, in both hemispheres, the correlations associated with primary visual, primary auditory, primary somatosensory and primary olfactory cortex were invariably lower in the autistic compared to the non-autistic group. In contrast, seed masks placed in the left or right thalamus identified higher overall thalamocortical correlations in the autistic group.

Conclusions: The observed pattern of atypical interregional resting state correlations in autism spanned all sensory systems examined, consistent with the domain-independent character of previously documented perceptual differences. The regional pattern and reliability of our results suggests that reduced cortico-cortical and increased thalamocortical resting state correlations in the systems involved in early sensory processing could be a useful physiological marker for atypical function in autistic perceptual systems.

118.107 107 Disrupted Network Differentiation in Autism: An fMRI Study of Intrinsic Brain Activity in Children. A. Di Martino*[1], C. Kelly[1], R. Grzadzinski[1], M. Mairena[1], L. Q. Uddin[2], C. Lord[3], F. X. Castellanos[1] and M. P. Milham[1], (1)*NYU Child Study Center*, (2)*Stanford University*, (3)*University of Michigan*

Background: Functional imaging studies of autism spectrum disorders (ASD) have focused on regional abnormalities, identifying hypo-activations in task-related areas and greater activation in task-irrelevant regions. Recently, authors have drawn attention to ASD-related disruptions in functional connectivity (FC) in networks involved in social and executive processes. Building upon the existing literature, we propose the hypothesis that the previously observed findings reflect disruptions in the differentiation of functional networks during development. Resting-state fMRI (R-fMRI) approaches are useful for testing this hypothesis. They provide measures of intrinsic brain activity simultaneously in multiple networks with moderate to high test-retest reliability. R-fMRI has been fruitful in characterizing development and aging of

brain functional networks and has been used to detect abnormalities in adults with autism. Here, we present the first examination of R-fMRI in children with ASD.

Objectives: To systematically examine the pattern of FC in multiple nodes of two classically examined networks: the default mode network (DMN) and the task positive network (TPN) in children with ASD compared to typically developing children (TDC).

Methods: Twenty children with DSM-IV ASD (10.4 y ± 1.7; 3 girls) and twenty age-matched TDC (4 girls) completed a 6.5 min R-fMRI scan (field strength= 3 T; TR = 2000 ms; 3x3x3mm voxels). Signed consent and assent were provided by all children and parents, respectively. Preprocessing included slice-time correction, motion correction, bandpass temporal filtering, spatial filtering, and spatial normalization. Spherical regions of interest (seeds) were selected for FC analyses at: medial prefrontal cortex (MPFC), retrosplenial complex, bilateral lateral parietal cortex (LatPar), parahippocampal complex and hippocampal formation, within the DMN; and bilateral intraparietal sulcus (IPS), ventral IPS (vIPS), inferior precentral sulcus, and middle temporal area within the TPN. Multiple regression (using FSL FEAT) FC analyses were carried out including the timeseries of each 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. Gaussian random field theory was used to correct for multiple comparisons at the cluster level (min $Z > 2.3$; cluster significance: $p \leq 0.05$, corrected).

Results: Preliminary analyses show that children with ASD lack functional segregation between nodes of the TPN and DMN, compared to TDC. In the DMN, a pattern of 'promiscuous' FC was observed, with areas that are typically negatively correlated or unrelated with a seed of interest. Specifically, in ASD, the MPFC showed significantly increased FC with dorsal paracingulate areas, bilaterally. Similarly, the right LatPar seed was significantly correlated with the right lateral temporal occipital junction. These areas are typically negatively connected with the seeds of interest. In children with ASD, within the task-positive network, the right vIPS and the left IPS showed reduced negative FC with posterior cingulate and precuneus.

Conclusions: Our data support the hypothesis that functional abnormalities in ASD reflect abnormal network differentiation as indexed by disrupted patterns of segregation and integration. If confirmed, these findings may also account for the variegated imaging literature which contains both hypo- and hyperactivations in ASD.

118.108 108 Functional Integrity of Dorsal and Ventral Visual Streams in Children with Autism. M. R. Pennick*, H. D. Deshpande and R. K. Kana, *University of Alabama at Birmingham*

Background: Visual information in the brain is processed by two distinct pathways (the dorsal and the ventral visual streams) which operate in a parallel and distributed manner. The dorsal stream extends from the occipital towards the parietal lobe and is associated with locating objects in space, and the ventral stream is commonly activated during tasks that involve recognizing objects, and information in this system travels in the direction of the temporal lobes (Ungerleider and Mishkin, 1982). Since people with autism may identify objects differently (enhanced ability to locate objects in space) from typically developing persons, it will be particularly relevant to examine the functional integrity of the brain areas mediating these functions. It is also equally relevant considering the recent findings of widespread functional underconnectivity among several brain areas in autism (Just et al., 2004; Kana et al., 2006).

Objectives: The primary objective of this study is to examine the functional integrity of cortical networks, especially the dorsal and ventral visual streams, involved in visual processing in children with autism.

Methods: Four high-functioning children (age range: 10-15 years) with autism, and two typical control participants took part in this fMRI study (data collection is in progress). The fMRI data collected from the Siemens

3.0T Allegra scanner at the UAB Civitan International Research Center is analyzed using SPM2 (Wellcome Department of Cognitive Neurology, London, UK). The stimuli consist of a series of common household objects presented in blocked design format in two experimental conditions. In the *object recognition* condition, the participants named an object from four choices, and in the *location identification* condition, they identified the location of a given object with respect to a cross on the screen.

Results: The fMRI data from this study showed that the dorsal and ventral visual streams were differentially recruited in the control participants for location and object conditions respectively. While the control participants activated inferior parietal area in the location identification condition and inferior temporal gyrus in the object recognition condition, participants with autism showed activation in parietal areas in both experimental conditions. In addition, unlike control participants, the participants with autism showed no activation in left inferior frontal gyrus in the object recognition condition. Behavioral results showed that the autism group made more errors in their responses; however both groups showed no differences in latency for either condition. The results are preliminary at this point and reveal only a trend.

Conclusions: The participants with autism seem to recruit more posterior brain areas, such as intraparietal sulcus in accomplishing both tasks suggesting their increased reliance on visuospatial processing. This type of processing is also reflected in the lack of reliance on language areas (reduced activation in left inferior frontal and left posterior superior temporal areas) when recognizing and naming an object. As the data collection is progressing, functional connectivity analysis with adequate sample size will be important in determining the integrity of the dorsal and ventral visual streams in autism.

118.109 109 Functional Neuroimaging of Cognitive Flexibility in Autism. A. M. D'Cruz, M. W. Mosconi, M. E. Ragozzino, L. Ankeny and J. A. Sweeney*, *University of Illinois at Chicago*

Background: Individuals with ASD demonstrate impairments in flexibly shifting to new adaptive response strategies. This cognitive impairment may underlie aspects of behavioral rigidity and insistence on sameness evident in some individuals with ASD. Animal and healthy adult neuroimaging studies indicate that frontostriatal circuitry is involved in cognitive flexibility, but few studies have directly examined the neural circuitry involved in cognitive flexibility impairments in ASD.

Objectives: To examine the neural systems supporting cognitive flexibility using reversal learning in individuals with ASD.

Methods: To date, eight individuals with ASD (3 females; mean age 16.4, SD 6.3) and eight age-matched healthy controls (3 females; mean age 15.6, SD 5.7) have performed 2- and 4-choice spatial reversal learning tests during fMRI. Recruitment of additional subjects is ongoing. Individuals selected the correct stimulus location from identical stimuli (2 or 4 boxes), and continued selecting it over repeated 3 second trials. The correct location changed after 4, 5 or 6 consecutive correct responses, at which point individuals received feedback that their choice was now incorrect, indicating that they needed to choose a new correct location. Thus, in the 2-choice condition individuals knew what the new correct location would be, but in the 4-choice condition they needed to learn which of the 3 alternative locations was correct.

Results: Control subjects engaged bilateral premotor cortex, anterior cingulate cortex, posterior parietal cortex (PPC), thalamus and caudate when shifting to a new response ($P<.05$ corrected). This replicates results in an independent pilot study of 15 healthy controls who performed this task. In contrast, individuals with ASD showed significant activation only in PPC. Neither group showed activation in frontostriatal circuitry in the 2-choice task. No behavioral differences in the number of errors or reaction times were found for individuals with ASD compared to that of controls.

Conclusions: These preliminary data indicate that there is reduced frontostriatal network

activation during reversal learning in ASD compared to that of age-matched healthy individuals. These results were specific to the 4-choice condition, in which individuals needed to flexibly search for a new response strategy. The lack of frontostriatal activation during reversal learning between unknown alternatives may reflect a distinct pattern of neural system dysfunction associated with behavioral rigidity in ASD.

118.110 110 Heart Rate Variability and Brain Function During Emotional Face and Voice Processing in Autism. K. M. Dalton*[1], N. Adluru[2] and R. J. Davidson[1], (1)*University of Wisconsin*, (2)*University of Wisconsin-Madison*

Background: Heart rate variability (HRV) refers to the beat-to-beat alterations in heart rate. HRV is predominantly mediated by parasymphathetic influences on the heart. In general, the greater the HRV, the stronger the parasympathetic influence, or vagal tone. HRV can be affected by acute stress or mental load. Central nervous system regulation of HRV is believed to play an important role in the relationship between psychological state (e.g. stress, mental load) and acute changes in HRV.

Objectives: The aim of this study was to investigate HRV during rest and during multisensory integration of visual and auditory emotional cues and it's relation to underlying brain activation patterns associated with these processes in individuals with autism versus typically developing individuals.

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) typically developing (TD) individuals served a comparison group. Pulse oximetery and 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. Participants were asked to judge the emotional facial expression by pressing one of two buttons.

Results: The 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 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 = .02). The two groups did not differ in HRV during a 7 min resting phase nor did they differ in heart rate (HR) during rest or the task. HRV was negatively associated with SCQ (used here as an index of autism severity) in the ASD group (r = -.709, p =.04) but not in the TD group (r = .38, p = .26; Z = -2.21, p = .027). The TD group showed significant negative correlations between HRV and brain activation in the right anterior insula (r = -.63, p =.002), right amygdala (r = -.52, p = .01) and left fusiform gyrus (r = -.53, p = .01) during the task. These correlations were not found for the ASD group.

Conclusions: While the ASD groups had similar resting state HRV, the ASD group's HRV did not change during the emotional face/voice task while the TD group showed an increase in HRV during the task. HRV was associated with brain activation in predicted regions during the task for the TD group, but not for the ASD group. These findings suggest differences in central and peripheral nervous system integration during emotion processing in ASD vs. TD group.

118.111 111 Heschl's Gyrus and Planum Temporale Volume in Autism: Does Morphology Reflect Language Function?. M. B. DuBray*[1], N. Lange[2], E. D. Bigler[3], P. T. Fletcher[1], K. M. Maasberg[1], A. L. Froehlich[1], A. L. Alexander[4] and J. E. Lainhart[1], (1)*University of Utah*, (2)*Harvard University*, (3)*Brigham Young University*, (4)*University of Wisconsin*

Background: Functional imaging studies of language and auditory processing in autism show abnormalities in the location and asymmetry of neural activation. Despite the striking clinical significance of language impairment and auditory sensitivity in autism, the development of the cortical regions underling these deficits remains largely unknown. Objectives: The present study compares volume and asymmetry of the primary auditory cortex (Heschl's gyrus) and auditory association cortex (planum

temporale) in children with autism to typically developing children using 3 Tesla structural MRI. We also investigate how speech onset and language function are related to Heschl's gyrus and planum temporale structure in autism. Methods: Manual segmentation of Heschl's gyrus and planum temporale of 17 male individuals with autism and 12 male control participants (age range 4-12 years; mean age: autism=8.3, control=8.7) were made on coronal 3T MRI images using itk-SNAP. The autism group was further divided into those with normal language onset or delayed language onset assessed with the ADI-R. Group differences in volume and asymmetry were examined. Results: No autism-control differences were found in Heschl's gyrus or planum temporale volume or asymmetry controlling for age and performance IQ. Interestingly, the individuals with autism with delayed language onset (n=8) showed reduced Heschl's gyrus L>R asymmetry (p=.002) compared to the autism group with normal language onset (n=9). This difference was driven by larger volume in the right Heschl's gyrus in the delayed language onset autism group compared to the normal language onset autism group (p=.002). Data collection is ongoing and future analyses will examine Heschl's gyrus gray and white matter differences in a larger participant sample. Conclusions: These preliminary findings suggest abnormalities in the development of cortical regions responsible for early auditory and language processing in individuals with autism with aberrant language development. Results also suggest that differences in brain morphology may subdivide individuals with autism into meaningful subgroups. These cross-sectional findings will be combined with longitudinal data on this same group of participants to understand the structural development of cortical areas involved in early stages of language processing.

118.112 112 Longitudinal Surface Morphometry Changes in Children with Autism. D. S. Hong*[1], N. J. Minshew[2], M. S. Keshavan[3] and A. Y. Hardan[4], (1)*Stanford University*, (2)*University of Pittsburgh School of Medicine*, (3)*Harvard Medical School*, (4)*Stanford University School of Medicine/Lucile Packard Children's Hospital*

Background: Cortical folding and gyrification are closely associated with the establishment of neuronal connections early in brain development. Advances in techniques to measure surface morphometry have shown promise in defining markers of pathological change of this process. Several studies have indicated that this aspect of neural development may be dysregulated in autism, including findings of increased cortical folding in frontal regions and excessive decrease in cortical thickness over a longitudinal course in childhood. However, no previous study has specifically examined the role of sulcal and gyral area and curvature in autism. A surface-based morphometric approach may yield more information, especially in light of data from functional imaging studies implicating frontal and temporal sulcal anatomy in social cognition. Additionally, these measures may provide more insight on the pathophsysiology of autism compared to volumetric analyses.. **Objectives:** The primary purpose of this longitudinal study was to examine developmental changes in sulcal and gyral anatomy in children with autism, utilizing magnetic resonance imaging (MRI). **Methods:** Participants included male children with autism and age- and gender-matched controls, between the ages of 8-12 years at baseline. Diagnosis was confirmed utilizing expert clinical evaluation and through structured research diagnostic instruments, the Autism Diagnostic Interview- Revised and the Autism Diagnostic Observation Schedule. Scans were obtained using the same acquisition protocol at baseline and follow-up. All scans were obtained on the same GE 1.5-Tesla Signa whole-body MRI system. Image processing of MRI scans was done on a SGI workstation, utilizing Brain Research: Analysis of Images, Networks and Systems software (BRAINS2), which was used to generate sulcal and gyral area and curvature measurements. Between-group differences in demographic data were analyzed with two-tailed Student's t tests. Within-group differences of neurobiological measurements over time were analyzed using paired t-tests. **Results:** 18 boys with autism (mean age=10.9, SD=1.2) and 16 healthy control boys (mean age=10.7, SD=1.2) participated in this study. No differences were observed between participants in the autism and the control group on any of the demographic characteristics except for FSIQ. Mean time

difference between the baseline and follow-up scans was 2.1 years with no significant difference in the time interval between the two groups (t=1.414, p=0.167). Over time, boys with autism showed a significant increase overall surface area of temporal gyri (t=-.4.519, p=0.000), as well as significant changes in parietal sulci (t=-2.341,p=0.032) and total sulcal curvature (t=-2.279, p=0.036). Controls only demonstrated a longitudinal increase in temporal sulcal (t=-3.105, p=0.006) and gyral (t=-2.325, p=0.032) surface areas.

Conclusions: Abnormal developmental changes in sulcal and gyral area and curvature were found in this sample of children with autism. These preliminary findings are consistent with previous observations that morphological changes at the level of sulci and gyri reflect underlying white matter structural abnormalities. Furthermore, the pattern observed here is suggestive of alterations of short- and long-distance neuronal connections. Additional studies are needed to elucidate this correlation between regional surface morphology with deeper cortical structure and function.

118.113 113 Aberrant Reward System Responsivity to Social and Non-Social Reinforcers in Autism as Revealed with Event-Related Brain Potentials and Functional MRI. G. Kohls*[1], J. Peltzer[2], M. Schulte-Rüther[2], B. Nehrkorn[2], R. T. Schultz[3], B. Herpertz-Dahlmann[2] and K. Konrad[2], (1)*The Children's Hospital of Philadelphia*, (2)*RWTH Aachen University*, (3)*Children's Hospital of Philadelphia*

Background: According to social motivation deficit theories of autism (e.g., Schultz, 2005), the lack of interest to attend to social stimuli and to seek and enjoy reciprocal social interactions in individuals with ASD might at least partly be attributed to dysfunctions in brain regions implicated in reward processing such as fronto-striatal limbic circuitry.

Objectives: Since we currently have very little understanding of neural reactivity to motivational incentives in ASD, the present study aimed to investigate ERP and fMRI correlates in boys with and without autism while processing social compared to non-social rewards.

Methods:

Twenty ASD boys and 21 male TDCs, matched for age (mean age 14.4 years), full-scale IQ, and handedness, participated in the study. In both ERP and fMRI sessions, we applied an incentive go/nogo task with social (positive facial expressions), monetary, and non-reward contingencies for successful task performance. FMRI data were collected on a 3T scanner and analyzed with BrainVoyager. High-impedance EEG recordings were obtained from 64 electrodes and processed with BrainVision Analyzer.

Results: On the behavioral level, we found that both social and monetary incentives enhanced performance accuracy and response speed in all participants, with highest improvement under monetary reinforcement, confirming previous findings (Kohls et al., 2009). Contrary to our prediction, children with ASD showed comparable performance benefit and task motivation under social reward conditions as TDCs. By contrast, both imaging methods revealed aberrant brain responses in patients to social and to monetary reinforcers. Concerning ERPs, we found compromised P300 amplitudes to reward-predicting cues in children with ASD, which were most pronounced when social rewards were at stake, and particularly when a timely reaction was required to obtain a reward. Taken the recent locus coeruleus-norepinephrine (LC-NE) P300 theory into account (Nieuwenhuis et al., 2005), the ERP data imply an attenuated state of motivational attention allocation to incentives which trigger active approach behavior in individuals with ASD, - probably mediated by malfunctions in the reward circuitry which intervenes into the LC-NE system to boost the processing of motivational signals against other neutral stimuli. This interpretation is supported by our fMRI data which clearly demonstrate broad hypoactivations in the extended mesocorticolimbic pathway in patients including substantia nigra/VTA, dorsal striatum, and prefrontal cortex/ACC for both social and monetary reinforcement. Moreover, during facial reward processing we could replicate the typical lower brain

reactivity in amygdala and fusiform gyrus in children with ASD relative to controls.

Conclusions: In sum, our findings are in line with recent social motivation deficit theories of autism which highlight a hyporesponsivity in the extended reward circuitry particularly to social incentives, what might cause the reduced socially motivated behavior in affected individuals. Noteworthy, our brain data strongly suggest that the processing of non-social incentives (such as money) is compromised, too, which deserves closer attention. Furthermore, the discrepant finding of undisturbed behavioral responses and the aberrant reward circuit responsivity in children with ASD indicate that imaging methods might be better suited to uncover deviant reward functioning in patients with neurodevelopmental disorders than behavioral measures.

118.114 114 Alexithymia, Metarepresentation, and the Dorsomedial Prefrontal Cortex in Autism. M. V. Lombardo*[1], B. Chakrabarti[1], E. Bullmore[2], S. J. Wheelwright[3], M. R. C. AIMS Consortium[4] and S. Baron-Cohen[3], (1)*Autism Research Centre, Department of Psychiatry, University of Cambridge*, (2)*Brain Mapping Unit, Department of Psychiatry, University of Cambridge*, (3)*University of Cambridge*, (4)*University of Cambridge; Institute of Psychiatry, King's College London; University of Oxford*

Background: Individuals with autism spectrum conditions (ASC) report much difficulty in understanding their own emotions; a trait termed 'alexithymia'. Research in typical development has shown that the appraisal of subjective emotional experience relies heavily on the engagement of dorsomedial prefrontal cortex (dMPFC). In autism, dMPFC is hypoactive during stimulus-driven emotional self-appraisals (Silani et al., 2008, Soc Neurosci). However, this observation could be due to something inherent about stimulus-driven (i.e. bottom-up) processing, or a more general deficit involved in metarepresentational (i.e. top-down) processing. To disentangle these explanations, we examined whether alexithymic traits would covary with dMPFC activity during a task that has a metarepresentational component (reflecting on one's own mental states), but does not evoke stimulus-driven bottom-up processing. Based on work showing that dMPFC is increasingly engaged during earlier stages of development (Blakemore, 2008, Nat Rev Neurosci) and is increasingly engaged during higher levels of metarepresentation (Coricelli & Nagel, 2009, PNAS), we hypothesized that dMPFC activity would be increased in individuals with higher levels of alexithymia (i.e. a positive correlation). However, because this region is both structurally and functionally atypical in autism, we expected that the hypothesized association between dMPFC activity and alexithymia would either be reversed (i.e. negative correlation) or non-existent (i.e. correlation near 0) in ASC.

Objectives: To assess the association between dMPFC function and individual differences in alexithymia during high-level self-representation.

Methods: 29 adult males (18-45 years old) with a diagnosis of an autism spectrum condition (ASC), and 33 age-, sex-, and IQ-matched neurotypical adults were scanned with fMRI at 3T while making mentalizing or physical judgments about themselves or a non-close other. Regions analyzed were dMPFC, medial orbitofrontal cortex (mOFC), bilateral anterior insula (AI), and bilateral amygdala (Amyg).

Results: Replicating past research, individuals with ASC report more alexithymic traits than neurotypical individuals. In the neurotypical group, Increases in alexithymia were associated with increases in dMPFC activity ($r = 0.57$, $p = 0.0005$). However, in the ASC group this association was absent ($r = -0.01$, $p = 0.95$). The difference in these correlations between-groups was significant ($z = 2.45$, $p = 0.01$). No other region was associated with individual differences in alexithymia in either group ($-0.16 < r < 0.21$, $p > 0.23$).

Conclusions: The dMPFC is critical for metarepresentational ability; particularly in appraising subjective emotional experience. In the absence of stimulus-driven processing, increasing alexithymia was strongly associated with increased recruitment of dMPFC during self-mentalizing in the neurotypical group. However, although individuals with ASC report more alexithymia

than that of neurotypical individuals, the magnitude of alexithymia was not associated with dMPFC activity. It is likely that the altered neurodevelopment of dMPFC in autism derails the normative role of dMPFC in metarepresentational function. However, the magnitude of alexithymic difficulty in ASC is likely to involve deficits in other aspects of emotion processing besides metarepresentation (e.g., bottom-up emotion processing).

118.115 115 Applying Machine Learning Techniques to Brain Imaging Characteristics to Distinguish Between Individuals with Autism and Neurotypical Controls. S. E. Schipul*[1], S. Aryal[1] and M. A. Just[2], (1)*Center for Cognitive Brain Imaging, Carnegie Mellon University*, (2)*Carnegie Mellon University*

Background: Autism spectrum disorder is a genetic neurodevelopmental disorder characterized by deficits in language, social interaction, and repetitive behaviors. Although many neuroimaging studies have shown underlying differences in the brain structure and function of individuals with autism as compared to neurotypical controls, currently the only method of diagnosing autism is through interviews and evaluations with trained clinicians. Previous studies (Ecker et al., 2009; Fahmi et al., 2007) have explored the potential of structural brain measures to predict a diagnosis of autism. However, brain activation and synchronization may also be able to contribute to such predictions.

Objectives: This project investigated the potential of machine learning algorithms to distinguish between individuals with autism and neurotypical individuals based on their brain structure, activation, and synchronization.

Methods: fMRI and MRI data were collected for 43 high-functioning individuals with autism and 43 neurotypical control participants. During the fMRI scan, participants read sentences and decided if they were true or false, interspersed with a fixation condition. The data submitted to the machine learning algorithms included activated voxel counts within several regions of interest (ROIs) during fixation, functional connectivity (synchronization) measures between pairs of ROIs obtained during the task performance, and white matter measurements from MRI scans. The classification algorithms that were used to predict a diagnosis of autism included Gaussian Naïve Bayes, logistic regression, and support vector machines.

Results: Our classifiers were able to distinguish between individuals with autism and neurotypical controls with an accuracy of 66%, where the group membership was established using ADOS scores and expert clinical diagnosis.

Conclusions: These findings suggest that brain imaging data has potential to play a role in diagnosing autism. Using several different machine learning algorithms, we were able to distinguish between individuals with autism and neurotypical controls with an accuracy well above chance based on brain imaging data concerning structure, activation, and synchronization.

118.116 116 Atypical Patterns of Effective Connectivity with Biological Motion Processing in ASD. F. E. Pollick*[1], L. S. McKay[1], P. McAleer[1], D. R. Simmons[1] and J. Piggot[2], (1)*University of Glasgow*, (2)*University of California, Los Angeles*

Background: Increasing evidence suggests that autism affects the recognition of biological motion. It has been proposed that this could be either a consequence of motion processing or social cognition, and could involve brain areas thought to be involved in the putative human mirror-neuron system.

Objectives: To investigate the neural mechanisms of biological motion recognition for evidence of different processing strategies between ASD and TD populations. In particular, to examine the effective connectivity between regions implicated in understanding the actions of others.

Methods: Participants in the study included an ASD group of 10 adult males and an age and IQ matched TD group. Every participant first performed a psychophysical task that involved recognizing the direction of locomotion of a point-light walker in visual noise (McKay, et al, 2009 Vision Research). This produced stimuli levels that equated to 50%(chance) and 84% correct performance

thresholds for each individual. Following this all participants were scanned in a 3T Tim Trio scanner using a rapid, event-related design with three runs, each run showing 45 repetitions of every stimulus level. The experimental design was optimized for Granger Causality Mapping (GCM) so that each stimulus type had to cover a large enough number of continuous volumes for the analysis to compare over. Functional T2 weighted images were acquired with a TR of 1000ms. We collected 18 slices for each of 272 volumes at a resolution of 3mm x 3mm x 4.5mm slice thickness and dimensions 70 x 70 per image. Brainvoyager QX 1.10 was used for processing all stages of the data.

Results: An analysis of the behavioural data revealed that there was no difference between the stimulus thresholds for the ASD and TD groups. For the brain imaging analysis, a random-effect GLM was carried out on the group data. We first applied a mask generated from the regions derived from a preliminary experiment to restrict the analysis to only those regions that responded to these stimuli. Contrasts of brain activity for the 84% vs 50% thresholds revealed regions in the Inferior Parietal Lobule, Precentral Sulcus, Inferior Temporal Gyrus and Middle Frontal Gyrus for the TD group and the Middle Occipital Gyrus, Middle Temporal Gyrus, Fusiform Gyrus and Middle Frontal Gyrus for the ASD group. Each of the regions found from these contrasts were entered into the GCM analysis as seed regions. Results of this GCM analysis for the 84% condition indicated that the primary difference between TD and ASD groups was that the TD group engages processing between the temporal and parietal cortices while the ASD group engages areas only within the temporal cortex, including the Fusiform Gyrus, Lingual Gyrus and Parahippocampal Gyrus.

Conclusions: The TD group recruits processing in the dorsal stream to recognize biological motion while the ASD group relies on more extensive ventral processing. This is consistent with the ASD group recognizing biological motion in a more static template matching strategy while the TD group can engage further mechanisms of motion and social processing in the parietal cortex.

118.117 117 Brain Mechanisms for Perceiving Emotional Information in Body Movement in Children with Autism. D. L. Williams*[1], E. J. Carter[2], N. J. Minshew[3] and K. A. Pelphrey[4], (1)*Duquesne University*, (2)*Carnegie Mellon University*, (3)*University of Pittsburgh School of Medicine*, (4)*Yale University*

Background: Researchers and clinicians have suggested that individuals with autism might find faces aversive to look at, particularly the eyes. The tendency to not look at faces, be it driven by aversion or a failure to understand the significance, has been used to explain poor performance on emotion identification tasks using faces (Adolphs et al., 2005; Pelphrey et al., 2002), and lower levels of FFA and AMY activation during emotional face viewing (Dalton et al., 2005; Hadjikhani et al. 2004). Research by Blake et al. (2003) demonstrated that children with autism exhibit deficits in the perception of biological motion. However, we do not know if children with autism process emotional information conveyed through biological movement differently than TD children. Do children with autism have difficulty with emotional processing in general whether it is conveyed through facial features or through body movement? Are these difficulties related to underlying neurological processing differences in autism in emotional brain areas?
Objectives: This fMRI study used a male silhouette (with no observable facial expressions) that moved with a happy, angry, or sad gait. We examined whether the different walks triggered emotion-based brain regions and whether these patterns differ between children with high-functioning autism and age and IQ-matched TD control children.
Methods: Data collection is ongoing. We have analyzed data for eleven children with autism (ages: 7-15 years, mean=11.6; FSIQ: 83-135, mean=108) and five TD children (ages: 9-13 years, mean=10.8; FSIQ: 98-134, mean=115). The children passively viewed the video while lying in a 3T Siemens Allegra scanner. The stimuli were created to convey three different emotional conditions—happy, sad, and angry---using parameters from previous research about emotional information conveyed by gait.
Results: Overall, preliminary results indicate that viewing the angry walk elicited a greater

BOLD response than viewing a happy walk in both the children with autism and the TD children in the right STS. The autism group also had greater activation than TD in right parietal and right STS when viewing the angry walk and in bilateral STS when viewing the sad walk. The TD children had greater activation than the autism children in bilateral middle temporal and left STS when viewing the happy walk. The children with autism had no greater BOLD response when viewing the happy walk than when viewing the non-moving figure during the baseline condition. Conclusions: As in previous studies with typically developing adults with emotional processing in faces, the amount of activity in the STS was modulated by happy and angry emotional body movement such that anger elicited a greater BOLD response than happiness for both groups of children. Differential processing is evident in that the children with autism have a greater response than the TD children in right STS for anger, the strongest of the three emotions. Significant differences between the groups occurred during the processing of the positive emotion of happy with the autism children failing to respond differently than a neutral condition.

118.118 118 Brain Serotonin and Dopamine Transporter Bindings in Adults with Autism. K. Nakamura*[1], Y. Ouchi[1], M. Tsujii[2], K. J. Tsuchiya[1], G. Sugihara[1], Y. Iwata[1], K. Suzuki[1], H. Matsuzaki[3], S. Suda[1], T. Sugiyama[4], N. Takei[1] and N. Mori[1], (1)*Hamamatsu University School of Medicine*, (2)*Chukyo University*, (3)*Osaka University School of Medicine*, (4)*Aichi Chilren's Health and Medical Center*

Background: Autism is a neurodevelopmental disorder that is characterized by repetitive behavior/obsessive interests and deficits in sociability and communication. Although its neurobiological underpinnings are postulated to lie in abnormalities of the serotonergic and dopaminergic systems, the details remain unknown.

Objectives: The purpose of this study was to determine the occurrence of changes in the binding of serotonin and dopamine transporters, which are highly selective markers for their respective neuronal systems.

Methods: Twenty male subjects (age 18-26 years; IQ 99.3±18.1) with autism and 20 age-and IQ-matched controls were employed. Participants recruited from the community. Using PET, we measured the binding of brain serotonin and dopamine transporters in each individual with the radioligands [^{11}C](+)McN-5652 and [^{11}C]WIN-35,428, respectively. SPM was used for between-subject analysis and for within-subject correlation analysis with respect to clinical variables.

Results: Serotonin transporter binding was significantly lower throughout the brain in autistic subjects, compared with control subjects ($P < .05$). Specifically, the reduction in the anterior and posterior cingulate cortices was associated with the impairment of social cognition in autism ($P < .05$). A significant correlation was also found between repetitive behavior/obsessive interests and the reduction of serotonin transporter binding in the thalamus ($P < .05$). In contrast, the dopamine transporter binding was significantly higher in the orbitofrontal cortex of the autistic group ($P < .05$). In the orbitofrontal cortex, the dopamine transporter binding was significantly inversely correlated with serotonin transporter binding ($r = -0.61$; $P = .004$).

Conclusions: The brains of people with autism have abnormalities in both their serotonin transporter and dopamine transporter bindings. The current findings indicate that the gross abnormalities in these neurotransmitter systems may underpin the neurophysiology of autism.

118.119 119 Calibrating Different MRI Scanners From Multiple Sites, and the Effect of Inter-and Intra Site Variation On Neuroimaging Data. J. Suckling*[1] and M. A. Consortium[2], (1)*Brain Mapping Unit, Department of Psychiatry, University of Cambridge*, (2)*University of Cambridge; Institute of Psychiatry, King's College London; University of Oxford*

Background:

Imaging studies conducted across multiple centres, like AIMS, are an effective way to increase recruitment rates, but bring with them their own particular operational and statistical challenges. In particular, the negative impact of the inflation of variance

arising from the introduction of a between-centre factor.

Objectives:

Thus, the AIMS consortium undertook a calibration study in which a group of healthy volunteers, matched demographically to AIMS cohort, were scanned at each centre under the study protocol.

Methods:

High resolution structural images from T1-weighted and DESPOT sequences were segmented into their component tissue types with a common processing pipeline. At each intra-cerebral voxel in standard MNI space the partial volume estimates were then regressed onto a random effects model to estimate the within-centre error variance. Subsequently, based on the known sample size, type II error rate and distribution of recruitment across participating centres, power calculations estimated maps of the minimum effect size (MES) that could be observed.

Results:

Strong spatial inhomogeneity in MES was observed with segmentations derived from both sequences and a direct comparison between them informed the design of the main AIMS study.

Conclusions:
Furthermore, the MES maps provides additional information for the interpretation of regions where significant differences were observed between autistic and control participants and, moreover, gives context to the discussion of type II (false negative) errors.

118.120 120 Delayed Brain Activation in Autism by Intersubject Phase Correlation. J. S. Anderson[1], N. Lange[2], J. A. Nielsen*[1], M. A. Ferguson[1], T. J. Druzgal[1], A. Froehlich[1], M. B. DuBray[1], E. D. Bigler[3] and J. E. Lainhart[1], (1)*University of Utah*, (2)*Harvard University*, (3)*Brigham Young University*

Background: Neural processing delays have been observed in autism with behavioral and electrophysiologic metrics. In particular, MEG investigations have shown delays in auditory processing in superior temporal gyrus. The low temporal resolution of fMRI has limited its applicability to measuring small phase differences in the timing of neural activity.

Objectives: We measured language network activation using an auditory phrase recognition fMRI task in a sample of 45 high-functioning autism and 20 typically developing (TD) subjects, group matched for age and IQ. The task consisted of subjects listening to spoken phrases, with instructions to think of a word being described by each phrase. To evaluate for differences in neural timing, we used a novel method of intersubject phase correlation wherein normalized time series data were compared across individuals to obtain voxel-level maps of synchronous activation between subjects.

Methods: For each pair of 65 subjects, fMRI time series were compared at each voxel for significant correlation in time between the pair of subjects. For each pair of subjects at each voxel, a cross-correlation curve was computed and the optimal phase recorded. For TD vs. TD, TD vs. autism, and autism vs. autism pairs of subjects, the average phase difference for each sample was recorded at each voxel in the brain.

Results: Classical language areas showed significant intersubject correlation in a spatial distribution similar to the activation map obtained from conventional general linear model analysis for the language task. In addition to language areas, areas of the default mode network also showed synchronous timing across subjects to the language task. Within TD subjects, intersubject phase correlation was able to accurately measure the phase delay of left Broca's area activation relative to left primary auditory cortex as 2.3 +/- 0.08 seconds, compared to average duration of spoken phrases of 2.2 +/- 0.2 seconds, as expected in a language task where subjects listen to the sentences and then respond covertly. Phase delays of 1.3 seconds in left Broca's area, 1.8 seconds in right Broca's area, 1.1 seconds in precuneus, 0.8 seconds in supplementary motor area, and 0.5 seconds in left Wernicke's area were observed in

autism group relative to the TD group. Within the autism sample, intersubject correlation was slightly but significantly less than for TD population in primary auditory cortex, left Broca's area, left Wernicke's area, and supplementary motor area.

Conclusions: Intersubject phase correlation was able to measure significant delays in activity in autism relative to TD subjects, including both language regions and the default mode network. This finding may represent propagation of small phase delays in early sensory processing areas to cause widespread dyssynchrony in distributed cortical networks in autism responsible for allocation of attentional resources and processing complex cognitive tasks. Intersubject phase correlation may represent a useful technique for assessing spatial distribution of neural timing delays in autism and other neurological disorders.

118.121 121 Describing the BRAIN IN AUTISM IN FIVE DIMENSIONS – A MULTI-PARAMETER CLASSIFICATION APPROACH. C. Ecker*[1], A. Marquand[2], J. Mourao-Miranda[3], P. Johnston[1], E. Daly[1], M. Brammer[2], C. M. Murphy[1], D. Robertson[2], S. C. Williams[2] and D. G. Murphy[1], (1)*Institute of Psychiatry, King's College London*, (2)*Institute of Psychiatry, King's College*, (3)*University College*

Background: Autism spectrum disorder (ASD) is a neurodevelopmental condition with multiple causes, co-morbid conditions, and a wide range in the type and severity of symptoms expressed by different individuals. In addition, several aspects of cerebral morphology are implicated in people with ASD – including both volumetric (i.e. cortical thickness, surface area) and geometric features (i.e. cortical shape). This makes the neuroanatomy of ASD inherently difficult to describe. Recently, we have introduced a framework for automatic image classification using whole-brain structural MRI scans, and were able to identify individuals with ASD at an accuracy of 80%[1]. The present study replicates these findings in an independent sample using an improved multi-parameter classification approach.

Objectives: The objective of this research was therefore to characterize the complex and subtle structural pattern of gray matter abnormalities in adults with ASD on the basis of multiple morphometric parameters, and to disentangle spatially distributed patterns of regional differences with potentially different neuropathological underpinning. Furthermore, we aimed to examine the predictive value of individual morphometric parameters for group membership (i.e. diagnostic value).

Methods: Structural MRI data was collected on 20 well-characterized male adults with ASD (mean age = 33 yrs, mean FSIQ = 103), and 20 age/IQ matched healthy controls. All individuals with ASD met algorithm cut-offs for ASD on both the ADI & ADOS. For each participant, a set of 5 morphological parameters including both volumetric and geometric features were obtained at each spatial location on the cortical surface (i.e. vertex) was obtained using FreeSurfer software. This set of measures was then used to (1) discriminate between individuals with ASD and controls using a Support Vector Machine (SVM) analytical approach, and to (2) find a spatially distributed pattern of regions with maximal discriminative power.

Results: Overall, SVM achieved good separation between ASD and control group and was able to identify individuals with ASD at a sensitivity and specificity of up to 90% and 80% respectively using cortical thickness measures. In addition, SVM revealed spatially distributed, independent patterns of regions with maximal discriminative power for each of the five morphometric features describing brain volume and geometry. For all parameters, the left hemisphere provided higher classification values than the right hemisphere.

Conclusions: Our results confirm the hypothesis that the neuroanatomy of ASD is truly multi-dimensional, i.e. affecting multiple brain regions with a differential involvement of individual areas. These differences also provided significant predictive power for group membership, and could thus be used as a potential biomarker for ASD to facilitate and guide the behavioural diagnosis. The spatial patterns detected using SVM may also help further exploration of the specific genetic and neuropathological underpinnings of ASD, and

provide new insights into the most likely multi-factorial aetiology of the condition.

[1] Ecker et al. (2009). Investigating the predictive value of whole-brain structural MR scans in autism: a pattern classification approach. NeuroImage [Epub ahead of print]

118.122 122 Disrupted Long-Range Connectivity in the Mirror Neuron System in Children with Autism Spectrum Disorders. J. D. Rudie*[1], Z. Shehzad[2], N. Colich[1], S. Y. Bookheimer[1], M. Iacoboni[1] and M. Dapretto[1], (1)*University of California, Los Angeles*, (2)*Yale*

Background: Converging evidence from neuroimaging and neurobiological studies of autism has led some to propose that autism spectrum disorders (ASDs) result from a failure of coordinated neural activity across long-range networks required for complex reciprocal social behavior (see Geschwind & Levitt, 2007, for review). In addition, dysfunction in the mirror neuron system (MNS), which rely on "long-range" fronto-parietal circuits subserving sensorimotor integration, has been linked to social communication deficits observed in ASD (see Oberman & Ramachandran, 2007, for review). We have previously shown that high-functioning children with ASD display less MNS activity in the right pars opercularis of the inferior frontal gyrus (IFG) compared to typically-developing (TD) controls while observing and imitating emotional expressions.

Objectives: We sought to further test the hypothesis that individuals with ASD have diminished functional connectivity across long-range networks that underlie complex social behavior. Specifically, we were interested in examining functional connectivity within the MNS. In order to test this hypothesis, we used a seed based functional connectivity analysis to characterize differences in connectivity in the MNS between TD and ASD children.

Methods: Twenty-three high-functioning children with ASDs and twenty-five typically developing children (matched by age, gender, IQ and head motion) passively observed faces displaying different emotions (angry, fearful, happy, sad, and neutral) while undergoing functional Magnetic Resonance Imaging (fMRI). Using an event-related design, each face was presented for two seconds according to an optimized random sequence. In order to minimize connectivity between regions simply due to task-related activity, we removed task effects by using the residuals from the general linear model that included the stimuli timings convolved with a double gamma-HRF. The right pars opercularis, as defined from the Harvard-Oxford probabilistic atlas (25% probability), was used as a seed region in our whole brain functional connectivity analysis.

Results: Direct contrasts of whole-brain corrected connectivity maps showed that in TD children, activity in the right pars opercularis was more strongly correlated with other long-range mirror neuron regions, including contralateral IFG and bilateral inferior parietal lobule. Children with ASD showed stronger local connectivity with anterior cingulate and ventromedial prefrontal cortex. While we regressed out the task effects, these "pseudoresting state" networks may still reflect enhanced correlations in networks involved in processing facial expressions.

Conclusions: Building on our previous findings of significant between-group differences in the frontal component of the MNS, the current results found during the observation of facial expressions provide supporting evidence of a relationship between deficits in ASD and the MNS. Additionally, increased connectivity with the anterior cingulate in participants with ASD is interesting in light of recent studies showing hyperactivity or the inability to deactivate the anterior cingulate cortex in individuals with ASD (Tesink 2009, Dichter 2009). The present findings highlight the importance of functional connectivity approaches in autism neuroimaging research and add to the literature implicating dysfunction in long-range networks in ASD etiology.

118.123 123 Functional Neuroimaging of Phonological Processing in Parents of Individuals with Autism. L. B. Wilson*[1], J. R. Tregellas[1], E. Slason[1], B. E. Pasko[1], S. Hepburn[2] and D. C. Rojas[1], (1)*University of Colorado Denver*, (2)*University of Colorado Denver School of Medicine*

Background: Delayed or absent language acquisition is a diagnostic criterion in two of the three autism spectrum disorders, with deficits involving phonology (i.e., the sound system of language) seen in a large subset of individuals with autism. In addition, deficits in phonological processing have been shown to be familial in autism (Folstein, et al. 1999; Schmidt, et al. 2008). To date, however, no neuroimaging studies have investigated phonological processing in autism.

Objectives: In the present study, we used functional magnetic resonance imaging (fMRI) to investigate the neurobiological substrates of phonological processing in parents of individuals with autism.

Methods: Fourteen parents of a child with autism and eighteen controls performed a phonological priming task while undergoing fMRI. The task consisted of four prime-target conditions including homophones (e.g., PAUSE-paws), pseudohomophones (e.g., BRANE-brain), unrelated (e.g., ARCH-gash), and word-nonword (e.g., FRAIL-clute) stimuli. Stimuli presentation was as follows: 500ms mask, 30ms prime, 30ms blank screen, 400ms target, and 1040ms blank screen. Primes were presented below perceptual threshold at 30ms in order to investigate the initial, automatic stages of visual word recognition and to avoid possible differences in the use of strategic or controlled processes between groups. Subjects were not informed that stimuli consisted of word pairs and performed a lexical decision task (i.e., is it a word or nonword?) on all lowercase targets. Functional images were acquired using a GE 3T whole-body magnet with a gradient-echo T2* Blood Oxygenation Level Dependent (BOLD) contrast technique. Data were realigned to the first volume, normalized to standard space, smoothed with an 8mm FWHM kernel, and evaluated using the GLM in a random effects whole-brain analysis in SPM8.

Results: Controls, as a group, exhibited enhanced hemodynamic responses for phonologically primed stimuli (i.e., homophones and pseudohomophones) relative to unrelated stimuli in regions known to be involved in phonological processing, including left lateralized inferior frontal and inferior parietal cortex, with no response differences observed between homophone and pseudohomophone stimuli (FDR, $p<0.05$). The parent group did not exhibit greater responses for phonologically primed relative to unrelated stimuli. Parents, however, exhibited greater responses for pseudohomophone relative to homophone stimuli in several regions including left lateralized superior temporal, middle temporal, and insular cortex (FDR, $p<0.05$). Direct group comparisons revealed that controls exhibited greater responses than the parent group for primed relative to unrelated stimuli in the left inferior frontal cortex (SVC, $p<0.05$). Furthermore, parents exhibited greater responses than controls for pseudohomophone relative to homophone stimuli in left lateralized inferior parietal, supramarginal, middle temporal, and inferior temporal gyri (SVC, $p<0.05$).

Conclusions: These results provide evidence for possible neurobiological correlates of the phonological processing deficits that have been observed in parents of individuals with autism. By clarifying the familiality of these deficits, our long-term aim is to identify endophenotypes that could be used to guide future genetic linkage studies and clinical interventions in autism.

118.124 124 Fusiform Gyrus and Face Processing: Intrasubject Stability, Hemispheric Asymmetry, and Effective Connectivity. J. D. Herrington*[1], D. W. Grupe[2], E. T. Hunyadi[1], C. S. Shin[1], A. H. Foss[3], J. M. Taylor[1] and R. T. Schultz[1], (1)*Children's Hospital of Philadelphia*, (2)*University of Wisconsin-Madison*, (3)*University of California-Berkeley*

Background: Abnormalities in the structure and function of fusiform gyrus (FG) are promising biomarkers of autism spectrum disorders (ASD). There is quite a large neuroimaging literature on FG function in healthy, non-ASD participants, but nearly all samples are relatively small (< 20). Larger samples are needed to study issues such as hemispheric asymmetries and regional brain connectivity. In addition, statistical and image processing methods have greatly

advanced in recent years, and past studies have often used approaches that were suboptimal. A more complete understanding of FG function and connectivity in typically developing samples is critical for the study of ASD.
Objectives: The present study tested 3 primary hypotheses. First, FG would not only show a sample-wide main effect for faces (versus a non-face condition), but would prove highly stable on a per-participant basis. Second, FG activity would be significantly right-lateralized. Third, FG would show effective connectivity with amygdala – another brain structure implicated in ASD. Exploratory analyses tested unilateral versus bilateral connectivity models between FG and amygdala.
Methods: 46 typically developing adults (22 female, Mean/SD age 23.7/3.0) completed a 5-minute fusiform "face localizer" task in which side-by-side pairs of faces and non-faces (houses) were presented. Participants were asked to indicate whether the pairs represented the same or different person or house (subordinate-level processing).
Statistical analyses consisted of a) per-voxel GLMs of task effects, b) per-voxel tests of task X FG and task X amygdala effects (i.e., psychophysiological interactions), and c) dynamic causal modeling of FG-to-amygdala connectivity. In order to formally test the rightward asymmetry typically associated with FG, fMRI data were registered to a symmetrical brain template via non-linear algorithms. This symmetrical registration procedure – to our knowledge the first applied to face processing data – allowed for direct, focal (per-voxel) asymmetry tests.
Results: Support was obtained for each of the three primary hypotheses. 45 participants (98%) showed significantly increased FG activation during face perception. 43 participants (94%) also showed significantly increased amygdala activation during face perception. Group findings were remarkably robust in these and other brain areas (including the lateral occipital complex and dorsolateral prefrontal cortex), surviving Bonferroni correction. As predicted, these analyses revealed a strong rightward asymmetry within FG and adjacent temporal regions, including superior temporal sulcus (also implicated in ASD). Lastly, exploratory connectivity analyses using psychophysiological interactions and dynamic causal modeling supported a bidirectional model of FG-to-amygdala connectivity above unidirectional models (i.e., FG-to-amygdala or amygdala-to-FG).
Conclusions: Data from this study verify, and quantify, hypothesized asymmetry and connectivity models of FG function. These data underscore the relevance of FG, amygdala, and their connectivity, in the processing of facial information – a network implicated in the pathobiology of ASD. It is likely that findings on FG-amygdala connectivity differences in ASD would appear most robustly in studies using relatively brief face tasks that are widely deployed (i.e., large samples and short scan durations).

118.125 125 Long-Range Fronto-Parietal Connectivity Is Related to Language Abilities in Children with and without Autism Spectrum Disorders. A. A. Scott*[1], B. S. Abrahams[2], A. I. Alvarez-Retuerto[2], L. Sonnenblick[2], D. Ghahremani[2], J. Mumford[2], R. A. Poldrack[2], M. Dapretto[2], D. H. Geschwind[2] and S. Y. Bookheimer[2], (1)*Scripps Translational Science Institute*, (2)*University of California, Los Angeles*

Background: Autism is a neurodevelopmental disorder characterized by impairments in language and social communication, and accompanied by restricted interests and stereotyped behaviors. A growing body of evidence implicates disruption of frontal cortical connectivity in autism spectrum disorders (ASD). Recently we found that an autism risk gene, *CNTNAP2,* modulates frontal functional connectivity in children with and without an ASD. This risk gene has been linked with language ability in both autism, and specific language impairment (SLI). Together, these findings suggest that variation in *CNTNAP2* may confer disease risk by biasing the brain towards different patterns of connectivity. These findings prompted us to test the hypothesis that variation in frontal functional connectivity is associated with language abilities in children with and without autism spectrum disorders.

Objectives: The aim of this investigation was to determine whether patterns of functional connectivity with the medial prefrontal cortex (mPFC) are related to verbal ability (verbal

IQ and receptive language) across children with and without an ASD.

Methods: We conducted task-independent functional connectivity analysis on functional magnetic resonance imaging (fMRI) scans collected from sixteen typically-developing (TD) boys (12.3 ± 1.76; FSIQ: 119.0 ± 8.41) and 16 age- and IQ-matched high-functioning boys with ASD (12.4 ± 2.14; FISQ: 112.3 ± 13.6). Briefly, a nuisance model including prewhitening with task as an explanatory variable, white matter average timeseries, cerebrospinal fluid average timeseries and motion included as covariates was run and residuals computed. The average timeseries from the seed ROI (mPFC) was extracted from the residual image. Both the extracted timeseries and residual image were normalized and entered into subject-wise correlations to create mPFC functional connectivity maps for each subject. Whole-brain regressions on the functional connectivity maps using verbal IQ (VIQ) and receptive language scores from the Peabody Picture Vocabulary Test (PPVT-III) were conducted.

Results: A whole-brain regression on mPFC functional connectivity with verbal IQ scores revealed a positive correlation in posterior cingulate cortex ($MNI_{x,y,z}$= -10, 41, 48; Z = 4.23), bilateral angular gyri (Right $MNI_{x,y,z}$= 52, -54, 30; Z = 4.34; Left $MNI_{x,y,z}$= -52, -56, 24; Z= 3.13), and right superior cerebellum ($MNI_{x,y,z}$ = 40, 076, -34; Z=4.52). An additional whole-brain regression on mPFC functional connectivity with receptive language scores from the PPVT demonstrated a positive correlation with right angular gyrus ($MNI_{x,y,z}$ = 46, -66, 40; Z = 3.81) and right superior cerebellum ($MNI_{x,y,z}$ = 44, -70, -34; Z = 4.18).

Conclusions: These results indicate that children with higher verbal IQ scores had increased anterior-posterior functional connectivity between medial prefrontal cortex and posterior heteromodal speech, language and attention areas. Similar to the positive correlation observed with VIQ, which taps expressive language ability, we found that children with better receptive language abilities, as measured by the PPVT, also demonstrate stronger long-range connectivity between the mPFC and parietal cortices. These findings support the contribution of long-range frontoparietal networks to verbal abilities and reflect the importance of these connections for language development and autism pathogenesis.

118.126 126 A MEG Study of Functional Connectivity During Preparation for Saccades in ASD. T. Kenet*[1], E. Orekhova[2], H. Bharadwaj[3], N. Shetty[1], A. K. Lee[3], M. Vangel[1], M. Elam[4], M. R. Herbert[5], M. S. Hämäläinen[1] and D. S. Manoach[6], (1)*Massachusetts General Hospital*, (2)*Institute of Neuroscience and Physiology, Sahlgrenska Academy, Gothenburg University*, (3)*Massachusetts General Hospital-Harvard Medical School*, (4)*Sahlgrenska University Hospital*, (5)*Massachusetts General Hospital / Harvard Medical School*, (6)*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 make more errors than controls on an antisaccade task.

Objectives: Given compelling evidence of cortical hypo-connectivity in autism, we investigated long-range coherence in ASD during fixation and in preparation for prosaccades and antisaccades. We hypothesized that coherence in the network subserving volitional ocular motor control would be reduced in ASD. 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 11 age and gender matched neurotypical controls (NTC) 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 during the preparatory interval in between the instructional cue and stimulus appearance.

Results: In sensor space ASD participants showed significantly reduced coherence relative to NTC participants, most prominently in the alpha band, with the right hemisphere showing significantly greater reduction in coherence relative to the left hemisphere. Accordingly, in source space, we focused on alpha coherence and used the superior and inferior frontal eye field (FEF), the key cortical region for saccade generation, as the seed region. In the NTC group, the FEF region had significant coherence values primarily with the intraparietal sulcus (IPS), dorsolateral prefrontal cortex (DLPFC), and the dorsal anterior cingulated cortex, both ipsilaterally and contralaterally, depending on the region and the condition. In the ASD group, FEF showed significant coherence values with many but not all of the same regions, but those were often reduced in the alpha band relative to the NTC group. In particular, the left FEF to left IPS and left FEF to right FEF showed condition dependent group differences, with the strongest effects between the antisaccade and prosaccade conditions.

Conclusions: Our data indicates that when preparing for a saccade, participants in the NTC group show increased coherence in the alpha band between the FEF bilaterally and other cortical regions, relative to the ASD group. The extent of the group differences was task dependent. These findings likely correspond to the neural substrates of deficient inhibition of prepotent saccades observed in ASD.

118.127 127 Basal Ganglia, Amygdala and CEREBELLAR WHITE MATTER Volume and Asymmetry Differences BETWEEN AUTISM Spectrum Disorder and Typically DEVELOPING Boys. N. Shetty*[1], K. Singh[2], T. Kenet[1], J. Fanelli[1], G. Chapman[1], H. Bharadwaj[2], A. Orinstein[3] and M. R. Herbert[1], (1)*Massachusetts General Hospital*, (2)*Massachusetts General Hospital-Harvard Medical School*, (3)*University of Connecticut*

Background: Brain morphometry in autism spectrum disorders (ASD) has yielded heterogeneous findings. Diverse clinical features of autism may theoretically be associated with a range of brain regions. Abnormalities in amygdala are thought to be correlated with emotion and particularly with fear, while abnormalities in caudate are thought to be associated with repetitive and restricted behaviors (e.g. stereotypies) and with movement abnormalities. Increased brain volume does not have a clear cut behavioral correlate but might be related to abnormalities in functional connectivity.

Objectives: Using whole brain gray-white brain segmentation, we sought to identify total and regional brain volume and asymmetry differences between ASD and typically developing (TD) subjects.

Methods: MRI scans were acquired on a 3T Siemens, and segmentation data was analyzed for volume differences between groups, as well as for regional asymmetries and asymmetry differences between groups. Participants included 10 ASD (8.5 +/-1.27y) and 11 TD (8.55 +/-1.97y). The analyses were performed on both raw data (non-normalized) as well as after normalizing for cerebral volume. Effect sizes were calculated [(Mean volume for autistics-mean volume for typical)/Pooled Standard deviation] on right side, left side and bilaterally (right+left) for all segmentation volumes. Then, mean ASD and TD segmentation volumes were compared between groups using the Multivariate ANOVA for correlated data (Proc Mixed in SAS) to obtain significance (p) values for each of the segmentation volume. Finally, Symmetry Indices (SI) [2*((Volume Left-Volume Right)/(Volume Left+Volume Right))*100] were calculated and compared between groups. Also, a one-sample t-test was performed to test whether the SIs in each group were significantly different from 0. All between-group analyses included adjustments for age, handedness and non-verbal IQ.

Results: Total cerebral volume asymmetry was significant for autistics (t -2.39; p 0.0406) but not for TD (t -0.98; p 0.3496). However there were no significant between

group differences in either total cerebral volume (F 0.04; p 0.85) or total cerebral volume asymmetry (F 3.00; p 0.1090). Analysis of the data normalized to cerebral volume showed that Caudate was significantly smaller in ASD than TD on right (ES -0.68; p 0.0316), left (ES -0.787; p 0.047) and bilaterally (ES -0.77; p 0.03), although there were no differences in raw caudate volume between ASD and TD groups. Total Amygdala volume adjusted for cerebral volume was smaller in ASD than TD (p=.0375, ES = -.43) but neither right nor left nor any raw volumes of amygdala were different between groups. Significant asymmetries were found in both ASD and TD in putamen (ASD: p=.0015; TD:p=.0002) and pallidus (ASD: p=.0011,TD: p=.0008) and in TD only for cerebellar white matter (p=.0495) and amygdala (p=.0371).

Conclusions: Our preliminary findings are consistent with other studies showing differences in caudate and amygdala between ASD and TD subjects. We also note a modest loss of regional asymmetry in ASD. Given the lack of difference in total brain volume between groups, the source of differences in significance of amygdala and caudate measures between raw and adjusted volumes remains unclear.

118.129 129 Category Representation in Autism and Unaffected Siblings. B. C. Vander Wyk*[1], C. M. Hudac[1], C. Cheung[1], S. M. Lee[1], A. Berken[1], M. R. Dillon[1], C. A. Saulnier[2] and K. A. Pelphrey[1], (1)*Yale University*, (2)*Yale University School of Medicine*

Background:

Although autism spectrum disorders (ASD) are highly heritable no single genetic mechanism has yet been identified. Neuroimaging studies have converged on functional impairments in regions of the brain dedicated to processing social stimuli, such as faces. However, it is unclear which dysfunctions are necessary correlates of autism, which may indicate vulnerability, and which are epiphenomenal.

Objectives:

Unaffected siblings of children with autism did not develop an ASD, but share many genetic and environmental factors with their affected siblings, especially when compared to standard control groups. Therefore, they are an ideal population for investigating brain systems associated with increased vulnerability to an ASD. Our objective is to characterize differences and similarities in brain activation to several kinds of social and nonsocial stimuli. Target groups include children with autism, unaffected siblings of children with autism, and typically developing children.

Methods:

To date, 34 children and adolescents have participated in this fMRI study. Children with autism (n = 12) were characterized by scores on the ADOS and ADI-R, the SRS, and the Vineland II. ASD and other neurodevelopmental disorders were ruled out in a group of age and IQ matched unaffected siblings (n = 14). In addition, we targeted typically developing children (n = 8), who did not have siblings on the spectrum. In a blocked design, participants viewed black and white exemplars of stimuli from several categories: neutral faces, houses, objects, letters, and Arabic numerals.

Results:

Regions that preferentially responded to faces (left amygdala, left inferior frontal gyrus, & right fusiform gyrus), houses (bilateral parahippocampal gyrus), and letters (left middle temporal gyrus) were defined from the data of typically developing adults. Among the child groups, no differences were found in response to houses in the parahippocampal gyri, or in response to letters in the middle temporal gyrus. However, differential patters were observed in regions that preferentially responded to faces. Within the left amygdala, both the children with autism (ASD) and the unaffected siblings (UAS) exhibited hypoactivation relative to typically developing children (TDC). Within the right fusiform, only the children with ASD showed hypoactivation. Within the left inferior frontal gyrus, the UAS showed hyperactivation relative to TDC and ASD.

Conclusions:

Uniform activation to houses and letters among the groups suggest that neither generalized cortical hypoactivation nor global deficits to visual information processing are part of the neuroendophenotype of autism. Consistent with previous neuroimaging studies of individuals with autism, we found reduced activation to faces in the amygdala and fusiform gyrus. Unaffected siblings also exhibited reduced activation to faces in the amygdala, but showed normal activation in the fusiform. So although hypoactivation in the limbic system to social stimuli may be associated with autism, it is not sufficient to cause the disorder. Interestingly, unaffected siblings showed increased activation, relative to typical controls, in the left inferior frontal gyrus. It is possible that increased activation in the left inferior frontal gyrus is either a buffer against susceptibility to autism, or is part of a system of compensatory mechanisms.

118.130 130 Cognitive Control of Social and Non-Social Information in Autism: An fMRI Investigation. A. Sabatino*[1], A. Rittenberg[2], N. Sasson[3], J. W. Bodfish[4] and G. Dichter[2], (1)*University of North Carolina at Chapel Hill*, (2)*University of North Carolina*, (3)*University of Texas at Dallas*, (4)*University of North Carolina - Chapel Hill*

Background: Individuals with Autism Spectrum Disorders (ASDs) are characterized by fMRI activation differences in frontostriatal brain regions during tasks that require cognitive control (Schmitz et al, 2006). This finding has been conceptualized to reflect the repetitive behaviors that are a core feature of autism. Our research group has demonstrated that frontostriatal functioning in ASDs during a cognitive control task is moderated by the presence of social stimuli (Dichter et al, 2009).

Objectives: The purpose of the proposed study was to extend this line of research to investigate frontostriatal functioning in response to nonsocial stimuli presented in a cognitive control context.

Methods: Participants with and without autism completed an oddball target-detection task. On half the runs, targets were neutral faces taken from the Nimstim set of face stimuli. On half the runs, targets were so-called "High Autism Interest" (HAI) stimuli, derived from a passive-viewing eye-tracking study of children with autism (Sasson, et al. 2008). To date, we have assessed 16 typically developing individuals [mean age= 24.10 ± 3.58] and 5 individuals with Autism [mean age= 23.45 ± 4.83]. Primary analyses will contrast response to "HAI targets" and "Face targets."

Results: Data collection is ongoing; however, analysis on our current sample reveal two important findings. First, replicating our previous findings, the ASD group demonstrated relatively greater dorsal anterior cingulate activation in response to face targets. However, the opposite pattern was observed in response to HAI targets: the ASD group displayed relatively *decreased* dorsal anterior cingulate activation in response to HAI targets.

Conclusions: Research has demonstrated that autism is characterized by aberrant functioning of frontostriatal brain systems during tasks requiring cognitive control. The overarching goal of our research is to examine frontostriatal functioning in autism when task stimuli are relevant to core symptoms. We have previously reported that ASD is characterized by dorsal anterior cingulate (dACC) hyperactivation during a cognitive control task that used social stimuli (Dichter et al, 2009). We interpreted this pattern to reflect the greater cognitive "effort" required to response to social targets in autism. dACC hyperactivation to face targets may represent a compensatory mechanism that is engaged to respond appropriately to social stimuli during a cognitive control task. We have extended this line of research to assess cognitive control of stimuli relevant to repetitive behaviors in autism, namely nonsocial stimuli that elicit greater visual attention in children with ASDs. In contrast to the pattern of brain activation observed in response to social targets, nonsocial targets prompted the opposite pattern of findings in the dACC: the ASD group demonstrated *less* dACC than their neurotypical counterparts. This finding suggests that cognitive control abilities in ASD may be superior to neurotypical individuals in the presence of certain nonsocial stimuli. These findings indicate that functioning of neurobiological mediators of cognitive control

in autism is dependent on the types of stimuli processed: relevant brain systems may function more poorly in social contexts and less poorly in nonsocial contexts. Relations between fMRI activation patterns and core autism symptoms will be assessed, and implication for the executive function theory of autism will be discussed.

118.131 131 Corticocerebellar Resting State Correlations in Autism. T. A. Zeffiro*[1], I. Soulières[2], S. Whitfield-Gabrieli[3] 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)*, (3)*Massachusetts Institute of Technology*

Background: Altered cerebellar function has been suggested as the source of speech and movement atypicalities in autism. The cerebellum is strongly connected with motor control systems in the cerebral cortex. Evidence from both neurophysiologic and neuroimaging studies have identified four spatially distinct body maps in the cerebellum, with two representations in each hemisphere, one in the anterior cerebellum (Lobule IV/V) and the other in the posterior cerebellum (Lobule VIII). These body maps are connected to cortical motor areas via the thalamus and receive reciprocal connections via corticopontine and pontocerebellar projections. Recent work has demonstrated that functional MRI can be used to record spontaneous BOLD-contrast fluctuations at rest. Modeling these data using correlation techniques allows estimation of low frequency interregional influences in corticocerebellar systems responsible for supporting a range of sensorimotor and cognitive activities.

Objectives: Our goal was to examine the resting state correlations in four different corticocerebellar systems in autistics. The strength of these correlations may provide information concerning the operation of the structural and functional infrastructure supporting movement in autistics.

Methods: Our sample included 19 autistic and 21 non-autistic participants, matched for age, sex, manual preference and IQ. Using a 3T MRI system, we examined interregional BOLD-contrast bivariate correlations in time series collected over a 10 min period while participants rested with eyes closed. Noise sources were removed using linear regression, including estimated head motion, and average ventricular and white matter signals. Seeds were placed in various parts of the visuomotor control system, including primary motor cortex, supplementary motor area, thalamus, posterior parietal cortex, and cerebellar lobules IV/V and VII. We calculated Pearson's correlation coefficient between the band-pass filtered time series of the seed regions and all brain voxels. The resulting r-maps were then converted to z-scores using the Fisher transform for between-group comparisons.

Results: The between-group analysis was restricted to regions which exhibited positive correlations with the seed regions. Compared to the non-autistics, the autistics had atypical interregional correlations in both hemispheres in frontocerebellar loops, with the lobule IV/V -> thalamus correlations increased, the thalamus -> primary motor cortex correlations increased and the primary motor cortex -> lobule IV/V correlations decreased. The parietocerebellar loops also showed differential influences, with the lobule VIII -> thalamus correlations unchanged, the thalamus -> superior parietal lobule correlations increased and the superior parietal lobule -> lobule VIII correlations increased. In addition, the autistics exhibited reduced correlations between the left and right thalami, suggesting a relative decoupling of their respective hemispheric systems.

Conclusions:

The observed pattern of atypical interregional resting state correlations encompassed anterior and posterior corticocerebellar systems in both hemispheres. Examination of interregional neural influences at rest provides useful information about the functional organization of the distributed neural subsystems responsible for movement execution. In autistics, the corticocerebellar systems involving both frontal and parietal cortex are characterized by generally higher synchrony, perhaps reflecting developmental differences in local synaptic organization. These differences in interregional

corticocerebellar activity may be the neural substrate for the delays and atypicalities in speech and movement commonly seen in autism.

118.133 133 Default Mode Connectivity in Children with and without Autism, and Their Siblings. B. Deen*, A. Westphal, R. J. Jou and K. A. Pelphrey, *Yale University*

Background: Recent fMRI research has used temporal correlations between BOLD signals in the resting-state as an assay of functional connectivity in the human brain. In particular, this research has identified two large-scale, anticorrelated functional networks: the task-positive network, active during the performance of cognitively or attentionally demanding tasks, and the default mode network (DMN), engaged during reflective or ruminative cognition (such as self-reflective thought, theory of mind reasoning, and autobiographical episodic recall). Given that the default mode network has been linked to cognitive functions that are putatively impaired in autism, this network may function abnormally in those with autism; prior research has shown reductions in DMN connectivity in adults with autism, but research has not investigated this network in children with autism. Such research will be relevant to the question of whether connectivity abnormalities play a role in the etiology of autism.

Objectives: To assess functional connectivity in the default mode and task-positive networks in children with autism, and their siblings.

Methods: A collection of children (age 5-15) with and without autism, and unaffected siblings of kids with autism, were scanned in a 3T magnet for 6:40 minutes in the absence of stimulus presentation. Seed voxel-based connectivity analyses were performed in each subject, using time series from precuneus and left anterior insula as predictors, to assess connectivity in default mode and task-positive networks, respectively. Motion artifacts are common in fMRI data acquired in children, and have a particularly strong effect on connectivity analyses; thus any dataset with more than 1mm of motion within a period of 3 TRs (6s) was discarded from the analysis.

Results: Preliminary results suggest that default mode and task positive network connectivity are both largely intact in children with autism, and their siblings, with minimal differences in correlation strengths between kids with and without autism.

Conclusions: Together with prior studies demonstrating DMN abnormalities in adults with autism, these results suggest either that these abnormalities develop after childhood, or that the previously observed differences resulted from the presence of artifacts (e.g., from head motion) in data from subjects with autism. The findings suggest against the claim that abnormalities in long-range connectivity play a central role in the development of autism.

118.134 134 Default Network Correlates of Obsessive Compulsive Symptoms in Autism Spectrum Disorders. M. Carrasco*, J. L. Wiggins, S. J. Peltier, S. J. Weng, K. Clancy, S. Risi, C. Lord and C. S. Monk, *University of Michigan*

Background: Autism Spectrum Disorders (ASD) are characterized by disturbances in social function and communication, and the presence of repetitive behaviors. In addition, ASD is associated with other co-ocurring symptoms, including obsessions and compulsions. These symptoms are reported in 37 - 95% of individuals with autism and have been observed to share some overlap with characteristic symptoms of obsessive-compulsive disorder (OCD). Given these observations, both ASD and OCD are hypothesized to share similar neurocognitive circuits that may underlie the presence of obsessions and compulsions in both disorders. The literature has suggested a possible role for default network dysfunction in ASD and OCD. Objectives: We hypothesized that an alteration of the interplay between structures of the default network may underlie obsessive and compulsive symptoms associated with ASD. We determined whether there are differences in default network connectivity between ASD individuals exhibiting high vs. low obsessive-compulsive symptoms. Methods: 25 ASD children (ages 10-18) and 25 controls matched for age, gender and IQ took part in this functional MRI (fMRI) study. The Autism Diagnostic Interview-Revised and the Autism

Diagnostic Observation Schedule were used to assist in the ASD diagnosis. None of the ASD children received a formal diagnosis of OCD. Obsessive and compulsive symptoms were evaluated by using the Obsessive–Compulsive Inventory-Revised (OCI-R). Categorization into ASD (high obsessive-compulsive symptoms) or ASD (low obsessive compulsive symptoms) groups was based on OCI-R scores: patients with scores <20 were categorized as having "low symptoms," whereas patients with scores >20 were categorized as having "high" symptoms. During fMRI acquisition, 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 posterior cingulate cortex (PCC) and other areas of the default network. Results: Initial efforts in our lab (including a sample of 12 adolescents with ASD and 12 controls) indicated that there are differences in default network functional connectivity between adolescent ASD individuals with high vs low obsessive-compulsive symptoms. Increased obsessive and compulsive symptom severity, as evidenced by higher OCI-R scores, was found to correlate with decreased functional connectivity between the bilateral parahippocampal gyrus, the bilateral angular gyrus, the superior frontal gyrus, and the PCC. Conclusions: Preliminary results show group differences in default network functional connectivity between adolescent ASD individuals with high vs low obsessive-compulsive symptoms. Upcoming analyses will yield additional information on the functional connections between default network structures thought to underlie obsessive and compulsive symptoms associated with ASD.

118.135 135 EEG Coherence of Adolescents with High Functioning Autism During Social Perception. M. Jaime*[1], H. A. Henderson[1], C. Hileman[1], L. C. Newell[2] and P. C. Mundy[3], (1)*University of Miami*, (2)*Indiana University of Pennsylvania*, (3)*UC Davis*

Background: Previous studies have reported reduced cortical connectivity during a resting state in individuals with autism. However, little is known about the nature of cortical connectivity during the processing of social information in autism.
Objectives: (1) To compare differences in EEG coherence during a social perception task between adolescents with high functioning autism (HFA) and typical development (TD). (2) To examine relations between individual differences in EEG coherence and performance on a social cognition task.
Methods: Thirty-seven adolescents (11-19 years old) participated in this study (HFA =19, TD =18). Participants watched 12 videos of a male looking towards a dot appearing at one of the four corners of the screen. During congruent videos, the male's direction of gaze matched the area in which the dot appeared. For the incongruent videos, the male's direction of gaze did not match the location of the dot. EEG was continuously recorded during video presentations and during a baseline (BL) condition in which participants sat still with their eyes open but no video stimulus was presented. Due to no differences in EEG coherence between congruent and incongruent videos, an average was calculated to obtain a single social perception (SP) coherence measure. Coherence was calculated, bilaterally, between pairs of sensor sites located over a short distance frontal area, a short distance temporal-parietal area, a short distance temporal-central area, and a long distance frontal-posterior area. Coherence was calculated for the alpha, beta, delta, and theta frequency bands. Participants were administered the Reading the Mind in the Eyes task.
Results: Overall, attenuated coherence among HFA participants was observed only in the alpha frequency band. This result was qualified by interactions with condition and hemisphere. Specifically, the HFA group showed reduced left coherence during BL and reduced right coherence during the SP condition $F(1, 35) = 6.95$, $p < 0.05$. Both groups showed reduced bilateral EEG (alpha) coherence during the SP condition in the temporal-central area, $F(3,33) = 5.55$, $p < 0.05$. A planned diagnostic group comparison showed HFA participants with reduced EEG (alpha) coherence in the following areas: BL left temporal-parietal ($p < 0.05$) and BL temporal-central ($p < 0.01$). In

addition, greater right frontal (r = .58, p < 0.05) and temporal-central (r = .59, p < 0.05) EEG coherence in the alpha frequency band in the SP condition was associated with better performance in the Eyes task for the TD group but not for the HFA group. No associations were observed in the other frequency bands. Conclusions: Results indicate that adolescents with HFA show reduced cortical connectivity over areas associated with social information processing during a resting state. However, connectivity does not differ significantly from TD adolescents during social perceptual processing suggesting that the neural basis of social information processing deficits in autism may be one of greater effort exerted by the cortex when transitioning from a resting state to social perceptual processing. These results also support the validity of using EEG coherence to study inter/intra-group differences on cortical connectivity and social information processing in autism.

118.136 136 Empathy Deficits Associated with Alexithymia but Not Autism: Evidence From Brain Imaging. G. Bird*[1], G. Silani[2], R. Brindley[3], S. White[4], U. Frith[4] and T. Singer[2], (1)*Birkbeck College, University of London*, (2)*University of Zurich*, (3)*Kings College London*, (4)*University College London*

Background:

A lack of empathy is often described as a feature of Autism Spectrum Conditions (ASC). However, empirical studies of empathy in ASC have produced mixed results, with some evidence for an empathy deficit in ASC being provided by tasks that rely on skills that may be impaired in ASC (e.g. facial expression recognition). More problematic for claims of an empathy deficit in ASC is the high rate of alexithymia in ASC. Alexithymia is described as a subclinical phenomenon marked by difficulties in identifying and describing feelings and difficulties in distinguishing feelings from the bodily sensations of emotional arousal. Our previous work suggests that alexithymia results in empathic deficits, thus making it possible that ASC *per se* does not result in reduced empathy, but that previous findings of an empathy deficit may be due to the increased numbers of alexithymic individuals in this population.

Objectives:

To directly test empathy in individuals with ASC and to determine whether any deficits are due to their autism spectrum condition and/or a result of the increased level of alexithymia in this group.

Methods:

Using functional magnetic resonance imaging (fMRI), we tested empathy in a group of individuals with ASC selected to ensure a wide distribution of alexithymia scores and a matched control group (of individuals without an ASC) with the same wide distribution of alexithymia scores. Empathic brain responses were measured using an 'empathy for pain' paradigm which involves a real-life social setting and does not rely on attention to, or recognition of, facial affect cues. In this task participants lie in the scanner while a partner sits next to the scanner and rests their hand next to the participant's hand. Both the participants and their partner receive brief electric shocks to the back of their hand. Coloured cues indicate whether the participant, or their partner, will receive the shock. This paradigm allows pain-responsive areas of the participant's brain to be identified. Activity can be measured in these areas when the partner receives pain as an index of the participant's level of empathy.

Results:

Importantly, after controlling for alexithymia, there were no differences in the level of empathic brain activity between the ASC and Control groups. In contrast, the degree of alexithymia was significantly associated with empathic brain activity in both groups. The relationship between alexithymia and empathic brain activity did not vary as a function of group.

Conclusions:

These findings suggest that the empathy deficits observed in ASC may be due to the large co-morbidity between alexithymic traits and ASC, rather than representing a necessary feature of the social impairments in autism.

118.137 137 Functional Activation and Connectivity of Dorsal and Ventral Attention Networks in Autism Spectrum Disorder: An

fMRI Study of Visual Search. B. Keehn*[1], L. A. Brenner[2], P. Shih[3], A. J. Lincoln[4] and R. A. Müller[3], (1)*San Diego State University / University of California, San Diego*, (2)*University of California, Los Angeles*, (3)*San Diego State University*, (4)*Alliant International University*

Background: Prior studies have demonstrated that children and adults with autism spectrum disorder (ASD) evidence superior visual search abilities compared to typically developing (TD) individuals. Corbetta and Shulman (2002; 2008) have proposed a dual-system model of visual attention for TD individuals: a dorsal frontoparietal network (bilateral frontal eye fields [FEF] and intraparietal sulci [IPs]) that mediates top-down, directed visual attention and a right-lateralized ventral frontoparietal network (inferior frontal gyrus [IFg] and temporal-parietal junction [TPJ]) that is responsible for reorienting attention to behaviorally-relevant stimuli. Additionally, recent functional magnetic resonance imaging (fMRI) studies investigating visual search have suggested that TPJ suppression may reflect filtered visual processing and assist in reducing the influence of task-irrelevant distractor stimuli.

Objectives: The goals of the present study were 1) to examine the fMRI activation in nodes of dorsal and ventral attentional networks during visual search in ASD and TD individuals, and 2) to investigate the functional connectivity within and between dorsal and ventral attentional networks, using activation-derived regions of interest from a visual search task.

Methods: Twenty children and adolescents with ASD and twenty age, handedness, and IQ matched TD individuals participated in an event-related fMRI visual search experiment. Participants' task was to indicate the presence or absence of a target ("T") embedded within arrays of heterogeneous or homogeneous distractors that varied in set size (6, 12, or 24 items). Baseline trials consisted of a solitary target (target present baseline) or a single distractor (target absent baseline), displayed in the center of the screen.

Results: Behaviorally, there were no significant differences between ASD and TD groups for mean error rates or median response time (RT); however, individuals with ASD showed increased search efficiency for heterogeneous search trials compared to TD individuals, as measured by RT by set size slope. FMRI results indicate increased activation of TPJ in individuals with ASD relative to TD individuals for heterogeneous versus baseline comparisons. Functional connectivity MRI results indicate that individuals with ASD exhibit increased functional connectivity between TPJ and cerebellum. Furthermore, correlations between TPJ-cerebellum connectivity reveal that increased functional connectivity is related to increased search efficiency (RT by set size slope) for ASD, but not TD, individuals.

Conclusions: Contrary to previous reports, the current study did not find accelerated visual search RT in children and adolescents with ASD; however, individuals with ASD demonstrated increased search efficiency for the most difficult search trials as compared to TD individuals. Functional activation and connectivity analyses revealed abnormally increased activation and connectivity of the ventral attentional network in ASD. Decreased TPJ suppression relative to baseline in ASD may suggest abnormal top-down filtering of distractors during visual search. Additionally, functional connectivity between TPJ and cerebellum was correlated with search efficiency, suggesting that increased search efficiency in ASD may be related to atypical functional connectivity between these regions.

118.138 138 Investigating White Matter Abnormalities in Autism Using Voxel Based Morphometry and Voxel Based Relaxometry. Y. Gagnon*[1] and R. Nicolson[2], (1)*University of Western Ontario*, (2)*The University of Western Ontario*

Background: Although there is strong evidence that autism is associated with abnormal brain development, the anatomical extent and timing of any neurobiological differences are unknown. Findings of volumetric studies in children with autism often implicate increased white matter volumes, with more recent studies focusing

on evaluating regional contributions to an overall white matter volume increase. 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 follow-up studies finding disproportionally localized increases in the frontal and parietal lobes, as well as radiate and bridging white matter. This pattern of increased T2 parallels that of increased white matter volume of some volumetric studies in autism.

Objectives: The purpose of this study was to further investigate any possible relationship between white matter volumes and T2 differences in patients with autism with a voxel-wise multimodal image analysis mapping method known as biological parametric mapping (BPM).

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. 10 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.

Results: Data have been collected and preprocessed and results are pending BPM analyses. Both an ANCOVA will be performed using T2 data as the principal modality and white matter VBM data as the imaging regressor. Given the changes in T2 described in childhood, the statistical analysis will be covaried for age. Furthermore, a correlation analysis between these two datasets will be performed on a voxel-by-voxel basis using BPM's correlation model.

Conclusions: Conclusions are pending analyses

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118.139 139 Clustering of Autistic Patients Based On Pathogenetic Components. R. Sacco[1], P. Curatolo[2], B. Manzi[2], R. Militerni[3], C. Bravaccio[4], C. Lenti[5], M. Saccani[5] and A. M. Persico*[1], (1)*Univ. Campus Bio-Medico*, (2)*Tor Vergata University*, (3)*II Univ. of Naples*, (4)*University Federico II*, (5)*Univ. of Milan*

Background: We have recently identified four principal components providing major contributions to autism, namely (I) a disruption of the circadian cycle associated with behavioral and sensory abnormalities, (II) a dysreactive immune process, surprisingly linked both to prenatal obstetric complications and to excessive postnatal body growth rates, (III) a generalized developmental delay, and (IV) an abnormal neural circuitry underlying stereotypies and early social behaviors.

Objectives: To identify clusters of ASD patients characterized by specific patterns of principal components and to estimate their frequency.

Methods: We performed a k-means clustering of the same 245 patients assessed in our principal component analysis, using regression-based factors, each representing one cumulative component score. The K-means method is an unsupervised learning algorithm that assumes k clusters fixed a priori and defines k centroids, one for each cluster.

Results: ASD patients could be categorized into four clusters: (a) 43 patients (17.6%) have intense immune-related symptoms, accompanied by circadian and sensory issues; (b) 44 patients (18.0%) display intense circadian and sensory symptoms, with some developmental delay and stereotypies, but little or no immune dysfunction; (c) verbal and/or motor stereotypic behaviors predominate over the other three components in 73 (31.0%) patients, and (d) 83 (33.9%) patients show a mixture of all four components, with developmental delay somewhat more pronounced, and the other

components less pronounced, compared to the remaining three clusters. The "immune" component II exerts the highest discriminatory power ($F=111.247$, df 241, $P=2.7 \times 10^{-45}$), followed by "stereotypic" component IV ($F=98.165$, df 241, $P=1.4 \times 10^{-41}$).

Conclusions: Despite the long-recognized interindividual variability in clinical phenotype, it seems possible to begin dissecting clusters of autistic patients based on a set of clinical, patient and family history variables. We are in the process of replicating and extending these results using a neural network approach. If replicated, these clusters may be used to explore differences in genetic underpinnings, disease course and severity, as well as in response to therapies.

118.140 140 Cranial Width (not Macrocephaly) Is Markedly Increased in Multiplex Autism and Predicts the Extent of Craniofacial Dysmorphology. R. E. Butler*[1], C. Lajonchere[1], S. S. Nazarian-Mobin[2], B. S. Chambers[1], R. W. Francis[3], A. R. Shell[3], J. R. Cuomo[4], M. M. Urata[2] and C. Deutsch[5], (1)*Autism Speaks*, (2)*Children's Hospital Los Angeles*, (3)*Eunice Kennedy Shriver Center*, (4)*Harvard University*, (5)*Shriver Center and McLean Hospital, Harvard Medical School*

Background: Several laboratories have reported a statistical overrepresentation of macrocephaly in autism. This begs the question of how cranial enlargement is manifested. Also, earlier studies point to an excess of dysmorphic features in autism, but the phenotypic relationship between cranial dimensions and other forms of craniofacial dysmorphology has not yet been explored.

Objectives: We now ask whether these dimensions are proportionately increased or, rather, are disproportionately increased along the principal axes of the cranium: width and length. Further, we determined the extent to which increased dimensions predict craniofacial dysmorphology. This was measured by quantitative morphometry of 3D craniofacial surface images, providing objective and reliable measures of anomalies.

Methods: Subjects were recruited from the Autism Genetic Resource Exchange (AGRE) and the testing was conducted at Children's Hospital, Los Angeles. Craniofacial surface images were obtained by a stereo-photogrammetric image capture system (3dMD, Atlanta), and quantitative analyses were performed using 3D landmark-based morphometry. Spreading calipers (GPM, Zürich) were used to directly measure cranial length and width. The study was limited to subjects who were Caucasian (N=40), for whom normative data are most extensive. Measurements were converted to standardized (z-) scores, conditioned on demographics using a new digitized version of the Farkas norms (FaceValue; N = 1312).

Results: There was a substantial increase in cranial width (biparietal diameter) among subjects with autism. In contrast, cranial length (anterior-posterior distance) was decreased. Width approached a full standard deviation (mean/SD z-score = + 0.80/ 1.43) above the population mean ($p < .0001$), yet length was approximately half of a standard deviation in the opposite direction (mean/SD z-score = - 0.49/ 1.10; $p < .004$). In contrast, head circumference was only slightly increased (mean/SD z-score = + 0.18 / 1.06; ns) above population norms. The proportion of head width to length (expressed as the cephalic index), was correspondingly high (mean/SD z-score = + 0.89/ 1.49; $p < .0001$); this disproportionate pattern is classically described as brachycephaly. Moreover, increased width was predictive of increased craniofacial dysmorphology (full-scale anomaly score; $r = 0.46$, $p < .006$).

Conclusions: Cranial width was markedly increased in autism, but there was a corresponding decrease in cranial length. This excessive head width (termed eurycephaly) was seen in 23% of probands using a 3rd percentile cut-off point, constituting over a 7-fold increase above population values. This finding --- combined with the fact that eurycephaly predicted the extent of craniofacial dysmorphology --- suggests that eurycephaly may present a distinct subtype of individuals with ASD and this may help to resolve some of the heterogeneity in studies of genetics and neurobiology.

118.141 141 Diagnosing ASD in Adults: The Use of the ADOS Module 4. A. de Bildt*[1], J. A. C. J. Bastiaansen[2], H. Meffert[2],

S. Hein[3], P. Huizinga[3] and R. B. Minderaa[1], (1)*University Medical Center Groningen*, (2)*University of Groningen*, (3)*Lentis*

Background: Diagnosing Austism spectrum disorders (ASDs) in adults is complicated due to behavioral overlap with other disorders and limited access to developmental historical information. Standardized instruments may serve as tools to facilitate the diagnostic procedure in order to help the clinician judge on the presence of an ASD. The Autism Diagnostic Observation Schedule (ADOS) has a module for adults with fluent speech. After publication of the manual and the initial research underlying the validity and reliability of the ADOS module 4, there has been little research on the use of the ADOS in adults, while the need for instruments that assist the clinician's diagnosis in adults has been growing. Therefore, more research on module 4 of the ADOS in an independent sample is valuable.

Objectives: The current study aims to investigate the psychometric qualities of the ADOS module 4 with respect to the classification and the domains.

Methods: The ADOS module 4 was administered to 93 males aged 18 through 66, in four groups based on clinical diagnosis: ASD (n=38), Psychopathy (n=16), Schizophrenia (n=18) and no clinical diagnosis (n=21). Groups did not differ with respect to age and IQ. The ADOS was administered and scored by trained and experienced examiners, who all had reached inter-rater reliability. Scoring was obtained from two different researchers and discrepancies between their scores were discussed to reach consensus.

Results: ANOVA's showed significant main effects of group on the social and communication subdomains. Post-hoc tests showed that the group with ASD scored significantly higher compared to the Psychopathy group ($p<0.005$) and the Control group ($p<0.001$) on both domains. The group with Schizophrenia also scored significantly higher than the control group ($p=0.05$) on Communication and higher than the Psychopathy ($p<0.05$) and the Control group ($p<.005$) on the Social domain. Compared to the group with Schizophrenia, the group with ASD did not score higher on the Communication ($p=.471$) nor Social domain ($p=.118$). However, when comparing the participants with AD (n=8) with the group with Schizophrenia, the group with AD did obtain higher scores on the social domain ($p=.026$, Mann-Whitney U-test). Outcome on the ADOS for participants with Schizophrenia was related to their scores on the Positive and Negative Symptom Scale (PANNS): more negative symptomatology was associated with higher scores on the social domain ($r=.586$, $p<.05$) and total score ($r=.553$, $p<.05$).

Conclusions: The ADOS module 4 assists the clinician in differentiating ASDs from Psychopathy and from persons with no clinical diagnosis. Additionally, autism is distinguishable from Schizophrenia on the social domain. Difficulties in distinguishing ASDs from Schizophrenia seem to be related to the nature of both disorders and to the relatively high-functioning ASD group in this study.

118.142 142 Diagnosing Autism in Fragile X Syndrome with the Revised ADOS Algorithms and Severity Score. A. Harris*, M. Losh and G. E. Martin, *University of North Carolina at Chapel Hill*

Background: Fragile X syndrome (FXS) is associated with an increased risk of autism, with prevalence rates ranging from ~25-50%. A key step in studying the phenotypic overlap of autism and FXS (and potential role of *FMR1* in autism symptomatology) will be to improve the sensitivity and specificity of autism diagnostic instruments. Revised algorithms for Modules 1-3 of The Autism Diagnostic Observation Schedule (ADOS; Lord et al. 2000), a gold standard measure for autism diagnosis, were recently developed with this goal in mind (Gotham 2007, 2008). Additionally, a standardized severity metric based on the revised algorithm scores has also been developed (Gotham, Pickles & Lord, 2009). Importantly, emerging research comparing autism diagnosis using the previous Western Psychological Services (WPS) algorithms to the new algorithms has revealed a shift in classification of autism

spectrum disorders (ASD) in individuals with FXS (Harris et al., 2009).

Objectives: This study compared autism classifications derived from the new severity metric with those based on the original WPS version of the ADOS algorithm and the new research algorithms in children with FXS with and without autism, as well as children with autism only. We also examined the association between autism classification and severity scores to determine the utility of considering such scores to characterize autism symptomatology in FXS.

Methods: The new algorithm classifications for Modules 2 and 3 were examined for a group of 68 boys and 25 girls with FXS, and 14 boys with ASD only (no FXS). Participants ranged in age from 4-15 years. Raw scores of the new algorithm were mapped onto the calibrated severity scores provided in Gotham et al. (2009). The classification of each individual based on the calibrated severity scores was then compared to classifications from the new algorithm, and the original WPS algorithm. We examined changes in classification across groups and frequency of severity scores within groups.

Results: The new severity index classification (SIC) resulted in substantial changes in autism classification among males with FXS. Twenty-seven percent (12/45) previously assigned a "spectrum" diagnosis using the old algorithm, were re-classified as autistic using the new SIC.. The frequency of the severity scores was also most varied in males with FXS. Twenty-five percent of males with FXS (31% in Module 2) received a score of 6 (the autism cut-off score for the SIC). This mirrors the percentage of diagnostic change seen using the new algorithms and the SIC classifications. We found no significant classification changes or frequency differences in girls with FXS or children with ASD only.

Conclusions: Findings indicate a considerable increase in autism classification in boys with FXS using the new algorithms and severity index. Such changes may be related to the severity score cut off. Future work may profit from considering the severity metric in tandem with classifications to better capture the heterogeneity of autism in FXS, particularly in treatment and intervention studies.

118.143 143 Differences in Early Symptom Presentation Between Children with a History of Autism Who Achieve An "Optimal Outcome," and Children with Persisting Autism. M. Helt*[1], T. Dumont-Mathieu[1], I. M. Eigsti[1], M. L. Barton[1], E. Troyb[1], K. E. Tyson[1], M. A. Rosenthal[1], A. Orinstein[1], L. Naigles[1], E. A. Kelley[2], M. C. Stevens[3], R. T. Schultz[4] and D. A. Fein[1], (1)*University of Connecticut*, (2)*Queen's University*, (3)*Institute of Living, Hartford Hospital / Yale University*, (4)*Children's Hospital of Philadelphia and the University of Pennsylvania*

Background: A study is currently following children who have a history of autism spectrum disorder (ASD), but who no longer meet diagnostic criteria for such a disorder. These children have achieved social and language skills within the average range for their ages and receive little or no school support. Several recent studies suggest that this small subset of children, once diagnosed with ASD, achieve an "optimal outcome" (Sutera et al., 2007, Kelley et al., 2006, and Helt et al., 2008).

Objectives: The purpose of the current study was to investigate differences in the early presentation of autistic symptoms in children who later go on to achieve optimal and sub-optimal outcomes.

Methods: Complete medical history forms and Autism Diagnostic Interviews (ADI) were collected from parents of children and young adults with an "Optimal Outcome" (OO) (n = 28), ages 8-21 (M =13.0), and children with High Functioning Autism (HFA) (n = 18), ages 8-18 (M = 13.4). Groups did not differ in gender (p = .42), age (p = .77), or WASI full-scale IQ (p = .35). Full-Scale IQ means were M = 110.35, and M = 114.04, for the HFA and OO groups, respectively. **Results:** Parents of OO children were significantly more likely to report that their child had lost skills (28.5 %) than parents of HFA children (5 %), c^2 (3) = 0.048. Parents of OO children were also more likely to report that they never perceived any differences in the intonation, volume, rhythm, or rate of their child's voice (29%) or that any perceived differences in these qualities of the child's voice were quite mild (46%). In contrast,

parents of children with HFA were more likely to report moderate (56%) or severe (14%) differences in their child's prosody at the time the child began to speak, c^2 (3) = 0.049. No differences were found between these groups on average age of diagnosis, household income, additional medical diagnoses, multiplex/simplex status, or any other specific ASD symptoms appearing early in the course of the disorder.

Conclusions: The high number of OO children reported to have lost skills is consistent with previous studies that have reported a high number of regressive cases among children who go on to lose their ASD diagnosis (Fein, Dixon, Paul, & Levin, 2005) and may imply that there are distinct subtypes of ASD with distinct developmental trajectories.

Differences in prosody are common (perhaps even universal) amongst children and adults with ASD and may be the most disabling symptom for high functioning indiviudals (McCann & Peppe, 2003; Paul et al., 2005). Early differences in prosody between OO and HFA groups may imply its potential for aiding in the determination of the severity of an ASD at the time of diagnosis.

118.144 144 Face Processing as An Endophenotype for the ASD Population. J. L. Ward-King*[1], J. J. A. Holden[2] and X. Liu[1], (1)*Queen's University*, (2)*ASPIRE, Queen's University*

Background: In an attempt to identify genes that contribute to different aspects of the autism spectrum disorder (ASD) phenotype, we examined an endophenotype of ASD and correlated this with specific gene variants, particularly functional variants that impact the outcome of two relevant biochemical pathways. Face processing – the process of perception, reaction and recognition that the brain goes through when it perceives a visual stimulus that is configured like a face – is both a social and communicative behaviour that appears early in development, and is linked with many early milestones. Converging evidence from brain imaging studies, event related brain potentials and eye-tracking indicates that the physiological responses that are associated with face processing in typically developing individuals are atypical in individuals with ASD. Furthermore, there is a relationship between abnormalities in face processing in subclinical autism spectrum traits (thought to be present in those genetically related to those with ASD) and those who actually have an autism spectrum condition which indicates that this trait may be a genetically determined marker for ASD. Thus we identified face processing abnormalities as an endophenotype of ASD.

Objectives: This electroencephalogram study addresses the question of whether the relevant polymorphisms of either of the candidate genes (COMT and 5-HTTLPR) that are associated with behavioural effects in response to the viewing of the human face (changes to the N170 and N400 event-related potentials) occur more or less frequently in the autism spectrum disorder (ASD) population and in their first-degree relatives. Given the association of variants in the COMT and 5HTTLPR genes with latency and amplitude of the N170 and N400 waveforms, respectively, it is hypothesized that there is an increased frequency of COMT158Val allele and 5HTTLPR short allele in individuals with ASD and that these variants are associated with poor face processing (i.e. increased N170 latency and reduced N400 amplitude.)

Methods: For genetic assays, a non-invasive saliva or cheek swab sample is collected from each individual with ASD and any consenting first-degree relatives as well as from any unaffected and unrelated age- and gender-matched control participants. A 128-channel EEG is recorded while the participant is asked to look at both faces and objects that appear on the computer screen. The stimuli consist of one face (which elicits the N170 waveform), presented with three expressions: joy, anger, neutrality (which elicits the N400 waveform). There are also three photos of objects. Each face and each object is displayed twenty times for 1300 milliseconds (ms) each time, in a random order, with 1200-1600 ms of black screen between each stimulus presentation.

Results: These data comprise an evolving dataset rendering conclusions preliminary. Individuals with ASD and their first-degree relatives show atypical face processing

relative to controls. Genetic correlations are modest; a larger sample is required for more complete analysis.

Conclusions: The study of face processing as an endophenotype in this small sample of the ASD population and their first-degree relatives is fruitful and continues to be pursued. Atypical face processing is present in these samples and a related genotype is hypothesized.

118.145 145 Investigating the Female Profile of Autism. V. Miller, M. A. Stokes*, J. Manjiviona and T. Attwood, *Deakin University*

Background:
To date, there has been very little research conducted on the female profile of autism, particularly at the high functioning end of the spectrum. This group has been largely overlooked in research. The focus upon the male profile has continued despite the absence of clear genetic or neuroanatomical evidence in support of the reported sex ratio of approximately 4:1. However, some clinical anecdotal evidence suggests that many HFA females are not currently diagnosed because the female phenotypical expression of autism is not congruent with the current male-centric conceptualization of autism.
Objectives:
To systematically examine the profile of HFA females and compare to HFA males and NT females in the areas of behaviour, personal care, verbal and non-verbal communication, conversation, social interactions, peer relationships, play and obsessive interests, at home and at school.
Methods:
Participants in the study comprised of parents and teachers of children and adolescents (aged between 5 and 18 years of age) with or without a diagnosis of HFA, AS or PDD-NOS without the presence of an intellectual disability. Parents were recruited from Australia, the USA, the UK and the Republic of Ireland. Teachers were only recruited from Australia. The parent group included 283 parents of HFA males, 82 parents of HFA females, 27 parents of NT males and 30 parents of NT females. Parents and teachers completed a questionnaire about their child or student. Results were analyzed utilising by tau-equivalence confirmatory factor analysis, discriminant function analysis, and MANOVA.
Results:
Males and females differed significantly on all investigated domains including behavior (__(66)=882.11, p<.001), personal care (__(57)=2413.85, p<.001), verbal and non-verbal communication (__(92)=858.79, p<.001), conversation (__(45)=550.73, p<.001), social interactions (__(45)=837.93, p<.001), peer relationships (__(11)=983.81, p<.001) and play (__(66)=411.77, p<.001). Evidence was also found for a camouflage effect whereby HFA females, in spite of underlying autistic symptomatology, presented in a similar fashion to NT females for the domains of behavior (__(66)=226.27, p<.001), verbal and non-verbal communication (__(93)=285.83, p<.001), conversation (__(45)=155.27, p<.001), social interaction (__(45)=284.80, p<.001) and play (__(70)=4605.49, p<.001). Gender was found to be significantly related to obsessive interests $F(17,402)=14.69$, *p<.001).* It was found that HFA females could be adequately distinguished from HFA males on the basis of imaginative, creative, unstructured play, self focused play on the computer or in rules based fantasy play, indirect social interactions over the phone and internet and poor independent care skills with 74% accuracy. It was also found that HFA females could be significantly distinguished from NT females on the basis of indirect, parallel play with peers, peer relationships, social withdrawal from peers and family and personal hygiene, presentation and grooming with 74% accuracy.

Conclusions:

Males and females with HFA appear to express their autistic symptomatology in different ways, thus indicating that gender mediates the phenotypical expression of autism. As such it is likely that there are females in the community not being adequately identified. The current male-centric conceptualization of autism will need to be reviewed in the context of these results

118.146 146 Male:Female Ratio Is Related to Autism Spectrum Disorder in the Family and to Maternal Age. E. Ben Itzchak*[1] and D. A. Zachor[2], (1)*Ariel University Center of Samaria*, (2)*Tel Aviv University / Assaf Harofeh Medical Center*

Background:

Research suggests that biological factors such as heredity, gender and parental ages may play a causal role in autism spectrum disorder (ASD). Male:Female (M:F) ratio of 4:1 was documented in most studies. The prevalence of ASD among siblings of individuals with ASD ranges from 2% to 6% in comparison to 0.5-1% in the general population. Increased autism risk was documented with both advanced maternal and paternal ages.

Objectives:

1. To define gender ratio, prevalence of ASD in first and second relatives and maternal ages in a cohort with ASD. 2. To examine possible relationships between gender, familial genetic factors and maternal ages and autism severity, adaptive skills and developmental trajectories (developmental regression/non-regression)

Methods:

The study included 564 children who came to a tertiary autism center in Israel for a comprehensive evaluation. A pediatric neurologist obtained birth and developmental histories and performed a neurological examination. Evaluations of autism severity and of adaptive skills were performed using standardized tests [Autism Diagnosis Interview (ADI-R), Autism Diagnosis Observation Schedule (ADOS, the new ADOS severity scale and Vineland Adaptive Behavior Scales].

Results:

Of the 564 participants, 461 (81%) children, (M=39.8 months SD=26.3) were diagnosed with ASD.

Gender: M:F ratio in ASD cohort was (6.8:1) which was significantly higher than the known ratio (4:1) ($\_^2$=14.8, p<.001). Autism severity was not different between boys (M=7.5, SD=2.0) and girls (M=7.4, SD=2.1). However Vineland composite scores were significantly better in boys (M=67.1, SD=10.0) than in girls (M=63.1, SD=13.1) [F(1,308)=4.7, p<.05, h^2=.015]. Of the specific Vineland domains, only in motor skills boys showed significantly better scores (M=83.3, SD=13.9) than girls (M=73.7, SD=21.6) [F(1,276)=13.4, p<.001, h^2=.015]. Developmental regression was significantly higher in girls (33%) than in boys (23%) ($\_^2$=3.1, p<.05).

Familial genetics: Of 441 participants, 32 (6.8%) had a sibling diagnosed with ASD, and 51 more (12%) had a second-order relative diagnosed with ASD in the extended family. No difference was noted in adaptive skills, autism severity or developmental trajectories between the groups with and without ASD in the family. Male/female ratio was significantly lower in the group with a first-order relative with ASD (2.5:1) than in the group without ASD in the family (7.5:1) ($\_^2$=54.3, p<.001).

Maternal ages: Mean maternal age of the ASD group at birth was 31.1 years (SD=5.8) which was significantly higher than the mean newborns maternal age (29.7y) in Israel (t=5.8, p<.001). M:F ratio in the >35y group (N=100) was 4.5:1 which was significantly lower than M:F ratio of 11.2:1 in the < 25y group (N=49) ($\_^2$.=12.9, p<.001). The two maternal age groups did not differ significantly in the ADOS severity score, Vineland composite scores and developmental regression rates.

Conclusions:

Changes in Male:Female ratio is related to familial ASD and to maternal age. Male predominance is observed in idiopathic ASD, while more females are affected in families with first-and second-order relatives with ASD and with advanced maternal age. Females showed more delayed motor skills and developmental regression than males. This pattern may suggest genetic and epigenetic influences in the etiology of ASD.

118.147 147 Psychopathology and Adaptive Functioning in Individuals with Autism Spectrum Disorders, First Episode Schizophrenia, and Clinical-High-Risk for Psychosis. B. E. Seymour*[1], M. Solomon[2], T. A. Niendam[3], J. D. Ragland[4], J. H. Yoon[4] and C. S. Carter[2], (1)*UC Davis Department of Psychiatry and Behavioral Sciences, MIND Institute, Imaging Research Center*, (2)*MIND Institute, Imaging Research Center*, (3)*UC Davis Department of Psychiatry and*

Behavioral Sciences, Imaging Research Center, (4)*Imaging Research Center*

Background:

Individuals with autism and schizophrenia share many common symptoms. However, few studies have systematically investigated similarities and differences in the behavioral phenotypes of adolescents with autism spectrum disorders (ASDs), first-episode schizophrenia (FEP), and clinical-high-risk for conversion to a psychotic disorder (CHR).

Objectives:

The goal of this study was to compare ASD, FEP, and CHR on measures of co-morbid psychopathology and adaptive functioning. This program of research can provide a means to improve "deep phenotyping" of autism and schizophrenia, assist in differential diagnosis, provide insights for psychosis risk prevention, and reveal differences in the neural mechanisms involved in symptom development and to enhance treatment matching.

Methods:

Four groups of age and IQ-matched ASD (n=19), CHR (n=12), and FEP (n=14) and typically developing (n=15) adolescents aged 12-20 were recruited from the MIND Institute, and the Imaging Research Center at UC Davis Medical Center. They were assessed using gold standard diagnostic measures for each disorder. Parents completed the Behavior Assessment System for Children 2 (BASC-2; Reynolds, 2004), which assesses current functioning. The BASC-2 consists of both clinical (hyperactivity, aggression, conduct problems, anxiety, depression, atypicality, withdrawal and attention problems.) and adaptive behavior scales (adaptability, social skills, leadership, activities in daily life and functional communication). Means from normed scores were compared using appropriate parametric and non-parametric univariate tests with correction for multiple comparisons.

Results:

All clinical groups evidenced significant levels of psychopathology relative to TYP. CHR demonstrated the highest overall level of psychopathology, driven by elevations on the depression, aggression, and conduct sub-scales. CHR resembled ASD in hyperactivity. The ASD group was distinguished by their high scores on the atypicality and withdrawal sub-scales. All clinical groups showed comparable levels of anxiety, and attention problems. The clinical groups exhibited similar deficits relative to typically developing adolescents across the adaptive functioning sub-scales, although the ASD and CHR groups tended to be the most impaired.

Conclusions:

These preliminary results suggest that the clinical groups showed relatively discrete patterns of current co-morbid psychopathology. Individuals with CHR, and to a lesser extent FEP, were most likely to display current aggression and conduct problems, suggesting that this form of externalizing behavior may be more characteristic of individuals on the schizophrenia spectrum and a risk marker for the development of psychotic disorders. Adolescents with ASDs were unique in their atypicality and social withdrawal, suggesting that these symptoms are more characteristic of ASD. Despite these patterns, the groups also exhibited considerable similarities. The ASD and CHR groups displayed comparable and elevated hyperactivity. All three clinical groups evidenced similar anxiety and attention problems suggesting that schizophrenia and autism may share common endophenotypes. All groups displayed significant deficits in adaptive functioning relative to TYP.

118.148 148 Relationships Between Social Functioning Among Children with ASD and Competencies/Problem Behaviors Among Siblings. C. M. Brewton*, K. P. Nowell, M. W. Lasala, S. Peters and R. P. Goin-Kochel, *Baylor College of Medicine*

Background:

Individuals with autism spectrum disorders (ASD) undoubtedly exhibit social-skill deficits, but the range of social-skill functioning can vary drastically from one affected child to the next. Just as with typically developing

children, sibling interactions have been shown to play an influential role in the development of children with ASD (Jones & Carr, 2004; Knott, Lewis, & Williams, 2007; Murray et al., 2008). However, most studies have focused on the proband's outcomes given the presence of an interactive sibling, and less is known about how sibling attributes may influence the social-skill functioning of the proband. It seems plausible that siblings who are less socially competent and/or exhibit some degree of psychopathology may not impart as many socially helpful cues to probands. Understanding more about specific sibling characteristics and how they may relate to probands' social-skill functioning could explain some of the variance in social-domain scores we see among children with ASD.

Objectives:

To investigate the relationship between social-skill functioning among probands with ASD and indices of their siblings' social competencies and problem behaviors.

Methods:

Participants were drawn from a larger population of children with ASD who participated in the Simons Simplex Collection (SSC; https://sfari.org/simons-simplex-collection), with a total sample size of 589 pairs of affected children and their designated siblings. Among probands with ASD, 84.3% were male (*M* age = 8.9 years, *SD* = 2.9); among siblings, 45.5% were male. The majority of sibling pairs were white (83.2%) and came from families with annual household incomes ranging from $66K—$130K per year (43.9%). Pearson correlations were used to examine relationships between (a) the probands' reciprocal social interaction (RSI) scores on the *Autism Diagnostic Interview-Revised* (ADI-R) and social-affect (SA) score on the *Autism Diagnostic Observation Schedule* (ADOS) and (b) the siblings' internalizing, externalizing, ADD/ADHD, and total-problem scores on the CBCL, as well as siblings' scores on the *Social Responsiveness Scale* (SRS).

Results:

Mean scores from the select CBCL subscales were compared to the available normative data (Achenbach, 1991), and no significant differences were found. Significant relationships were noted between proband RSI scores on the ADI-R and sibling CBCL internalizing-problems scores (r = .129, p < .05), ADD/ADHD-problem scores (r = .086, p < .05), and total-problems scores (r = .093, p < .05). Continued analyses include comparable correlations using sibling socialization scores on the *Vineland Adaptive Behavior Scales* (VABS), as well as linear regression to predict probands' RSI and SA scores from siblings' CBCL, SRS, and VABS socialization scores. Proband's IQ score will be considered as a potentially confounding variable in this analysis.

Conclusions:

Preliminary findings suggest a positive, albeit small, relationship between proband social-skill functioning and siblings' problem behaviors. It is difficult to say the direction of the effect, as the proband's difficulties could negatively influence sibling outcomes, or the sibling's competencies could favorably influence the proband's outcomes. Next-step analyses will explore the degree to which siblings' scores on the aforementioned measures predict probands' RSI and SA scores.

118.149 149 Screening for Autism Spectrum Disorders in Young Children Referred for Developmental Assessment: Guiding Efficient Assessment Practices within a Tertiary Clinic Setting. S. E. O'Kelley*, K. Guest, S. M. Munger, K. J. Bailey, F. J. Biasini and E. M. Griffith, *University of Alabama at Birmingham*

Background: While there is an increased awareness and demand for effective screening tools for young children at risk for ASD, there is not yet consensus on which measures are most effective. The M-CHAT and CSBS-ITC show tremendous promise for use in primary care settings to identify toddlers at risk for ASD, but these have not been investigated as closely among children who are referred for evaluation due to known or suspected developmental delays. Given high rates of referral and few clinicians skilled at diagnosing ASD, it is essential that clinics

identify children in need of ASD-specific evaluation as efficiently as possible.

Objectives: To evaluate the utility of two screening measures for ASD in young children in a tertiary care clinic setting, including:

- utility in a clinic-referred sample of children at risk for developmental disabilities

- identification of children without a referral question of ASD who were in need of ASD-specific evaluation

- utility in a more expanded age range (up to 48 months)

- how each measure individually and together predicted ASD diagnosis.

Methods: As part of the intake process for referred children under the age of 4 years, caregivers completed the CSBS-ITC and M-CHAT in addition to a general intake form requesting information about development and referral question. Screeners are used by clinic staff to inform assessment procedures, including whether the child will receive an ASD-specific evaluation in addition to other interdisciplinary assessments. Based on referral question and/or scores on screeners, children were routed to either ASD-specific or more general developmental evaluations. Final diagnoses utilized ADI-R/ADOS and were concluded by members of the interdisciplinary team.

Results: 138 children have been screened using these procedures; diagnostic assessments have been completed on a subset (n = 29). Within the available data, 69% of the children who had a question of ASD were confirmed to have an ASD diagnosis. Among the children with confirmed ASD, 85% were detected with the M-CHAT and 92% were detected with the CSBS-ITC. Within this sample, the positive predictive values for the M-CHAT and CSBS-ITC were 58% and 50%, respectively. Negative predictive values were 80% for the M-CHAT and 75% for the CSBS-ITC. Of the children who screened positive on one or both of the screeners but did not have a referral question of ASD, none received an ASD diagnosis upon specific evaluation. Evaluations are in progress or will be scheduled for an additional 60 children.

Conclusions: Preliminary data indicates that children at-risk for ASD are already being referred for an ASD-specific evaluation. The positive predictive values are lower in the current sample than has been previously reported in community-based samples, warranting additional analyses. The rates of false positives observed on the CSBS-ITC in this sample is likely related to the nature of the non-ASD referrals to our clinics, as most children referred in this age range have concerns regarding language and/or other developmental delays. Subsequent analyses will explore the utility of these measures both within and beyond the typical age ranges for these measures.

118.150 150 Screening the Levels of Reactive Nitorgen Species, Protein Oxidation, Lipid Oxidation and Energy Metabolite (pyruvate) in Autistic Children in Sultanate of Oman. M. M. Essa*, M. Waly, A. Ali and A. Manickavasagan, *Sultan Qaboos University, College of Agricultural and Marine Sciences*

Background: Autism is a developmental disorder. 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. Abnormal lipid oxidation, protein oxidation and energy metabolites (pyruvate and lactate) have been implicated in autism and other neuropsychiatric disorders such as depression and ADHD. No such biochemical data is available for normal and autistic children in Sultanate of Oman.

Objectives: This study was aimed to compare the status of circulatory reactive nitrogen species (RNS), protein oxidation, lipid oxidation and pyruvate in normal and Omani autistic children.

Methods: The blood/plasma samples were collected from SQU hospital, Oman from autistic and control children. Protein and lipid oxidation was assessed in the plasma by quantitation of protein carbonyls and TBARS using ELISA kits (Cayman Inc) respectively. Pyruvate was measured by using pyruvate assay kit (Bio vision). RNS was

measured by using Nitric oxide fluorometric assay kit from Bio vision.

Results: Altered protein carbonyls, lipid oxidation, RNS and pyruvate were found in Omani autistic children as compared with controls.

Conclusions: This is the first study in Omani autistic children and the outcome of this study may give a lead to develop a novel biomarker for early detection of autism. Also this study will give the relationship between oxidative stress and the pathophysiology of autism.

118.151 151 Social Responsiveness: a Quantitative Intermediate Phenotype in Parents of Children with An Autism Spectrum Disorder. W. De la Marche*[1], I. L. J. Noens[2], E. M. Scholte[3], S. Vertommen[1] and J. Steyaert[1], (1)*UPC-K.U.Leuven*, (2)*Katholieke Universiteit Leuven*, (3)*Universiteit Leiden*

Background: Although heritability of Autism Spectrum Disorders (ASD) is up to 90%, finding specific genetic causes has proven to be very difficult. There is genetic heterogeneity (e.g. copy number variants, single nucleotide polymorphisms). Though in some cases dominant genetic effects operate, additive effects seem more common. This means that, on average, both parents may contribute to the risk for ASD without having ASD themselves (Steyaert & De la Marche, 2008). Carrying such a risk factor might result in subclinical traits of ASD. The Social Responsiveness Scale (SRS) (Constantino et al., 2003) has proven to reliably measure traits of ASD in a quantitative way in the general as well as in the clinical population.

Objectives: To assess if parents of a child with ASD show traits of ASD, in-between general population adults and adults with ASD.

Methods: We requested general population (GP) adults, parents of children with ASD (ASD-P) and adults with ASD (ASD) and their partners or parents to complete the Dutch self-report c.q. other-report version of the SRS. Parents of children with ASD with a confirmed ASD diagnosis themselves were added to the ASD-sample. Only questionnaires without missing items were used for the analyses.

Results: So far, we have gathered SRS data on about 1000 GP subjects, 180 ASD-P subjects and 21 adults with ASD.
For male respondents there is a statistically significant ($p<.0001$) difference in SRS total scores between the three groups, on both the self-report (mean scores GP 31.99, ASD-P 36.34, ASD 88.50) and the other-report form (mean scores GP 29.51, ASD-P 41.21, ASD 99.84). In post-hoc pairwise analyses all differences remain significant ($p<.0001$) except for ASD-P versus GP on the self-report questionnaire ($p=.03$). By now, we only have data on two female ASD participants. Preliminary results however show a statistically significant ($p<.001$) difference between GP and ASD-P on the self-report questionnaire in women too.

Conclusions: These preliminary results indicate that (problems in) social responsiveness can be seen as an intermediate phenotype in fathers (and possibly in mothers) of children with an autism spectrum disorder. The results contribute to the hypothesis of genetic variants with each a small effect inherited by the parents as a cause of ASD.

118.152 152 A Comparison of Social and Communication Skills in Autistic Children, Their Clinically Unaffected Siblings and Typically Developing Subjects: Evidence for Genetic Susceptibility. A. Berken*[1], A. Voos[1], D. Sugrue[1], C. A. Saulnier[2] and K. A. Pelphrey[1], (1)*Yale University*, (2)*Yale University School of Medicine*

Background:

Limited research has investigated the possibility of impaired social and communicative behaviors in the siblings of children with autism spectrum disorders (ASD). Studies comparing children with autism to their siblings and to typically developing children using psychometric and behavioral indices have pointed to a broad phenotype of ASD. Social and communication behaviors of phenotypically normal siblings were found to resemble the ASD children more than they did those of typically developing children. *SRS* scores of siblings of children with autism have been shown to be

significantly increased relative to those of probands with PDD-NOS or a psychopathology unrelated to autism. These findings suggest that subsyndromal social impairment may be prevalent among children with an affected sibling.

Objectives:

This study compares the communication and socialization skills of children with ASD to their siblings and to those of typically developing children. The *SRS* and the *Vineland II* are being used to assess symptom expression and adaptive functioning, respectively. The results of this investigation will provide additional information regarding the broad autism phenotype in which "unaffected" siblings demonstrate greater communication and social impairments in relation to their typically developing peers.

Methods:

To date, 28 children and adolescents (mean age 9.68 years, FS IQ= 92.86) were characterized with an ASD according to performance on the *ADOS, ADI-R, SRS*, and *Vineland II*, as well as by the assessment of expert clinicians. Twenty-five unaffected siblings (mean age 10.65 years, FS IQ=115.36) met stringent exclusionary criteria to rule out ASD or other neuropsychological disorders. In addition those with scores of 70 or below on the Adaptive Behavior Composite or any subdomain of the *Vineland II* were excluded.

Results:

Independent samples t-tests indicated that these two groups differed significantly on full scale IQ (t=4.87, p<.001) but not on age (t=1.13, p=.265). Independent samples t-tests demonstrated that probands and their siblings differed significantly on the Communication (*Proband M*=77.08*, Sibling M*= 104.61; t=7.44, p<.001) and Socialization (*Proband M*= 70.60, *Sibling M= 100.18; t*=9.45, p<.001) domains of the *Vineland II*. Results from a Mann-Whitney U test also demonstrated that probands and their siblings differed significantly on the *SRS* (M=82.50, M=43.96; z=-6.07, p<.001). As expected, siblings showed less socialization and communication impairments than did probands. *SRS* and *Vineland II* subscores for typically developing children (age and IQ matched to the siblings) are currently being collected, with the hypothesis that siblings will show more impaired scores than typically developing children.

Conclusions:

Unaffected siblings demonstrated higher adaptive skills and lower symptom severity scores on the *Vineland II and SRS* rating scales, respectively, than did their ASD siblings. It is likely that the siblings of ASD children will show communication and socialization skills intermediate between the proband and typically developing individuals. The addition of a control group will allow for the potential differences between typical children and siblings of children with ASDs to be explored. In sum, these findings would support the notion of a genetic susceptibility of social deficits demonstrated in ASD.

118.153 153 Broad Autism Phenotype (BAP) - Personality Styles and Preferences in a Sample of Portuguese Families of Children with Autism Spectrum Disorders. J. Almeida*[1], S. Mouga[1], R. L. Abreu[1], C. Café[1], T. S. Miguel[1], F. Duque[1], L. Lapa[1], I. Lucas[1], A. M. Vicente[2] and G. Oliveira[1], (1)*Hospital Pediátrico de Coimbra*, (2)*Instituto Gulbenkian de Ciência/Instituto Nacional de Saúde Dr. Ricardo Jorge*

Background: The current researches have been pointing to the study of families of children with autism spectrum disorders (ASD) in order to identify a broad autism phenotype (BAP). The BAP is a set of personality and language characteristics that reflect the phenotypic expression of autism, in non-autistic relatives of autistic individuals. Social Responsiveness Scale (SRS) and the Broad Autism Phenotype Questionnaire (BAPQ), are the two most used scales to check this phenotypic expression.

Objectives: To characterize the BAP in a sample of Portuguese families, where one child has ASD and an unaffected sibling, to identify the autism traits in parents and unaffected siblings.

Methods: The sample consists of 95 families (proband, his parents and the unaffected sibling closest in age to the proband). Family

inclusion criteria were: (1) one child with ASD - ADI-R positive and ADOS (positive for autism or ASD); (2) one unaffected sibling (negative result on SCQ). To assess the BAP: (1) both parents completed the BAPQ about themselves and about their partners; (2) BAPQ was completed for siblings aged >16 years, by themselves and by their parents (3) the SRS was completed by parents about the proband, the sibling and about their partner.

Statistic analysis was performed comparing the different results of the scales with Mann-Whitney test for unpaired samples (_)=0.05, p<0.05.

Results: 95 families: 92M/3F probands, 100 months of median age.

On the BAPQ self-report, relative to published norms, parents exceeded cut-off scores for Aloof Personality (AP), for Pragmatic Language deficits (PRD), for Rigid Personality (RP) and for Total scale, respectively in 40 (21%), 49 (26%), 91 (48%) and 34 parents (18%); indicating that parents had multiple features of the BAP.

However, on the parents BAPQ informant report the percentages of abnormalities were lower than that observed in the self report view. Actually for parents cut-off scores were exceeded only in 16 (8%) for AP, 42 (22%) for PLD, 35 (18%) for RP and in 18 (9%) for Total scale.

Regarding to the results of the siblings (n=18) on the BAPQ self and informant report, 3 subjects (17%) exceeded cut-off scores in AP, PLD and Total. In the RP more siblings had exceeded cut-off scores in subject's report (n=7, 39%) than in informant (n=2, 11%).

Comparing parents self and informant report, we found significant differences in personalities traits between fathers and mothers. Fathers are more aloof (p<.03) and mothers more rigid (p<.02). Moreover in general fathers demonstrate more BAP characteristics (p<.01).

Relative to SRS, 47 parents (25%), 59 siblings (62%) and 90 probands (95%) exceeded cut-off for ASD traits total score ≥60. Comparing mother, father and siblings, there are significant differences (p<.028).

Conclusions: We found a remarkable percentage of fathers and mothers with autistic traits especially in the self report view. In general fathers demonstrated more autistic personality, mainly aloof type. Mothers are more rigid. Worrying is that in the SRS more than a half of the "unaffected" siblings exceeded the cut-off for pathology. These findings should be replicated in a larger sample and compared with families without autistic cases.

118.154 154 Cholesterol Levels in Young Children with Autism and Typically Developing Controls. S. J. Spence*, A. Thurm and S. E. Swedo, *National Institute of Mental Health, National Institutes of Health*

Background: High rates of autism are observed among patients with Smith Lemli Opitz Syndrome (SLOS), a rare genetic disorder with low cholesterol levels resulting from genetic defects in sterol synthesis (Tierney et al., 2001; Sikora et al., 2006). To investigate whether SLOS might go unrecognized in autism, Tierney et al., (2006) examined a large group of children with ASD for biochemical evidence of SLOS by measuring total cholesterol levels. While no patients with SLOS were detected, a subset of patients was found to have low cholesterol levels, leading to the hypothesis that other sterol deficits might contribute to the ASD phenotype.

Objectives: To determine if children with autism (AUT) have abnormally low cholesterol levels, in comparison with NHANES norms and a group of typically developing children (TYP).

Methods: AUT and TYP subjects were participants in a phenomenological study examining subtypes of autism. Autism is diagnosed by ADI-R, ADOS and clinical judgment. Children with typical development have normal scores on cognitive, adaptive behavior and ADOS assessments.
Cholesterol levels were taken from a clinical laboratory panel obtained at baseline evaluation. Normative cholesterol values

were drawn from NHANES data according to age and gender.

Results: Cholesterol measurements were available for 87 AUT (ages 2-8) and 35 TYP (ages 2-8). Table 1 shows mean cholesterol, and distributions of high, normal and low levels of cholesterol for both groups. In comparison with the NHANES norms, low levels were over-represented in both groups. 18.4% of AUT and 14% of the TYP sample had levels that were >1.65 SD (5th centile) below the mean. 11.5 % of AUT and 5.7% of TYP had levels that were >2 SD below the mean (2nd centile). The between group differences were not significant by Fisher's exact testing.

	N	mean (g/dl)	High (>1.65 SD above the mean)	Normal	Low (<1.65 SD below the mean)	Very Low (<2 SD below the mean)	Lowest (>2.5 SD below the mean)
AUT	87	140.2	4 (4.6%)	67 (77%)	16 (18.4%)	10 (11.5%)	2 (2.3%)
TYP	35	134	0 (0%)	30 (86%)	5 (14%)	2 (5.7%)	0 (0%)

Conclusions: Low cholesterol levels were found more often than expected in both the TYP and AUT groups. These results demonstrate the importance of having a local control group, as a comparison of the AUT results against the NHANES norms would have suggested a specific deficit in the affected individuals. Since the TYP group also differed from the larger NHANES sample, the increased rates of low cholesterol levels may be due to other factors, such as lab methodology, family history, or nutritional intake. Although no significant differences were seen in overall rates of abnormalities, it is interesting to note that 2 AUT children but none of the TYP children were in an "extremely low" group (>2.5 SD below the mean). Larger samples are needed to further examine the relationship of very low cholesterol levels and autism.

118.155 155 Cognitive Profiles, Phenotypic Heterogeneity and the Severity of Symptoms in Autism Spectrum Disorder. S. Brennan*[1], E. Heron[2], G. Hughes[1], R. J. Anney[2], M. Gill[2] and L. Gallagher[1], (1)*Trinity College Dublin*, (2)*Trinity College Dublin, Ireland*

Background: Autism spectrum disorder (ASD) is characterised by a high degree of phenotypic heterogeneity. This heterogeneity is primarily the result of individual differences in cognitive profiles and the severity of autistic symptoms. Previous research has suggested that cognitive abilities may ameliorate the severity of autistic symptoms in certain cases. Objectives: Thereby, implying that the autism spectrum could be composed of distinct subgroups with differing cognitive profiles that index different severity phenotypes as opposed to a severity gradient of autistic symptoms that exists independently of cognitive abilities. Methods: The verbal IQ, performance IQ and severity metric scores (severity of symptoms) of 534 participants were explored using hierarchical cluster analyses (namely single linkage, average linkage & complete linkage). Results: After subjecting the data to a series of hierarchical clustering analyses and validation techniques, a 5-cluster solution produced by the complete linkage hierarchical clustering algorithm was chosen as the best fit for the data. Conclusions: The results of this study are discussed in terms of previous research and their possible implications for defining ASD heterogeneity, genetics and the efficacy of autism specific interventions.

118.156 156 Descriptive Analysis of Autistic Regression in Families From the Autism Genetic Resource Exchange. A. Fedele*, V. Kustanovich, J. Furr and C. Lajonchere, *Autism Speaks*

Background: Given the heterogeneity of autism spectrum disorders (ASD), it's important to identify subgroups of individuals that may present with an etiologically distinct phenotype. Children with regression may represent a subgroup of individuals with ASD that may provide insight into the biological and genetic causes of the disorder.
Objectives: To provide a descriptive analysis of individuals with ASD enrolled in the Autism Genetic Resource Exchange who report a developmental regression. This analysis provides an evaluation of cognitive and social functioning as well as co-morbid medical conditions.
Methods: Subjects with confirmed diagnoses of autism according to the Autism Diagnostic Interview (ADI-R) and the Autism Diagnostic Observational Schedule (N=895) from 2-21 years of age were assessed as part of a study to collect data and biological samples for research into autism biology and genetics.

The ADI-R provided early developmental histories. A measure of cognitive functioning was provided by the Stanford-Binet V (SBV) and Ravens scales on a subset of the groups.
Results: The subjects were initially divided into two groups, those with a history of regression and those with no history of regression, according to the ADI-R. 598 (66.97%) subjects had no reported regression (AUT-NR) while 295 (33.03%) had some history of regression (AUT-R). We found no significant differences in age of onset between the AUT-NR (18.6 months) and AUT-R (19.23 months) groups. We did find significant differences in full scale IQ scores on a subset of subjects that had data from the SBV (n = 198). We found a significant difference (p = 0.0005152) between the full scale IQ of the AUT-NR vs AUT-R groups.
We subdivided the AUT-R group into three groups according to the focus of loss. Seventy two subjects had reported regression of language but not social skills (AUT-RL), 96 with loss of social skills but not language (AUT-RS), and 127 with loss of social and language skills (AUT-RLS). We found that full scale IQ scores in these groups differed significantly (Kruskal-Wallis chi-squared = 13.846, df = 3, p = 0.003122).
As previously reported, we found that subjects without regression had a later age of first word then those with regression (AUT-NR, mean = 34.58, SD = 18.08; AUT-R, mean = 22, SD = 16.55). When we divided the groups as previously shown, we found that the difference was provided by subjects with regression of language (AUT-RL, mean = 18.64, SD = 12.47) and (AUT-RLS, mean = 17.14, SD = 12.33) rather than from those with regression of social skills alone (AUT-RS, mean = 34.23, SD = 19.69). This is significantly later than previously reported.
Finally, we examined whether regression was associated with a medical illness. We found that approximately 26% of subjects who had regression had an associated illness whether the regression was focused on a loss of social skills, language skills, or both.
Conclusions: This study contributes to an understanding of social and language skills in children with autism with and without regression and supports the notion that children with regression may represent an etiologically-distinct phenotype.

118.157 157 Development of a Predictive Gene Classifier for Autism Spectrum Disorders Based Upon Differential Gene Expression Profiles Between Cases and Controls. V. Hu*, *The George Washington University Medical Center*

Background: Autism is a neurodevelopmental disorder which is currently diagnosed solely on the basis of abnormal behavior as well as observable deficits in communication and social functioning. Although a variety of autism candidate genes have been identified on the basis of genetic analyses, none have been shown to be unequivocally diagnostic for *idiopathic* autism or to account for more than a few % of autism cases.

Objectives: To identify limited sets of differentially expressed genes which can robustly distinguish between autistic cases and controls as potential biomarkers for diagnostic screening

Methods: DNA microarray analysis was employed to obtain the gene expression profiles of lymphoblastoid cell lines (LCL) of 87 autistic male individuals who were divided into 3 phenotypic subgroups (Hu et al., Autism Research, 2:78-97, 2009) based on cluster analyses of severity scores on the Autism Diagnostic Interview-Revised (ADI-R) assessment instrument (Hu and Steinberg, Autism Research, 2:67-77, 2009). We compared these expression profiles against that obtained from LCL of 29 nonautistic male control subjects. Using these datasets, we then utilized gene classification and cross-validation analysis software to identify sets of differentially expressed genes that have a high statistical probability of predicting cases and controls.

Results: We have identified panels of selected genes (less than 30) which correctly classify samples according to affected/unaffected status with an accuracy exceeding 90%. When autistic samples are subtyped according to ADI-R cluster analyses prior to the gene expression and classification analyses, the accuracy of correct assignment to cases and controls exceeds 98%. High throughput quantitative nuclease

protection assay of a subset of "classifier" genes (n=14) for one of the ASD subtypes further confirms the ability of the selected differentially expressed genes to identify autistic and control subjects with an accuracy of ~80%.

Conclusions: Limited sets of differentially expressed genes can distinguish between autistic cases and controls with high accuracy. We suggest that such panels of genes may serve as useful biomarkers for screening or diagnosis of idiopathic autism.

118.158 158 Diagnostic Instruments for EARLY IDENTIFICATION of AUTISM Spectrum Disorders. A. Mereu*[1], M. Carta[1], G. Doneddu[2] and R. Fadda[3], (1)*A.O. Brotzu*, (2)*Azienda Ospedaliera Brotzu*, (3)*University of Sheffield*

Background: Recent progress has been made in the early identification and diagnosis of children with Autism Spectrum Disorders (ASDs) (Fombonne & De Giacomo, 2000; van Daalen et al., 2009). On this basis, early identification of children with ASDs has come to be recognized as a critical aspect of their medical management and treatment (Itzchack & Zachor, 2009). However, the convergent validity of different tools for early diagnosis requires further investigation.

Objectives: The purpose of the current study was to investigate the relationships among four widely used diagnostic measures for ASDs in toddlers: ADOS-G, ADI-R, STAT, and clinical judgment based on DSM-IV criteria. Methods: The participants were 43 children with ASDs: 22 with a clinical diagnosis of Autism, 15 of PDD-NOS and 6 with Asperger syndrome (35 male, 8 female, mean chron. age= 48 months, mean developmental age= 22 months). The children were diagnosed in terms of clinical judgment based on DSM-IV criteria and with the ADOS-G, ADI-R and the STAT. We calculated the sensitivity, the specificity, and the positive predictive value of the three instruments (ADI-R, ADOS-G, STAT) measured against DSM-IV-based clinical judgment for diagnosing ASDs in very young children.

Results: Based on Cohen's kappa, there was significant agreement for the diagnosis of ASDs between clinical judgment and ADOS-G ($k=0.672$, $p<.001$), ADI-R ($k=0.811$, $p<.001$), STAT ($k=0.765$, $p<.001$), and between STAT and ADOS ($k=1.100$, $p<.001$). Sensitivity, specificity, and positive predictive values had similar rates for the ADOS. ADI-R had lower sensitivity but equal specificity compared to the other measures. STAT specificity was slightly higher for the diagnosis of PDD-NOS.

Conclusions: The results indicate that the ADOS-G, ADI, STAT and the clinical judgment based on DSM-IV criteria converge in showing agreement in the diagnosis of ASDs in toddlers. Considering their characteristics in terms of sensitivity, specificity and positive predictive values, all these instruments should be included as important tools in clinical protocols for early identification of ASDs.

118.159 159 Head Circumference in the Autistic Spectrum: a Comparative Study. A. K. D. Nguyen*[1], A. A. S. Meilleur[1], E. Chevrier[1], R. Godbout[2] and L. Mottron[1], (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*Hôpital Rivière-des-Prairies*

Background: A significant proportion of autistic children have a larger-than-typical head circumference (or macrocephaly) after 14 months of age. Most studies on autistic children show a macrocephaly prevalence of 16% - 20% against 3% in typically developing children. In adulthood, Lainhart and colleagues (1997) report an increased macrocephaly prevalence rate of up to 19.4% in autistic adults. Despite numerous head circumference studies involving autistic and non-autistic children, studies in well-defined groups of autistic adults remain limited. Moreover, few studies have controlled for height and IQ despite the fact that head circumference is usually proportional to the height of the individual (Bushby et al., 1992), and that IQ could be associated with brain size (Aylward et al., 2002).

Objectives: 1) To construct an adult head measurement reference chart for typically developing adults that takes height into consideration, and that could be used for clinical purposes. 2) To compare the proportion of macrocephaly among a group of autistic adults and a group of typically developing adults.

Methods: 1) 100 male adults will be recruited among personnel at Rivières-des-Prairies Hospital and students at the University of Montreal in order to construct the reference scale. Height, weight and head size will be measured. 2) Two groups of 40 male subjects, autistic and non-autistic (aged 18-40; IQ between 80 and 130), will be recruited within the hospital's database. Non-autistics who experienced past head trauma and who have a family history of psychological/neurological disorders, and autistics who have evident neurological/medical anomalies or other axis 1 disorders (except ADHD and dysphasia), are excluded from the study. Between-group differences will be tested using the scores obtained from the newly-made reference scale. Macrocephaly is defined as head circumference above the 97th percentile when controlling for height.

Results: 1) For the reference scale, so far, we have obtained measurements from 49 participants. Preliminary results show a positive relationship between head circumference and height (r=0.36). 2) So far, complete data have been obtained for 12 autistic and 20 typically developing participants matched on Wechsler full-scale IQ (F=0.378, p=.54). Preliminary results show a 16.7% prevalence of macrocephaly in the autistic group compared to no macrocephaly cases in the typically developing control group (according to Bushby's 1992 chart, as a temporary reference).

Conclusions: Preliminary findings in a reference group indicate the necessity of taking height into account when measuring head circumference. Preliminary findings in the head circumference comparison study indicate that macrocephaly in autism persists into adulthood.

118.160 160 Identification of Autism Specific Impairments through Behavioral Observation of Brief Parent-Child Interactions. S. Elmensdorp*, R. L. Koegel and L. K. Koegel, *University of California, Santa Barbara*

Background: Early identification of children with autism is crucial for the provision of early intervention services. Research suggests that autism-specific intervention provided before the age of 3 leads to improved long-term developmental outcomes. In order to identify children early, however, behavioral characteristics must first be identified that can discriminate young children with autism from children with other developmental delays.

Objectives: The purpose of this study was to identify behavioral characteristics of young children at risk for autism to determine if these characteristics could be used to effectively discriminate young children at risk for autism from children at risk for other developmental delays within a community-based setting.

Methods: This study utilized analysis of scores on the Vineland Adaptive Behavior Scales (VABS; Sparrow, Balla & Cicchetti, 1984) and video analysis of parent-child interactions during 10 minutes of free play in a community-based screening setting. Two groups of children were identified including one group with autism spectrum disorder (*n=15)* and one group with developmental delays (*n=18)* with a mean age of 26.3 months (*SD=4.4).* Videotaped behavior samples were coded using interval scoring for specific child behaviors including: looking at face (eye contact), directed affect, and the initiation of joint attention. A MANOVA was used to analyze group means on the VABS scores and behavior variables.

Results: Results showed that the VABS scores on the Adaptive Behavior Composite, Communication, Daily Living, and Socialization were significantly lower in children with autism and the use of all three behaviors were also significantly lower in children with autism. These behavioral characteristics were evident in all of the children with autism spectrum disorders during only ten minutes of parent-child interaction.

Conclusions: The low rates of the behavioral variables were evident during brief parent-child interaction, suggesting that abnormalities can be detected in a short period of time and may be used to improve early identification practices.

118.161 161 Language Discourse Profiles in the Broad Autism Phenotype. E. F. Dillon*[1], M. Losh[2], G. Goff[1] and E. J. Sanders[1], (1)*University of North Carolina, School of Medicine*, (2)*University of North Carolina at Chapel Hill*

Background: Impaired language discourse (i.e., connected speech such as conversation or narrative) is a hallmark of autism. Studies have documented similar but milder discourse features in relatives of individuals with autism (e.g. Landa et al., 1991; 1992), which have been referred to as one component of the broad autism phenotype (BAP). Prior studies using global rating scales have documented patterns of abrupt topic changes, topic preoccupation, over-talkativeness, detailed and confusing accounts, and insufficient background information (Landa et al., 1991; 1992; Ruser et al., 2007; Piven et al., 1997). While richly descriptive, it is unclear what discourse mechanisms might underlie these profiles. In attempt to address this question, this study employed a fine-grained discourse coding system to conversational samples obtained from parents of individuals with autism and parents of typically developing individuals. The coding scheme applied has been used in prior studies of high-functioning individuals with autism (Losh & Capps, 2003; Capps, Losh, & Thurber, 2000), and thus may afford direct comparisons of discourse profiles in autism and the BAP

Objectives: Analyses aimed to document the extent to which the discourse features of the BAP may be qualitatively similar to those documented in high functioning autism. We also aimed to identify specific discourse mechanisms that could underlie the global pragmatic language difficulties noted in prior work by examining associations between our microanalytic discourse coding system and global ratings of pragmatic language violations using measures employed in prior work.

Methods: Conversational samples were collected from 11 autism parents and 11 control parents using a semi-structured interview. Conversations were transcribed verbatim and coded for discourse elements by coders blind to group status. Coding focused on the use of evaluative devices, which are used to imbue narratives with a psychological perspective and integrate episodic elements within an overarching theme (e.g., Labov & Waletzky, 1967). The use of evaluation has been shown to be impaired in high functioning autism. Pragmatic language was also coded from video by independent coders using the Pragmatic Rating Scale (PRS) (Landa, et al, 1992) which has been used in prior work to document global pragmatic language violations in the BAP.

Results: No significant group differences were found in the length of conversations or in the frequency of evaluation. However, differences were detected in the use of specific types of evaluation that have been shown to be impaired in autism – autism parents differed from controls in their use of mental state language [$t(1, 20)=2.314$, $p=.031$] and hedges [$t(1, 20)=-2.194$, $p=.04$]. Parents' use of these evaluative devices was also correlated with more severe pragmatic language impairments as measured by the PRS ($p < .05$).

Conclusions: Results highlight particular discourse mechanisms (i.e., the use of evaluation) as potentially underpinning the pragmatic language features associated with the BAP and autism. Because the use of evaluation has also been shown to be impaired in autism, these findings may point toward this discourse device as a marker for genetic liability to autism.

118.162 162 Maternal, but Not Paternal, Interstitial Duplications of Chromosome 15q11.2-q13 Are Associated with ASD in 9 Individuals. N. Urraca*[1], J. E. Cleary[2], V. Brewer[1], K. Mcvicar[1] and L. Reiter[1], (1)*University of Tennesee Health Science Center*, (2)*The University of Memphis*

Background: It has been estimated that as many as ~3-5% of all autism cases may be the result of duplications of the 15q11-q13 region. Unfortunately, genotype-phenotype correlations have not consistently demonstrated that these duplications are the sole cause of ASD in these cases. Maternally transmitted 15q duplications consistently show autistic features with variable degrees of developmental delay. Only a few cases of paternally transmitted 15q duplication have

been reported and are associated with speech delay and behavior problems, but not autism.
Objectives: to perform an in depth phenotype analysis of individuals with interstitial 15q duplications and determine if maternal duplication is required for the diagnosis of autism spectrum disorder (ASD

Methods: We used neuropsychological, language and ASD diagnostic tools for phenotypic analysis in patients recruited through the IDEAS parent support group (www.idic15.org). In addition we performed High Resolution Melting analysis (HRM) of the maternally methylated SNRPN locus to determine the parent of origin of the duplications

Results: Nine pediatric subjects with interstitial duplication 15q have participated in the study. Eight patients scored as ASD upon ADOS/ADI-R analysis and one scored "no ASD" on both tests. In the neuropsychological evaluations 3/9 patients had a low average IQ score, 3/9 were borderline and the others had mental retardation, although the patients were noted to have a higher verbal IQ than performance, they had a low-moderate adaptive functioning score on the Vineland II evaluation. All patients performed below age corrected average for receptive vocabulary (Peabody Picture vocabulary test). HRM analysis was done in all patients: 8/9 had a maternal duplication and 1/9 had a paternal duplication. The sizes of the duplications ranged from 5Mb to 12.77Mb and included typical BP1-BP3, BP2-BP3 and duplications including the BP1-BP3 region plus additional regions upstream or downstream of the BP1-BP3 region. The size of the duplication involved does not appear to correlate with the severity of the phenotype or the ASD diagnosis.

Conclusions: in our study only maternally derived interstitial duplications result in ASD, not paternal duplications. It should be noted that several of our patients were adopted so parental DNA was unavailable for genotype analysis. HRM analysis for maternal specific methylation patterns at the SNRPN locus allowed us to determine the parental origin of the duplication in all samples tested.

118.163 163 Preliminary Evidence of the in Vitro Effects of BDE-47 On Innate Immune Responses in Children with Autism Spectrum Disorders. P. Ashwood[1], J. Schauer[2], I. N. Pessah[2] and J. Van de Water*[2], (1)*M.I.N.D. Institute, University of California at Davis*, (2)*University of California at Davis*

Background: Autism spectrum disorders (ASD) are complex neurodevelopmental disorders that manifest in childhood. Immune dysregulation and autoimmune reactivity may contribute to the etiology of ASD and are likely the result of both genetic and environmental susceptibilities.
Objectives: We examined a common persistent organic pollutant, 2,2',4,4'-tetrabrominated biphenyl (BDE-47), for differential effects on the immune response of peripheral blood mononuclear cells (PBMC) isolated from children with ASD (n=19) and age-matched typically developing controls (TD, n=18). Methods: PBMC were exposed in vitro to either 100 nM or 500 nM BDE-47, before challenge with an innate immune activator bacterial lipopolysaccharide (LPS), or the T cell mitogen phytohemagglutin A (PHA). Resultant cytokine production was then measured using the LuminexTM multiplex platform. Results: The cytokine responses of LPS stimulated PBMC from ASD and TD subjects diverged in the presence of 100 nM BDE. For example, cells cultured from the TD group demonstrated significantly decreased levels of the cytokines IL-12p40, GM-CSF, IL-6, TNF_, and the chemokines MIP-1_ and MIP-1_ following LPS stimulation of PBMC pretreated with 100 nM BDE-47 compared with samples treated with vehicle control ($p<0.05$). In contrast, cells cultured from subjects with ASD demonstrated an increased IL-1_ response to LPS ($p=0.033$) when pretreated with 100 nM BDE-47 compared with vehicle control. Pre-incubation with 500 nM BDE-47 significantly increased the stimulated release of the inflammatory chemokine IL-8 ($p<0.04$) in cells cultured from subjects with ASD but not in cells from TD controls. The T cell cytokine response following PHA stimulation was also differentially affected in the ASD subjects. There was an increase in the inflammatory cytokine IL-12p40 production in the ASD

samples following exposure to 100 nM PBDE-47 compared to a reduction in the TD controls (p=0.007). Conclusions: These data suggest that in vitro exposure of PBMC to BDE-47 affects cell cytokine production in a pediatric population. Moreover, PBMC from the ASD subjects were differentially affected when compared with the TD controls suggesting a biological basis for altered sensitivity to BDE-47 in the ASD population.

118.164 164 Regression Histories in Young Children with Autism: Timing and Associations. S. E. Swedo*, S. Shumway, S. J. Spence and A. Thurm, *National Institute of Mental Health, National Institutes of Health*

Background: Developmental regression is not uncommon in autism, yet little is known about the timing and acuity of the loss of skills. In particular, the acuity at which loss occurs (i.e. sudden versus gradual) has rarely been studied. The acuity of regression may provide clues to etiology or pinpoint associated events, such as physical illness, psychosocial trauma or other environmental factors.

Objectives: To explore the timing and acuity of language and social losses in young children with autism, and to determine if physical illnesses/medical conditions or psychosocial stressors were associated with the developmental regressions.

Methods: Parents of 185 children (146 autism, 39 PDD-NOS) with a mean age 53 months (range 21-153 months) were interviewed using the Autism Diagnostic Interview-Revised [ADI-R; a Toddler version of the ADI was administered for children under age 48 months (n=93)]. For this study, regression was defined as loss of at least 5 words and/or a significant loss of social engagement/responsiveness (score of 2 on ADI-R). Acuity of loss was explored through a question on the Early Development Questionnaire (EDQ; Ozonoff et al., 2005), "Was your child's loss of skills gradual or sudden? Please describe." Potential relationships with physical illnesses or psychosocial stressors were explored through answers to open-ended questions on the Early Development Questionnaire.

Results: Twelve of 185 children met criteria for language loss only, 30 children met criteria for social engagement/responsiveness loss only, and 38 met criteria for loss in both areas. Mean age of language loss was 20.7 months (SD = 6.7, range = 12-42), and mean age of loss of social engagement was 18.8 months (SD =6.3, range, 10-51 months).

Among the 80 cases with significant regression, parents of 26 children indicated physical illness/medical issues may have been related to loss of skills, and 21 responses indicated an associated psychosocial stressor (in 7 of these cases, both illness and psychosocial stressors were reported). However, only 8 reports clearly indicated a sudden loss of skills. Five of the 8 cases with sudden loss included both loss of language loss and social engagement/responsiveness. Two of the sudden loss cases were reported to be associated with a physical illness/medical issue and 3 were reported to be associated with a psychosocial stressor (with 1 reported to have both).

Conclusions: Most regression was reported to have been gradual in onset, making it difficult to identify illnesses or events that may have precipitated the developmental losses. Although a causal relationship can only be determined by prospective study of at-risk children, further clues to the nature, timing and events associated with regression may be provided by examination of the children's medical records, which is currently underway.

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118.165 165 Child Characteristics Associated with Motivational Biases and Diagnostic Stability of ASD in the First Three Years of Life. A. P. Inge* and R. Landa, *Kennedy Krieger Institute*

Background: Research from retrospective studies has suggested that child characteristics associated with motivational style may be related to symptom onset and expression in children with Autism Spectrum Disorders (ASDs). These suggestions have recently received support from prospective studies with high-risk infant sibling cohorts.

Specifically, among children who received a diagnosis of an ASD at 36 months, those who were rated by their parents as high approach were identified later (after 14 months), when compared to their high withdrawal counterparts (identified by 14 months), (Garon et al., 2009). Novel to this line of research is the investigation of the association between child characteristics and symptom course and expression as assessed via clinical impression of ASD diagnosis, over the first three years of life.

Objectives: The association of diagnostic stability and child characteristics (i.e., temperament traits and communicative style) was assessed. Diagnostic impression data were reviewed across study time points (14, 18, 24, 30, and 36 months) and stability ratings were assigned for 38 children with ASD. Diagnostic stability was operationalized as consistent ASD impression based on clinician ratings across all available data points. Subjects who were inconsistently rated as ASD positive or who received the diagnosis after 14 months of age were classified as having unstable diagnosis. Children with unstable profiles were expected to show more approach-oriented temperament traits (e.g., high approach, activity) and more frequent communicative behaviors.

Methods: Data on temperament characteristics were collected via parent report on the Toddler Temperament Scale (TTS) at 24 months of age. Behavioral assessment of communicative style was measured using the Communication and Symbolic Behavior Scales, Developmental Profile (CSBS DP) at 24 months. A Social Approach composite was computed by adding total frequency scores of behavioral regulatory communicative acts and shared positive affect. The Mullen Scales of Early Learning, Early Learning Composite (ELC) score was used as a covariate in all analyses given group differences on this measure (i.e., unstable diagnosis group demonstrated significantly higher ELC scores).

Results: Results indicated that children with unstable diagnostic profiles were rated by their parents as more distractible to extraneous environmental stimuli when compared to children with stable ASD profiles (TTS, Distractibility Scale, F (3, 35) = 8.48, p = .006). Additional analyses indicated that an unstable ASD diagnostic profile was associated with more social communication bids when compared to children with stable profiles (CSBS DP, Social Approach Composite, F (3, 35) = 4.24, p = .047).

Conclusions: This study suggests that child characteristics associated with motivational biases are meaningfully related to symptom course and expression as assessed by using clinician impression data. Children with unstable diagnostic impressions were more effectively (easily) distractible by extraneous environmental stimuli and more engaged communicatively both to share positive affect and regulate examiner behavior (e.g., requesting, refusing). Interestingly, frank motivational differences (approach vs. avoidance) were not apparent based on parent report, but were reflected in behavioral observation data of communicative style.

118.166 166 Defining the Characteristics of Distinct Neurological Diseases in Patients with Autism Spectrum Disorders and Epilepsy. G. Barnes*[1], C. Fu[1], D. Lai[2] and A. Popescu[2], (1)*Vanderbilt*, (2)*University of Pittsburgh*

Background: Autism spectrum disorder (ASD) is associated with an increased incidence of epilepsy over the general population. There is considerable variability in the reported incidence; ranging from 5 to 40%. Co-morbid epilepsy contributes negatively to the cognitive, adaptive, behavioral and emotional outcomes for individuals with autism. Early identification of those at particular risk can help target counseling, surveillance measures, and treatment. Various studies have reported risk factors for epilepsy in ASD, some of which are well established including lower IQ, underlying neurologic disorder, language disorders, and sex.
Objectives: To define distinguishing phenotypes of patients with diseases causing autism and epilepsy in a series of 129 patients with ASD and suspected seizures referred to Vanderbilt University Hospital for electroencephalography from January 2004 through February 2009.
Methods: We analyzed the medical records and 147 EEGs including routine (114) and

long term studies (37) to determine characteristics of the ASD patients with epilepsy vs ASD patients without epilepsy. We looked at these variables in both groups: gender, regression, head circumference, rates of epileptiform EEG, and genetic studies.
Results: There was a preexisting diagnosis of epilepsy in 31% of all patients and a history of developmental regression in 17%. Previously diagnosed epilepsy was more likely in patients with a history of developmental regression ($p=0.0085$). Among patients without a prior history of epilepsy, a history of regression significantly increased the risk of having epileptiform discharges on a screening EEG ($p=0.014$). When patients with regression were subdivided by age, we found significantly more epileptiform EEGs when the study was performed at age 10 years or older ($p=0.0015$). Further, the rate of increasing head circumference between < 10 years of age vs > 10 years was significantly less (1.5 cm vs 3.7 cm, $p<0.01$) in ASD patients with epilepsy as compared to ASD patients without epilepsy. The presence of single gene disorders, copy number variants (gains and deletions), and Trisomy 21 does not explain this difference in ASD patients with epilepsy as opposed to ASD patients without epilepsy.
Conclusions: Given the high frequency of epilepsy in this patient population, a high index of clinical suspicion should be maintained for subtle symptoms of seizures in ASD. There is inconclusive evidence to recommend screening EEGs in asymptomatic ASD patients without spells. We propose that screening EEGs should be considered in patients with ASD over 10 years of age with a history of developmental regression and a history of spells suspect for seizures. Further these data suggest ASD patients with epilepsy have a distinct developmental trajectory of head growth compared to ASD alone. A prospective study of ASD patients with and without epilepsy would be helpful to validate this data.

118.167 167 Diagnostic Yield in School-Age Children Referred for Possible ASD. C. A. Molloy*, D. Murray, R. Akers, S. L. Bishop and P. Manning-Courtney, *Cincinnati Children's Hospital Medical Center*

Background: With increased community awareness and media attention, many children are being referred for possible autism spectrum disorder (ASD) for the first time during their school age years. It is not clear how many of these older children are actually diagnosed with ASD and what impact this has on prevalence rates.
Objectives: To characterize school age children undergoing initial evaluation for possible ASD in a diagnostic referral center.
Methods: Medical records from 2008 were examined for all children ages 6 – 18 years evaluated for the first time for possible ASD in the division of developmental and behavioral pediatrics (DDBP) at Cincinnati Children's Hospital Medical Center. DDBP is the only diagnostic referral center for ASD in a 27 county region. Assessment for ASD consists of a multidisciplinary evaluation including the Autism Diagnostic Observation Schedule (ADOS) administered by a clinician research-reliable with the instrument. Final clinical diagnosis is conferred by a developmental pediatrician following the multidisciplinary evaluation. Descriptive statistics were examined. ADOS classification was compared to final diagnosis (Spectrum vs Not spectrum) and ANOVA was used to compare group means for cognitive and behavioral test scores.
Results: A total of 333 children ages 6 – 18 years had a first time evaluation for ASD. Mean age was 9.9 yrs (SD = 3.2yrs). Boys numbered 280 (84%). Final clinical diagnosis was available for 308. Of these, 153 (50%) had a diagnosis within the autism spectrum: 44 (29%) autism; 45 (29%) Asperger's syndrome and 64 (42%) ASD or PDD-NOS. There were 28 Module 1 ADOSs, 59 Module 2s, 192 Module 3s, and 54 Module 4s. Overall sensitivity of the ADOS compared to final clinical diagnosis was 91%. Specificity was 48% with little difference between original and revised algorithms. Comparison of ADOS classification to diagnosis for 209 children who had a Module 2 or 3 defined four groups in the 2x2 table: (a) 102 classified as spectrum by both ADOS and clinical diagnosis, (b) 75 classified as spectrum by ADOS but not clinical diagnosis, (c) 13 classified as spectrum by clinical diagnosis, not ADOS, and (d) 51 classified as not spectrum by both. Among the 75 children

classified as spectrum by ADOS but not clinical diagnosis, 47 (63%) had a diagnosis of anxiety and/or ADHD. Mean VIQ and NVIQ scores for this group were significantly higher than the other groups (p = 0.03). The Communication Domain and composite scores on the Vineland were also significantly higher in the group classified as Spectrum by ADOS but not final clinical diagnosis (p = 0.003 and 0.004 respectively). Mean core language scores on the CELF did not differ. Conclusions: Only half of school age children seen in a referral center for the first time for possible ASD are found to have a diagnosis in the spectrum. The most common non-spectrum diagnosis for this group is anxiety and/or ADHD. Children in this age group who meet criteria for ASD on the ADOS, but are not diagnosed in the spectrum have a characteristic profile with higher mean IQ and communication scores.

118.168 168 Elevated Urinary Levels of a Known Compound Derived From the Gut Flora in a Subgroup of Autistic Children. L. Altieri[1], C. Neri[2], P. Curatolo[3], B. Manzi[3], F. Muratori[4], R. Militerni[5], C. Bravaccio[6], C. Lenti[7], M. Saccani[7], A. Urbani[8] and A. M. Persico*[1], (1)*Univ. Campus Bio-Medico*, (2)*IRCCS Fondazione Santa Lucia*, (3)*Tor Vergata University*, (4)*University of Pisa – Stella Maris Scientific Institute*, (5)*II Univ. of Naples*, (6)*University Federico II*, (7)*Univ. of Milan*, (8)*University G. D'Annunzio*

Background: In recent years, several studies have reported gastrointestinal abnormalities accompanied by increased gut permeability in a consistent subgroup of autistic patients. Other studies have also unveiled an excess of unusual bacterial strains in the gut flora of autistic individuals.
Objectives: This study aims at measuring the urinary amounts of a known compound which cannot derive from human metabolism, but can instead exclusively come from the catabolism of the bacterial wall of strains previously shown to be overrepresented in the gut flora of many ASD patients. This compound could also derive from exposure to hydrocarbons, requiring controls for levels of active and passive smoking.
Methods: Urines were collected from 59 ASD patients and 59 age- and sex-matched controls, recruited from different clinical centers located in Central and Northern Italy (age range: 2-18 years; M:F ratio = 3:1). Compound concentrations were measured by HPLC. We also measured levels of cotinine, a urinary metabolite of nicotine, using a specific ELISA assay.
Results: All subjects were included, since we found no evidence of active smoking and the urinary amounts of the compound were totally unrelated to urinary cotinine levels. We found a significant difference in the concentration of the compound between autistics and controls (123.5 ± 12.8 vs 91.2 ± 8.7 _g/ml, Student-t = 2.091, 116 df, P<0.05). Moreover, this increase was interestingly limited to ASD patients up to 7 years old (134.1 ± 20.1 vs 70.3 ± 6.7 _g/ml, Student-t = 2.922, 60 df, P<0.01), whereas no difference at all was found between patients and controls aged 8 or older (111.0 ± 14.5 vs 112.7 ± 15.5 _g/ml, Student t= -0.81, 54 df, P=0.936). Before age 8, levels above 175 mg/ml were found in 8/32 (25%) ASD patients vs 0 controls (P=0.0046), whereas levels above 140 mg/ml were detected in 9/32 (28.1%) ASD patients vs 1/32 (3.1%) controls (P=0.0127).
Conclusions: Our results are consistent with the existence of a subgroup including approximately 25-30% ASD patients carrying an abnormal gut flora and/or possibly increased gut permeability. In young children, this compound could contribute to a panel of biochemical and genetic measures able to estimate autism risk or to support clinical diagnoses, whereas patterns of urinary excretion appear to normalize after age 7. Since this compound could conceivably exert behavioral effects, we are now assessing whether its urinary concentrations correlate with signs or symptoms of autism. Behavioral studies on rodents are also under way.

118.169 169 Evaluation of Autism Spectrum Disorders in Females with Fragile X Syndrome. M. J. Leigh*, F. Tassone, G. Mendoza-Morales, D. Nguyen, A. Boyd, J. Brodovsky, C. Ruiz, D. Hessl and R. Hagerman, *UC Davis*

Background: Fragile X syndrome (FXS) is the most common inherited form of intellectual disability and is associated with a behavioral phenotype which may meet the criteria for autism spectrum disorders including autism and pervasive developmental disorder not otherwise specified (PDD NOS). Previously reported rates for autism in males with FXS range from 15-33% depending on what

evaluation method is used. The prevalence of autism spectrum disorders (ASD) in females with FXS is thought to be lower, although predisposing molecular, medical, and cognitive factors for ASD have not been recently investigated.
Objectives: To estimate the prevalence of autism spectrum disorders in females with fragile X syndrome and to assess the relationship of molecular measures, medical problems, and cognitive factors to autism spectrum disorders in this population.
Methods: We utilized autism assessments including the ADOS, ADI-R, SCQ, as well as the DSM-IV-TR to estimate the prevalence of ASD in a population of females with the full mutation or mosaicism of the *FMR1* gene who were evaluated from 2000-2009. We also assessed the relationship of molecular measures, including *FMR1* CGG repeats, *FMR1*- mRNA level, activation ratio, and FMRP level in addition to IQ and selected medical co-morbidities, to the diagnosis of ASD in females with fragile X syndrome.
Results: One hundred and ten females with the full mutation or mosaicism of the *FMR1* gene were evaluated, with an age range of 2-53 years of age and mean age of 11.7 years. The assessment for ASD demonstrated autism in 10% and PDD NOS in 21%, leading to an overall percentage of ASD in this population of 31%. Molecular measures were also assessed. Our preliminary molecular data in 4 females with autism and FXS demonstrate mean *FMR1*- mRNA levels of 2.55 ±2.3 compared to mean *FMR1*- mRNA levels of 1.14 ± 0.5 in 27 females with FXS without ASD (NS).
Conclusions: There is a significant portion of females with FXS who meet criteria for autism (10%) or PDD NOS (21%), and this is important to document for treatment planning. Further details will be presented on *FMR1*- mRNA, activation ratio, and FMRP levels to assess whether deviations in the *FMR1* molecular variables are associated with autism in females with FXS. Additional risk factors for autism may include a lower IQ, medical problems that affect the CNS, or additional allelic variations, and all of these potential factors will be studied and presented.

118.170 170 Face Recognition Abilities in Children with ASD, Their Unaffected Siblings and Parents. L. Berry*[1], J. Pandey[1], C. Klaiman[2], K. Koenig[3], J. Wolf[3] and R. T. Schultz[1], (1)*Children's Hospital of Philadelphia*, (2)*Children's Health Council*, (3)*Yale University*

Background: Difficulties in person identity recognition via images of the face among individuals with an autism spectrum disorder (ASD) are widely documented (e.g., Wolf et al., 2008). However, reproducible estimates of the magnitude of the deficit from studies with large samples and appropriate measurement tools are lacking. To date, there are also no family data on whether the face recognition deficits among probands are shared by unaffected siblings and parents.
Objectives: (1) To estimate the effect size of face recognition deficits in a suitably large sample of typically developing controls (TDCs) and participants with ASD using a widely accessible clinical measure – the Benton Test of Facial Recognition (3Benton_). (2) To test for face recognition deficits in unaffected parents and siblings of the ASD probands.
Methods: 440 children, including 182 with ASD (160 males) and 258 TDCs (168 males) were administered the Benton. ASD diagnoses were confirmed with the ADOS and ADI-R. In addition, the Benton was administered to 173 parents of children with ASD (83 mothers, and 82 fathers), and 87 siblings (from 68 families). Benton scores were converted to standard scores that controlled for age (mean = 100, SD = 15) to facilitate comparisons. For each participant, a Full Scale IQ score was estimated using an age appropriate version of the Wechsler scales.
Results: Average Benton standard score for probands with ASD was more than a standard deviation lower than TDCs (79.6 vs. 96.5). However, groups were mismatched on FSIQ (94.4 vs. 109.5) and there were significant, but small positive correlations between FSIQ and Benton scores in both groups. After covarying FSIQ, significant group differences remained ($t=9.85$, $p < .0001$), with an estimated effect size (Cohen's d) of 0.83. Subsampling both groups to match on FSIQ (134 ASD, 123 TDC) yielded a nearly identical result: Cohen's d = .82. Within the ASD group, there were significant, but modest correlations between Benton scores and indicators of severity of social impairment.

Parents and siblings of probands with ASD scored significantly higher on the Benton compared to the probands. There were no difference between parents and TDCs, but siblings scored significantly lower than TDCs ($p<.002$, $d=.3$, after covarying IQ). Conclusions: The Benton is a sensitive measure of face recognition deficits among children with ASD, comparable to lengthier computerized test results (e.g., Wolf et al 2008). Deficits are independent of age and IQ and modestly correlated with degree of impairment. Unaffected siblings have much smaller deficits in face recognition, while parents appear unaffected. This pattern of results might suggest common environmental effects on all offspring, or some shared de novo genetic contributions.

118.171 171 Facial Phenotypes and Subgroups in Children with Autism Spectrum Disorders. K. Aldridge*, K. K. Pope, I. D. George, C. A. Hill, T. N. Takahashi, J. H. Miles and Y. Duan, *University of Missouri*

Background: The brain develops in concert and in coordination with the developing facial tissues, with each influencing the development of the other. Autism spectrum disorders (ASD) result from alterations in the embryological brain, suggesting that the development of the face of children with ASD may result in subtle facial differences compared to typically-developing children.

Objectives: The purpose of this study is to determine whether children with ASD display differences in facial phenotypes as compared to age-matched, typically-developing children.

Methods: The 3dMD Cranial system was used to acquire 3D stereophotogrammetric images for our study sample of 8-12 year old children diagnosed with essential ASD (N=60) and typically-developing children (N=69) following approved IRB protocols. Three-dimensional coordinates were recorded for 17 facial anthropometric landmarks from these images using 3dMD software. Age-matched comparisons of facial morphology in the two groups were completed using Euclidean Distance Matrix Analysis (EDMA).

Results: First, we find that there are significant differences in facial morphology in children with ASD compared to typically-developing children. Children with ASD have significantly broader orbits, philtrums, and mouths, and higher foreheads relative to typically-developing children. Additionally, this group displays significantly less anteriorly prominent foreheads and nasal bridges relative to children with ASD. Second, using a clustering technique, we also find a subgroup of children with ASD with facial morphology that differs from the majority of the children with ASD and the typically-developing children; this subgroup is defined by a superoinferiorly shorter midface. None of these results were correlated with either age or measures of head size.

Conclusions: Children with ASD display a distinct facial phenotype from typically-developing children. These differences may reflect alterations in the development of the brain during prenatal development in children with autism spectrum disorders. There is also a subgroup of children with ASD who display a facial phenotype that is distinct from the majority of the children with ASD. This subgroup may represent a different etiology compared to the larger group of children with ASD. Further investigations into the brain morphology and correlations with clinical and behavioral phenotypes will help to elucidate the causes for and significance of these subtle phenotypic differences.

118.172 172 Firstborn Child with Autism Spectrum Disorder: Effect of Birth Order Relative to Unaffected Sibs. R. K. Abramson*[1], A. Hall[2], S. Ravan[1], M. L. Cuccaro[3], J. Gilbert[4], J. Haines[5], M. Pericak-Vance[4] and H. H. Wright[1], (1)*University of South Carolina School of Medicine*, (2)*Univ. S. Carolina Sch. Public Health*, (3)*University of Miami*, (4)*University of Miami Miller School of Medicine*, (5)*Vanderbilt University*

Background: In families with no child with an autism spectrum disorder (ASD), birth order may affect communication, social development and parents' perception of development. Children with ASD may be first born or have younger, older, or both younger and older sibs without a diagnosis of ASD. Parents complete the ADI-R (Lord, 1994) which probes social, communication, and repetitive stereotyped behaviors (RSB) to help confirm diagnosis. However, little is written about whether birth order of the non-

ASD sibs relative to the birth order of the first child diagnosed with ASD affects parent perception of that child's social, communication and RSB behaviors.
Objectives: The aims of this study are (1) to evaluate whether parent perceptions of symptoms as reported on the ADI-R of their first child diagnosed with ASD are affected by birth order and (2) to evaluate whether parent report of symptoms differs in families where the child with ASD was an only child or had no younger siblings (stoppage) from families with a younger child born within 3 years of the child with ASD or had a younger child born over 3 years later than the child with ASD.
Methods: Children and adolescents (n=275) were enrolled from a genetic study of ASDs. The sample was predominantly Caucasian (n=214) and male (n= 214). The child's ADI-R social, communication and RSB domain scores were used to evaluate if there was a birth order effect on parent perception of the child's symptoms. In multiplex families, the first affected proband was included in the analysis. There were 150 firstborn children with ASD and 125 with older, younger, or both older and younger sibs. The analysis to evaluate the effect of stoppage included 156 probands (STOP) who were only children or had no younger siblings, 44 ASD children (YS<3) with younger siblings born within 3 years of ASD child, and 75 ASD children (YS>3) with younger siblings born over 3 years after ASD child.
Results: The results of multivariate ANOVA showed there were no significant main effects for birth order and ADI-R Social (firstborn, X=19.819±SE.532; not firstborn, X=20.025±SE.628), Communication (firstborn, X=13.959±SE.397; not firstborn, X=13.385SE.469), and RSB (firstborn, X=5.699±SE.213; not firstborn, X=5.945±SE.252) domain scores. A second multivariate ANOVA indicated no significant main effects for stoppage and ADI-R Social (STOP: X=19.611±SE.43; YS<3, X=18.799±SE.809; YS>3, X=19.42±SE.62), Communication (STOP, X=13.958±SE.317; YS<3, X=13.714±SE.597; YS>3, X=13.535±SE..458), and RSB (STOP, X=5.922±SE.177; YS<3, X=5.843±SE..333; YS>3, X=5.627±SE.265) domain scores.
Conclusions: Neither birth order of the first child identified with ASD nor stoppage after the birth of a child with ASD appear to affect parent perception of social, communication and RSB symptomatology at the time the parent completes the ADI-R. Research to evaluate whether birth order affects parent report of social and communication symptoms for the child with ASD 10 years later in families where there is an older or younger both unaffected sibs might better focus therapy. This data also highlights the fact that 43.3% of parents had at least one other child after the diagnosis of the first child with ASD.

118.173 173 Gender Differences in Symptom Presentation and Emotional Comorbidities in Higher Functioning Children with Autism. N. Kojkowski*[1], D. C. Coman[1], L. Mohapatra[2], C. Hileman[1], K. E. Ono[1], M. R. Schneider[1], P. C. Mundy[3] and H. A. Henderson[1], (1)*University of Miami*, (2)*Graduate Student*, (3)*UC Davis*

Background: Given the gender ratio of 4:1 for autism spectrum disorders, females tend to be underrepresented in research samples. As such, 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, symptom presentation and emotional comorbidity in a sample of High Functioning Children with Autism (HFA) and a sample of gender-, age-, and IQ-matched typically developing children.
Methods: Preliminary results are reported on sixty-eight children (34 HFA (17 female); 34 comparison (17 female). Parents completed the Social Communication Questionnaire (SCQ), Autism Spectrum Screening Questionnaire (ASSQ) and Social Responsiveness Scale (SRS). Additionally, each participant completed the Behavioral Assessment Scale for Children (BASC) self-report and the Autism Diagnostic Observational Schedule (ADOS).
Results: Preliminary analyses revealed an interaction between diagnostic group and gender on the SCQ total score, $F(1,66) = 5.57$, $p = 0.02$ and the ASSQ Total Score, $F(1,68) = 4.92$, $p = 0.03$. Specifically, HFA males were reported as more symptomatic than HFA females, whereas gender was

unrelated to symptom scores within the comparison sample. Moreover, analyses indicated a main effect of gender on SRS Total Score, $F(1, 60) = 7.68$, $p = 0.08$ as well as specific domains including Cognition, $F(1, 60) = 4.60$, $p = 0.03$, Communication, $F(1, 60) = 6.03$, $p = 0.01$, and Motivation, $F(1, 60) = 9.16$, $p = 0.04$. Regardless of diagnostic status, females were reported as more symptomatic on the SRS than males. Additionally, non-parametric analyses revealed that HFA males were scored as more symptomatic than HFA females on the ADOS Quality of Social Overtures, Quality of Social Response and Amount of Reciprocal Social Communication algorithm items. Further, analyses indicated a significant effect of gender on anxiety, $F(1, 58) = 7.98$, $p = 0.07$, and depression, $F(1, 58) = 9.52$, $p = 0.03$, on the BASC-SRP, such that females, regardless of diagnostic status, endorsed more internalizing problems than males. A series of regressions were run to examine the mediating role of anxiety on the relations between gender and SRS. Anxiety mediated the relationship between gender and the SRS motivation domain.
Conclusions: These data suggest that while still meeting diagnostic criteria, HFA females are reported as less impaired than HFA males when it comes to traditional diagnostic measures (SCQ, ASSQ, ADOS). However, when using a gender-normed diagnostic measure (SRS), females are reported as more impaired than males. These findings support the importance of combining traditional and gender-normed measures of symptoms to fully characterize the impairments of females with autism. For females, high levels of anxiety may contribute to low levels of social motivation. This suggests that clinicians should pay particular attention to internalizing problems in the diagnosis and treatment of females with HFA.

118.174 174 Global Autism Public Health Initiative Background Report: India, Chile, and South Africa. A. Simcoe-Matthews*, *(1)Autism Speaks Etiology Department Intern, (2)College of the Holy Cross*

Background: Autism Speaks, the world's largest autism advocacy and science organization, has begun to enter into partnerships with various countries through its Global Autism Public Health Initiative (GAPH) that aims to increase public and professional awareness of autism spectrum disorders (ASD) worldwide, improve service delivery, and enhance research expertise and international collaboration through training of international researchers. Little is currently known about the global epidemiology rates of autism because of major differences in culture and subsequent differences in screening and diagnostic techniques around the world. In addition, limited awareness and understanding of autism among both parents and professionals can lead to stigma, which in turn may limit access to autism diagnostic services. Objectives: To move forward in creating global partnerships, preliminary information must be gathered to inform Autism Speaks' unique plan of action for each territory. This research examines the existing awareness, research, and service infrastructure in India, Chile, and South Africa, and identifies potential challenges and specific areas of needed improvement in each country. Methods: The first step in creating a background report was to compile a list of ten core questions focused on the steps a family takes to receive a diagnosis and appropriate services for their child as well as the infrastructure currently in place for awareness, services, and research. Once questions were developed, the approach taken in finding answers was primarily internet based research. Information was collected regarding public and professional awareness of autism, research capabilities, and service provision in India, Chile, and South Africa. The results were organized as answers under each core question and then evaluated to determine which key organizations may be valuable GAPH partners, but also to identify specific challenges each country faces and areas where the current system of diagnosis and treatment needs improvement. Results: It was found that while each country is lacking in the three areas of awareness, services, and research to varying degrees, they each face unique challenges. India struggles most with the incredible diversity of its peoples which creates difficulties when unifying support systems and awareness campaigns across multiple languages and cultures. Chile, on the other hand, has to combat the

prevailing attitudes that Thimerosal-containing vaccines are the cause of autism and detoxification can cure the disease in some children. In South Africa, the greatest challenge is shared by all three countries: resources are limited and often inaccessible because of the area's physical size. Conclusions: To overcome the many present challenges, researchers, service providers, parents, and awareness groups must work together to bring about key changes to aid the autism community.

118.175 175 Polybrominated Diphenyl Ethers, Autism, Developmental Delay, and Immune Markers: A Pilot Study. I. Hertz-Picciotto*[1], A. Bergman[2], B. Fangstrom[3], P. Ashwood[4], J. Van de Water[1], M. Rose[1], D. Bennett[1], I. N. Pessah[1], R. L. Hansen[1] and P. Krakowiak[1], (1)*University of California at Davis*, (2)*Lundberg Laboratory for Cancer Research*, (3)*Stockholm University*, (4)*M.I.N.D. Institute, University of California at Davis*

Background: Polybrominated diphenyl ethers (PBDEs) are flame retardants used widely, with a rapid increase in body burdens in the U.S. over the last few decades. PBDEs and their metabolites cross the placenta and studies in rodents show neurodevelopmental toxicity from prenatal exposures. Objectives: To review PBDEs and the development of 100 children from CHARGE (Childhood Autism Risk from Genetics and the Environment), a case-control epidemiologic study of autism/autism spectrum (AU/ASD), developmental delays (DD) and typically developing (TD) population-based controls. Methods: Developmental diagnoses were confirmed by the ADOS, ADI-R, Mullen's Scales of Early Learning, and Vineland Adaptive Behavior Scales. Eleven PBDE congeners were measured by GC/MS from serum specimens collected after children were assessed. Immunoglobulins and cytokines were measured by LuminexTM multiplex platform. Multiple logistic and linear regression models were used to control confounding factors in the evaluation associations between plasma PBDEs and (a) case status; (b) plasma IgG, IgA, IgE, and IgM, and (c) 13 cytokines (IL-1beta, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12p40, IL-13, IFN-gamma, GM-CSF, TNF-alpha, and TGF-beta). Results: Levels of PBDEs are higher than reported for any other population worldwide. AU/ASD and DD children were similar to TD controls for all congeners, but levels were high for all three groups. Highly brominated congeners were associated with reduced IgM, IL-1beta, IFN-gamma and TGF-beta, and with increased IL-2. Lower brominated congeners were associated with increased IL-4, Il-6, IL-10, and IL-12p40, GM-CSF, and TNF-alpha. Conclusions: The similar PBDE body burdens in children diagnosed with AU/ASD as compared with TD controls may be explained by our inability to obtain plasma prior to the diagnosis or during critical windows of development. Current concentrations in plasma may not represent early life exposures due to changes in diet and introduction of new household products containing PBDEs. The strong links of lower brominated congeners with increased levels of several pro-inflammatory cytokines is consistent with autism as a neuro-inflammatory condition. At the same time, reduced IgM and TGF-beta have been reported in autism, but the associations of these markers with concurrently measured PBDEs were independent of case status, supporting PBDEs as a potential contributor to autism risk. Because timing of blood samples was not optimal, the lack of association of PBDEs with autism does not preclude a causal role of these compounds. Based on the strong, multiple associations with numerous immune markers in this pilot study, we hypothesize that early life exposures to PBDEs have the potential to disrupt immune development. Whether immunotoxicity at a critical time period could contribute to abnormalities in brain development requires further investigation.

118.176 176 Rapid Assessment of Autistic Social Impairment in a Taiwanese Population. J. W. Wang*[1], L. C. Lee[2], J. N. Constantino[3] and J. W. Hsu[4], (1)*Weill Cornell Medical College*, (2)*Johns Hopkins Bloomberg School of Public Health*, (3)*Washington University School of Medicine*, (4)*Taipei Veterans General Hospital*

Background: Autism spectrum disorders (ASDs) and other developmental disorders such as ADHD and specific development delay all present with some impairments in social interaction that can be confused with ASDs. Recognizing the spectrum of autistic traits in affected children is important both for differential diagnosis of these conditions

and for appropriate assessment and treatment in individual cases. The Social Responsiveness Scale (SRS) is an assessment tool that provides a quantitative rather than categorical measure of social impairment. Previous research has established the discriminant and concurrent validity of this scale in US populations; however no data are yet available from Chinese Mandarin-speaking populations.

Objectives: (1) To characterize the spectrum of autistic traits among children at an early-intervention clinic and among typical controls in Taipei. (2) To examine the cross-cultural validity of the SRS in a Chinese Mandarin-speaking population.

Methods: Participants are the primary caretakers of children referred for developmental evaluation at Taipei Veterans General Hospital and GuanDu Hospital in Taipei from July 2009- April 2010. Four study groups are included: (1) ASD (n=18): including autism syndrome, Asperger syndrome, and pervasive developmental disorder-not otherwise specified (PDD-NOS), (2) ADHD+DD (n=11): including comorbid ADHD and DD as described in 3 and 4, (3) ADHD (n=19): including inattentive, hyperactive-impulsive, and combined type, (4) Developmental Delay (DD, n=28): including speech/language, learning, motor development, and other specific and nonspecific DDs. Diagnoses are made based on DSM-IV and ICD-10 criteria, with a team of experienced clinicians coming to a consensus based on all available information obtained from assessments and clinical evaluations. Controls are parents of children attending local kindergartens. SRS total and five subscale scores (i.e. social awareness, social cognition, social communication, social motivation, autistic mannerisms) are compared between the ASD group and the other three groups.

Results: Preliminary results indicate that children with clinically-diagnosed ASDs have significantly higher SRS total and all five subscale scores than children with either ADHD or DD. However, children with ASDs are only statistically different from children with ADHD+DD in social communication, social motivation, and the SRS total scores (all $p<.05$). Results from unaffected controls are pending at this time.

Conclusions: Findings from these preliminary data support the cross-cultural validity of the SRS as a tool for distinguishing ASD from other developmental conditions (e.g. ADHD, DD), and as a tool for characterizing autistic traits in these non-ASD disorders. This finding is important for future research that may use the scale for differential diagnosis of autism from other neuropsychiatric conditions, as well as for large-scale epidemiologic studies of ASD. In addition, the SRS may be useful for identifying autistic traits in children who do not meet criteria for full-scale ASD diagnoses, yet may nevertheless benefit from special interventions to address their social impairment.

This study remains in progress. Additional data from unaffected controls and a larger sample size will be included for the meeting. Findings from the study will further clarify the spectrum of autistic traits in the Taiwanese population, and more fully examine the validity of the SRS as a cross-cultural diagnostic tool.

118.177 177 Reciprocal Social Conversation in Children and Adolescents with ASD and Asperger Syndrome. M. N. Park*, L. K. Koegel and R. L. Koegel, *University of California, Santa Barbara*

Background: Individuals with autism spectrum disorders (ASD) and Asperger Syndrome (AS) often have difficulty effectively using language in various social contexts. This difficulty is often demonstrated in deficits in reciprocal social conversation, or the ability to sustain a verbal exchange through initiations and expansion of conversational topics. The inability or reluctance to use language in a social manner severely limits social interactions and exacerbates the risk of social withdrawal and isolation that is commonly experienced by individuals with ASD and AS.

Objectives: The purpose of this study was to examine the effects of a behavioral intervention using an empirically supported motivation-based treatment combined with

self-management procedures to target reciprocal social conversation skills. The intervention incorporated an empirically supported, motivation-based behavioral intervention for autism spectrum disorder—Pivotal Response Treatment.

Methods: A non-concurrent multiple baseline across participants time series research design was implemented with measures collected longitudinally to examine the effectiveness of a self-management intervention. Children and adolescents diagnosed with ASD and AS aged 5 to 14 participated in the study.

Results: The results indicate improvements in sustained conversation exchanges through increased elaboration of conversation topics and reciprocal question-asking or initiations were observed with the implementation of intervention.

Conclusions: Meaningful social conversation skills are an important area for intervention and theoretical research. Continued efforts to understand and promote the development of complex conversation skills through effective interventions are warranted.

118 Human Genetics

105.003 3 RNA-Seq Studies of Gene Expression in Fronto-Insular Cortex of Autistic Subjects Reveal Gene Networks Related to Inflammation, Development and Synaptic Function. N. Tetreault*, *California Institute of Technology*

Background:

Fronto-insular (FI) cortex is part of the neural system involved in self-awareness and social reciprocity and contains von Economo neurons (VENs) that selectively degenerate in fronto-temporal dementia (FTD) and may also be involved in autism (Seeley, 2006; Allman, 2005). Deficits in self-awareness and social reciprocity are characteristic of both conditions. The activity of FI is reduced in autistic subjects relative to controls when they introspect their feelings (Silani, 2008).

Objectives:

Determine the networks of genes that are abnormally expressed in FI of autistic brains compared to controls. Quantify the number of quiescent, activated, and phagocytic microglia in autistic brains compared to age matched controls.

Methods:

We used RNA-Seq to quantify expression across the entire set of genes in FI obtained from well phenotyped autistic cases and controls, then determined which genes are most informative in discriminating the different groups using an information theoretic approach. The most informative genes were subjected to IPA and GO analysis. We used IBA1 immunocytochemistry and stereology to quantify the number of microglia in the brain.

Results:

Autism brains classified as group A display a greater number of activated microglia, the key cellular participants in the inflammatory response in the brain, compared to autism group B brains and controls. Including additional autistic and control subjects for microglia staining (Iba1) and classification we found autistic (n=11) subjects compared to controls (n=9) have significantly more activated and phagocytic microglia while the control subjects have significantly more quiescent microglia. An IPA analysis based on the 100 most informative genes revealed that autism-A brains exhibit a network of potentially interacting genes related to immune function and inflammation. IL-6 is the major hub in this network. The proteins for several of the genes in this network, including IL-6 receptor and ATF3, are preferentially immuno-stained in VENs. Previous studies have found significantly increased amounts of IL-6 protein in autistic subjects relative to controls in frontal cortex (Li, 2009) and anterior cingulate cortex (Vargas, 2005). There are many studies implicating IL-6 in social functioning (Ader, 2007). For the 1000 genes with the highest NMI values, we performed a GO analysis comparing autism-A, -B and controls, which revealed a set of significantly enriched GO terms related to stress, inflammation and apoptosis, reflecting the network of genes centered on IL-6 in autism-A. The comparison of the three groups also reveals

a subset of genes related to synaptic vesicles and neurotransmitter release that is enriched in the autism-B brains.

Conclusions:

Autism-A exhibits a gene network involved in inflammation, and Autism-A subjects have a greater number of activated and phagocytic microglia compared to controls. We counted the microglia in an additional group of autistic subjects for which we did not have RNA-Seq data, and all of these subjects had increased numbers of activated and phagocytic microglia compared to controls. Autism-B has increased expression of genes which are involved in the presynaptic active zone where a change in vesicle fusion can alter neurotransmitter release and may perturb cortical function.

118.029 29 ADI-R Profiles of Individuals with Fragile X Syndrome with and without Autism. A. McDuffie*[1], S. T. Kover[1] and L. Abbeduto[2], (1)*University of Wisconsin*, (2)*University of Wisconsin-Madison*

Background:

This study utilized the *Autism Diagnostic Interview-Revised* (Rutter et al., 2003) to examine diagnostic profiles and longitudinal change in autism symptoms for a group of children and adolescents with Fragile X syndrome with and without autism. FXS is the most common inherited cause of intellectual disability. Prevalence rates of autism in FXS may be as high as 50%, with many individuals displaying behaviors that are characteristic of autism, including eye gaze avoidance, repetitive behaviors and language delay. Previous studies have reported that individuals with comorbid FXS and autism are more impaired cognitively than individuals with FXS only, making it important to clarify the extent to which cognitive delay contributes to profiles of autistic behavior in FXS.

Objectives:

- To identify diagnostic and current symptoms of autism that distinguish participants with FXS-only from those with comorbid FXS and autism.
- To examine change over time in symptoms of autism within each diagnostic group.
- To identify diagnostic symptoms of autism that best predict group membership.

Methods:

Participants (N=51, 36 males) had a confirmed diagnosis of FXS and ranged in age from 10- to 16-years (*M* = 13-years, *SD* = 1.75). Participants were classified as having autism if they met the diagnostic cutoff scores for all domains of the *ADI-R* including age of onset, resulting in two subgroups: FXS-only (n = 26; 13 females) and FXS+AUT (n = 24; 2 females). The Brief IQ Screener of the *Leiter-R* (Roid & Miller, 1997) provided a measure of nonverbal IQ.

Results:

RQ1: After controlling for nonverbal IQ, significant between-group differences for lifetime and current symptoms of autism were not detected for the Reciprocal Social Interaction (RSI) domain of the *ADI-R*, but were revealed for both the Communication (COM) and Restricted Interests/Repetitive Behaviors (RRB) domains.

RQ2: On average, severity of autism symptoms improved over time for all participants, with the least improvement noted for behaviors in the RRB domain.

RQ3: In the RSI domain, group play with peers, nonverbal IQ, and social smiling discriminated significantly between the groups and correctly classified over 80% of participants. In the COM domain, stereotyped utterances/delayed echolalia, pointing to express interest, nodding, and nonverbal IQ discriminated significantly between the groups and correctly classified over 90% of participants. In the RRB domain, repetitive object use, circumscribed interests, and verbal rituals discriminated significantly between the groups and correctly classified over 70% of participants.

Conclusions:

Deficits in social reciprocity are considered to reflect the essential and defining feature of idiopathic autism. Lack of significant between-group differences for either algorithm or current items within the RSI domain suggests that autism symptoms in FXS may not reflect the same underlying mechanism as in idiopathic autism, but may reflect cognitive impairments that influence an individual's ability to share enjoyment and interest with a social partner. Symptoms of autism improved over time for participants regardless of autism status with less improvement noted for the RRB domain. Nonverbal IQ added to group separation for the RSI and COM domains, but not for the RRB domain.

118.030 30 Epigenetic Heterogeneity of Human Chromosome 15 Duplication Syndrome Brain Samples. H. A. Scoles*[1], W. T. Powell[2], A. Hogart[3], K. N. Leung[4], N. C. Schanen[5] and J. M. LaSalle[1], (1)*UC Davis School of Medicine*, (2)*University of California Davis*, (3)*UC Davis*, (4)*University of California, Davis*, (5)*Nemours*

Background: Chromosome 15q11-13 contains an imprinted cluster of genes necessary for normal mammalian neurodevelopment. Paternal and maternal deficiencies of the 15q11-13 alleles results in Prader-Willi (PWS) and Angelman (AS) syndromes, respectively. A distinct maternal duplication of 15q11-13 (dup15), often associated with autism spectrum disorders (ASD), occurs as both interstitial duplications [int dup(15)] and supernumerary pseudodicentric chromosome 15 [idic(15)]. Our previous analysis of two post-mortem brain samples with idic(15) showed heterogeneity between the two cases, with one showing gene expression in 15q11-13 $GABA_A$ receptor genes, *UBE3A*, and *SNRPN* in a manner not predicted by copy number or parental imprint.

Objectives: Determine the effect of 15q11-13 duplication on 15q11-13 transcript levels in additional brain samples and investigate potential epigenetic differences to explain heterogeneity in gene expression patterns between different chromosome 15 duplication cases.

Methods: Frozen human postmortem cerebral samples were obtained from the Autism Tissue Program, including 6 chromosome 15 duplication cases, 6 age- and sex-matched controls, and 2 Prader-Willi and Angelman samples with paternal or maternal 15q11-13 deletion. RNA was isolated by TriZol reagent and cDNA reverse transcribed with a mix of random hexamer and oligo-d(T) primers. Quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) was performed for 15q11-13 transcripts *SNRPN*, *UBE3A*, and *GABRB3* and two housekeeping genes *GAPDH* and *HPRT1*. In addition, fluorescence in situ hybridization (FISH) using probes to each of the 15q11-13 gene loci was used to determine homologous pairing, chromatin decondensation, and potential mosaicism in each brain sample.

Results: Prior experiments with two idic15 brain samples revealed two striking patterns with one sample showing increased and one showing decreased expression of 15q11-13 genes. Preliminary results with additional dup15 samples confirms a pattern of two distinct categories of gene expression: one subset of samples with lower levels of *SNRPN* and GABRB3 but no difference in *UBE3A* compared to controls and another subset with higher *GABRB3* and *UBE3A* compared to controls but no difference in *SNRPN*. Previous work showed the idic15 chromosomes interacting non-selectively with maternal and paternal chromosome 15 alleles. Ongoing experiments are being performed to investigate homologous pairing and chromatin structure in the dup15 samples to investigate epigenetic heterogeneity associated with this syndrome.

Conclusions: These findings suggest that allelic expression within 15q11-13 is not based on entirely copy number or parental origin but can be influenced by epigenetic mechanisms that may create the clinical heterogeneity observed in 15q11-13 duplication syndromes.

118.031 31 CNVs in Autism Spectrum Disorder. R. Canitano*, E. Katzaki, F. T. Papa, M. Mucciolo, A. Spanhol Rosseto, M. A. Mencarelli, M. Pollazzon, V. Uliana, V. Scandurra, F. Mari and A. Renieri, *University Hospital of Siena, Italy*

Background: Autism Spectrum Disorders (ASD) present a complex and heterogeneous

aetiology with a strong evidence of a genetic involvement. The identification of copy-number variants (CNVs) by the application of comparative genomic hybridization (CGH) is beginning to provide some insights into the underlying genetic causes of neurodevelopmental disorders, in particular susceptibility to mental retardation, autism and schizophrenia. Recently recurrent microdeletions at 16p11.2, 16p13.1 and microduplications at 15q13.3 have been associated to confer susceptibility to autism spectrum disorder in up to 1% of autistic patients

Objectives: In order to identify the genetic causes leading to the disorder and provide an appropriate recurrence risk to the families we evaluated in genetic counseling a group of patients with a diagnosis of ASD, namely Autistic Disorder or Pervasive Developmental Disorder-Not Otherwise Specified(PPD-NOS) according to DSM-IV classification. We have attempted the characterization in term of frequency, size, and nature of CNVs in our population of patients with ASD. We have searched for new CNVs that could be implicated as genetic causes or modifier factors in the patient's phenotype and looked for new genes that could correlate with the disease.

Methods: By the use of oligonucleotide array with 44.000 probes and an average resolution of about 100-130 kb (44K, Agilent) we have analyzed 50 unrelated subjects with ASD. Inheritance has been determined using the same technique.

Results: We have identified private rearrangements in 4 out of 50 patients analyzed. In one patient, a 16p13.11 duplication was identified, already reported to be associated with Autistic Disorder (AD). In another patient with AD, a 17q12 duplication was identified, inherited by an apparently normal father and a possible positional effect in a nearby gene was hypothesized (Mencarelli MA et al; 2008 and Katzaki E et al; 2009). Two patients with AD presented two inherited rearrangements each, in one, a deletion in 1p22.1 inherited by the mother and a deletion in 4q35.2 inherited by the father were detected. In the other with AD, a deletion in 9p21.3 inherited by the mother and a duplication in 11q23.1 inherited by the father were identified. A possible mechanism by which a double structural variation can impact the patients phenotypes, apart gene dosage and disruption (currently implicated by CNVs), is that of genes included in two different regions having a possible interaction in a common molecular pathway

Conclusions:

Array CGH analysis has been revealed a useful tool not only for the identification of the genetic cause in patients with MCA/MR but also in providing evidence of the pathogenetic role of CNVs in patients with ASD. Our results confirm that rearrangements involving the 16p13 region are recurrent (2%) in ASD. As well we have identified in the 4% of patients double rearrangements that can lead to hypothesize the possibility of digenic inheritance. Future studies on ASD will require the collection of a larger number of patients and the attempt to identify new disease genes should take into account the possible interaction between genes located in different chromosomal regions.

118.032 32 Exposure to Propionic Acid Induces Autistic-Like Gene Expression Profiles in Lymphoblastoid Cell Lines From Non-Autistic Individuals. T. Sarachana* and V. Hu, *The George Washington University Medical Center*

Background: Genetic and environmental factors, including dietary substances and chemical toxins, are believed to contribute to the etiology and pathobiology of autism spectrum disorders (ASD). There is evidence that some individuals with ASD exhibit increased symptoms after ingesting foods containing high levels of propionic acid (PPA). PPA is a short chain fatty acid known to be an intermediate product of fatty acid metabolism and a metabolic end product of enteric bacteria in the GI tract. MacFabe, D.F. and colleagues (2007) reported that intracerebroventricular (ICV) injection of PPA in rats resulted in altered neuroinflammatory response, social impairment, and repetitive behaviors, all of which are consistent with clinical symptoms observed in autism. However, the effects of PPA on gene expression profiles in cells from autistic cases

and controls have not yet been elucidated. We therefore hypothesize that PPA exposure causes deregulation in gene expression which may reflect that which is seen in autism.

Objectives: To investigate dysregulation of gene expression mediated by PPA exposure in lymphoblastoid cell lines (LCLs) derived from non-autistic individuals, which may contribute to pathological conditions observed in autism.

Methods: LCLs from non-autistic individuals (n=5) and their autistic siblings (n=5) were employed in this study. Each of the non-autistic cell lines was split into 3 groups and treated with PPA, propanol, or PBS, while each autistic LCL was split into 2 groups and treated with propanol or PBS. Gene expression profiling for each sample was performed using a TIGR40K human cDNA microarray containing 41,472 probes. Pavlidis Template Matching (PTM) and the Significance Analysis for Microarrays (SAM) analyses were employed to identify genes that were significantly differentially expressed and matched to expression in autistic samples. Ingenuity Pathway Analysis (IPA) and Pathway Studio 5 programs were employed for identification of biological functions and pathways associated with PPA-responsive genes.

Results: The PTM-SAM analyses revealed that a total of 177 genes in non-autistic LCLs were significantly differentially expressed, and exhibited autism-related gene expression profiles after 24 hr exposure to PPA ($p<0.05$; %FDR<5). Novel network prediction analyses of these PPA-responsive genes reveal significant association with autism and other co-morbid disorders, including cognitive impairment, epilepsy, bipolar affective disorder, muscular dystrophy, altered immunological response, and gastrointestinal diseases. Many interesting biological functions implicated in autism, such as memory and synaptic plasticity, were also highlighted.

Conclusions: Findings from this study indicate that PPA exposure leads to global changes in gene expression profiles of non-autistic LCLs toward autistic-like expression patterns. The PPA-responsive genes are associated with autism and co-morbid disorders, suggesting that PPA exposure may contribute to pathological conditions observed in autism.

Reference: MacFabe DF*, et al* (2007) Neurobiological effects of intraventricular propionic acid in rats: Possible role of short chain fatty acids on the pathogenesis and characteristics of autism spectrum disorders. *Behav Brain Res* 176, 149-169.

Supports: National Institute of Mental Health (R21 MH073393) and Autism Speaks (2381) to VWH.

118.033 33 Copy Number Variants Associated with Autism Spectrum Disorder in Extended Families. D. Salyakina*[1], H. N. Cukier[1], D. Ma[2], J. Jaworski[3], I. Konidari[1], J. Gilbert[3], M. L. Cuccaro[1] and M. A. Pericak-Vance[2], (1)*University of Miami*, (2)*Hussman Institute for Human Genomics*, (3)*University of Miami Miller School of Medicine*

Background:

Recent research has suggested that inheritance for idiopathic autism (IA, with one individual in the family affected) may be distinct from inheritance for multiplex autism (MA, with two or more individuals in the family affected). Rare copy number variations (CNV) have been associated with autism, but these have been observed more commonly in IA than in MA. In contrast, interactive effects in multiple common susceptibility alleles have been hypothesized as causes of familial autism.

Objectives:

The lack of association of CNVs with autism in multiplex families could be explained by the limitation of previous studies to relatively large CNVs. New genotyping platforms such as Illumina offer dense marker coverage, which allow testing for CNVs with lengths of several kilo bases. In order to explore the role of CNVs in autism we used two approaches: testing for association of all common CNVs in a unique data set including affected and unaffected members of extended families; as well as screening for rare CNVs segregating all affecteds within individual families.

Methods:

45 extended families with 2 or more children affected with autism were available for analysis. Samples were genotyped using Illumina's Human 1M Beadchip, containing 1,072,820 SNPs. Samples and markers with call rates below 95% were excluded from analysis. We excluded from the analysis all CNV that did not demonstrate clear inheritance within the families.

We used the PennCNV algorithm for CNV calling. Quality control was performed as recommended by the PennCNV algorithm authors. Association was tested using the pedigree disequilibrium test (PDT). CNV validation was performed in quadruplicates using Applied Biosystems Taqman Copy Number Assays.

Results:

In total, 13168 CNVs in 471 genomes passed all QC steps, 14948 of which had unique boundaries. Common deletions on chromosome 6p21.32 in C4A and C4B genes localized in the major histocompatibility complex (MHC) class III region on chromosome 6 showed association with autism (p-value = 0.0026). This association possibly implies etiological mechanisms involving autoimmunity and/or infection. Validation of CNVs in this region is ongoing.

Six regions on chromosomes 4p16.3, 6q11.1, 7p21.2, 10p12.31, 13q31.1, 15q24.1 showed perfect segregation with incomplete penetrance, each in one family. None of these six regions have been reported in the Database of Genomic Variants (DGV). The length of these CNVs varied from 5.2 to 348.5 kb. 3 of 6 regions were validated (4p16.3, 6q11.1, 10p12.31) with real time PCR, with the concordance rate between predicted and validated CNVs in tested assays 100%. The validation of remaining 3 CNV regions is ongoing.

Conclusions:

In our study we found a novel region on chromosome 6p21.32 to be associated with autism, as well as six rare CNVs segregating in autistic families. We were able to validate 3 of these rare CNVs with extremely high consistency. Our results confirm the heterogeneous nature of autism and suggest that, probably, both common and rare CNVs are involved in its etiology.

118.034 34 Exploratory Sequence Analysis of Candidate Genes for Repetitive and Restricted Behaviors in Autism. E. L. Crawford*[1], A. D. McGrew[1], E. Kistner-Griffin[2], N. Cox[3], E. H. Cook[4] and J. Sutcliffe[1], (1)*Vanderbilt University*, (2)*Medical University of South Carolina*, (3)*University of Chicago*, (4)*University of Illinois at Chicago*

Background: Autism is a common neurodevelopmental disorder that 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. Serotonin dysregulation has long been implicated in autism, and rare autism-associated variants in the serotonin transporter (SERT; gene symbol: SLC6A4) lead to gains of function involving increased activity and abnormal regulation. In autism families, these SERT variants result in more severe rigid-compulsive behaviors, but one has also been observed in multiple pedigrees with obsessive compulsive disorder (OCD). Selective serotonin reuptake inhibitors (SSRIs) that selectively target SERT are a key front-line therapy for OCD. Thus, SERT variants and SSRI treatment efficacy highlight a shared etiology between autism and OCD involving serotonin regulation via SERT.
Objectives: We are pursuing related hypotheses that genes and/or pathways related to SERT regulation and SSRI-responsive OCD behaviors harbor autism susceptibility alleles.
Methods: In this study, we tested these hypotheses following a rare variant susceptibility model. We sequenced exons for two loci, DLGAP3 and ADAMTS6, in unrelated autism probands and controls. DLGAP3 is also known as SAPAP3 (SAP90/PSD95-associated protein 3), and mutations have been described in cases of OCD and trichotillomania, and a mouse knock-out shows analogous behaviors that are responsive to treatment with SSRIs. ADAMTS6 encodes a disintegrin and metalloproteinase with thrombospondin motifs 6, and this locus was identified using

the SCAN database (www.scandb.org) based on SNPs within this locus that significantly predict variation of SLC6A4 gene expression in lymphoblastoid cell lines. Exonic sequences for these two genes were sequenced in a pilot sample of 200 cases and 200 controls.
Results: Preliminary sequence analysis of DLGAP3 shows similar numbers of synonymous and nonsynonymous variants between cases and controls. In contrast, analysis of ADAMTS6 for rare variants revealed 8 nonsynonymous and 4 synonymous variants in cases vs 3 nonsynonymous and 1 synonymous variants in controls, suggesting a greater burden of rare, transcribed variants in ADAMTS6 in individuals with autism.
Conclusions: We conclude that further studies of rare variation are warranted for ADAMTS6, while for DLGAP3, rare variants do not seem to be a significant contributor to autism risk.

118.035 35 Redefining Sibling "Recurrence": Language Delays Affect 21% of Otherwise-Unaffected Siblings of ASD Probands.

J. N. Constantino*[1], Y. Zhang[1] and P. A. Law[2], (1)*Washington University School of Medicine*, (2)*Kennedy Krieger Institute*

Background: A number of recently identified genetic mutations observed in excess in autism have (each) been associated with wide variations in clinical phenotype. Given these observations, we sought to determine whether specific language disorder phenotypes might constitute a form of "recurrence" among otherwise unaffected siblings of children with autism spectrum disorders (ASD).
Objectives: To examine the prevalence and characteristics of language delay among the ASD-unaffected siblings of children with autism, in a large national volunteer register.
Methods: Using data obtained from the Interactive Autism Network (IAN) registry, we studied 2,945 children from 1,242 unselected ASD-affected families who met the criteria of having at least one child clinically-affected by an autism spectrum disorder (ASD) and at least one full biological sibling. For each of the children in the study, parents provided data on whether or not the child had a) a clinically-documented ASD diagnosis or b) a clinically-diagnosed language delay or speech problem. In addition, parents completed the Social Communication Questionnaire (SCQ) and the Social Responsiveness Scale (SRS) on each child.
Results: The occurrence of a categorically-defined ASD in an additional child occurred in 11.7 percent of the families; this percentage was substantially lower (5.6%) when the proband was cognitively impaired, higher (14.0%) when the proband was verbal; and still higher (16.6%) when a verbal proband was in the top third of the quantitative severity distribution for social impairment. Across all family types, an additional 21 percent of presumed-unaffected siblings had a history of delayed language at age 4 years, which contrasts sharply with a published general population prevalence of 5-9% for such conditions. Half of the unaffected siblings with histories of delayed speech had distinctly autistic qualities of speech (use of odd or repetitive phrases, socially-inappropriate questions, pronoun reversal, or invented words) documented by the lifetime version of the SCQ. In the entire sample, positive endorsement of a history of these speech characteristics was significantly more pronounced in ASD-unaffected children with versus without parent-reported history of language delay ($p<.001$); was associated with a significantly higher level of sub clinical autistic social impairment than in unaffected children without these speech characteristics (mean SRS score 33.4 versus 16.7; $t= -12.5$; $df= 713$; $p<.0001$); and accounted for most of the excess prevalence of language delay designation in this sample over the general population prevalence.
Conclusions: These data suggest that language delays with autistic characteristics (including autistic qualities of speech and sub clinical social impairments) are extremely common among unaffected siblings of ASD probands, account for the excess in prevalence of language delay over what would be expected on the basis of general population prevalence, and constitute a form of sibling "recurrence" that may be highly relevant to genetic and neurobiologic studies of autism, as well as to studies of the development of infant siblings of ASD probands. Sibling recurrence in ASD exceeds previously published estimates, is highly variable with respect to severity, and its

frequency varies (in a complex manner) as a function of proband type.

118.036 36 Evidence of Abnormal Folate Metabolism and DNA Hypomethylation in Mothers of Children with Autism. S. J. James*, S. Melnyk, S. Jernigan, L. Seidel, M. Lopez, J. Fussell, T. Reid, E. Schulz, D. Gaylor and M. Cleves, *University of Arkansas for Medical Sciences*

Background: Folate-dependent one carbon metabolism is a highly polymorphic pathway that regulates the distribution of one-carbon derivatives between DNA synthesis (proliferation) and DNA methylation (cell-specific gene expression and differentiation). As such, normal functioning of this pathway is essential to support the rapid shifts between proliferation, differentiation and cell death that are essential for normal fetal programming and organogenesis. Maternal polymorphic variants, nutritional deficiencies and/or environmental exposures that negatively affect availability of folate one-carbon precursors have been associated with increased risk of structural birth defects, chromosomal anomalies, schizophrenia, and prematurity. We recently reported preliminary evidence suggesting that folate-dependent transmethylation and transsufuration metabolism was abnormal in some autism mothers (James et al, JADD 2009).

Objectives: To measure plasma transmethylation metabolites and DNA methylation status in a larger independent local cohort of autism and control mothers and to determine the frequency of folate-relevant polymorphisms in DNA from 530 case-parent triads and 560 controls obtained from the NIMH repository.

Methods: Fasting plasma samples were obtained from 58 local autism mothers and 80 matched control mothers and analyzed for concentrations of folate, methionine, S-adenosylmethionine (SAM), S-adenosylmethionine (SAH), adenosine, and homocysteine using HPLC with electrochemical detection. Global DNA methylation (% 5-methylcystosine/total cytosine) was measured by LC/mass spectrometry. NIMH repository DNA samples were analyzed using TaqMan primer-probe sets (ABI PRISM 7300) for *MTHFR C677T, MTHFR A1298C, MTRR A66G, TCII C776G, and RFC1 A80G* as potential contributors to abnormal maternal one-carbon metabolism.

Results: Maternal DNA from the autism mothers was found to be significantly hypomethylated relative to reference control DNA. Metabolic profiling indicated that plasma homocysteine, adenosine, and S-adenosylhomocysteine were significantly elevated among autism mothers which is biochemically consistent with reduced methylation capacity and global DNA hypomethylation. In the case-control analysis of over 2100 NIMH repository DNA samples, a significant increase in the reduced folate carrier (RFC1) G allele frequency was found among case mothers, but not among fathers or affected children. Subsequent log linear analysis of the RFC1 A80G genotype within family trios revealed that the maternal G allele was associated with a significant increase in risk of autism whereas the inherited genotype of the child was not. Plasma folate levels were significantly reduced among the local autism mothers.

Conclusions: Taken together, these results support a broader paradigm of autism gene-environment interaction that encompasses the mother as a genetic/epigenetic case as well as a potential fetal environmental factor. Inclusion of maternal genetic/epigenetics in the autism gene-environment paradigm could provide new insights into the etiology of this complex disorder.

118.037 37 *FAM120C* as a Novel X-Linked Candidate Gene for Autism. A. Crepel*, V. De Wolf, H. Peeters and K. Devriendt, *Center for Human Genetics, University of Leuven*

Background:

Unique *de novo* or X-linked maternally inherited CNVs are found in more than 10% of patients with syndromic ASD. (Jacquemont, 2006 and Qiao, 2009) These CNV regions are of unique value to ASD genetics because they may pinpoint to novel ASD candidate genes.

Objectives:

In this respect, we studied a unique discontiguous X-linked deletion on Xp11.22 in a boy with syndromic autism.

Methods:

We present genetic studies in a sporadic male patient with features reminiscent of Aarskog syndrome (caused by *FGD1* mutations) and in addition cleft lip and palate and an ASD.

Results:

Molecular karyotyping with 1Mb resolution array-CGH revealed the presence of a maximally 4Mb microdeletion on Xp11.22, confirmed by FISH using the probe RP3-501A4. The deletion was inherited from the unaffected mother, who skews the mutated allele completely. However, fine mapping by means of an Agilent 244K array revealed the presence of two discontiguous deletions, confirmed by qPCR. A small intragenic deletion was detected in the *FGD1* gene, explaining the Aarskog features. A second, centromeric deletion involved the *PHF8* gene and part of the *FAM120C* gene. Mutations in *PHF8* cause XLMR with cleft lip and/or palate. No autism has been described in these families. Of interest, Qiao et al. (2008) reported a family with autism segregating with an overlapping but larger microdeletion encompassing the *FAM120C* gene. This finding points towards the *FAM120C* gene as a novel positional X-linked candidate gene for autism. *FAM120C* belongs to a family of 3 relatively uncharacterized proteins with putative transmembrane domains, and shows enriched expression in human and mouse fetal brain. (Holden et al, 2003) Moreover, since its paralogue Fam120a (C9orf10) colocalizes with Fmrp at Puralpha-positive particles in the mouse hippocampus, *FAM120C* further represents a good biological candidate gene with regard to ASD. (Kobayashi, 2006)

Conclusions:

In a patient with a unique chromosomal rearrangement on Xp11.22, we identified *FAM120C* as a novel positional and biological ASD candidate gene. This study provides further support for the great value of unique rare variants in the understanding of ASD genetics. We will present the results of an ongoing mutation screen and additional expression studies in mice.

118.038 38 Association STUDY of Vesicle-ASSOCIATED Membrane PROTEIN 7 VAMP7/SYBL1 Gene with Autistic PATIENTS. T. Galli[1], P. Gorwood[2], B. Golse[3], L. Robel[3] and N. Ramoz*[2], (1)*INSERM U950*, (2)*INSERM U894-Team1*, (3)*AP-HP*

Background: Vesicle-associated membrane protein 7 (VAMP7/TI-VAMP/SYBL1) with syntaxins form an active SNARE complex and it is required for exocytosis involved in neurite growth. Recently, polymorphisms of syntaxin 1A (STX1A) gene were found associated to autism, by transmission disequilibrium test (TDT) analysis of 249 AGRE trios.

Objectives: Our goal is to identify association between autism and polymorphisms of *VAMP7/SYBL1* gene located on Xq28 and Yq12.

Methods: We carried out a case-control study by genotyping single nucleotide polymorphisms (SNPs) within *VAMP7* gene, using TaqMan® SNP Genotyping Assays, on 84 French autistic patients, parents, and 143 healthy French controls. Distributions of alleles and genotypes were compared between patients and controls. Transmission disequilibrium test was performed in autism families.

Results: SNPs were on Hardy-Weinberg equilibrium. No significant differences of frequencies for alleles or genotypes were found between autistic patients and controls. Transmission disequilibrium test is currently under study in autism families.

Conclusions: No association between polymorphisms in *VAMP7* gene was identified yet with autism in this study. Additional SNPs are needed to entirely cover the 62 kb of *VAMP7/SYBL1* gene.

118.039 39 Elucidating the Effects of Genetic Variants On Protein Coding and Noncoding Genes in Autism. C. Hicks*, *Loyola University Medical Center*

Background: The past few years have witnessed substantial advances in

understanding the genetic basis of autism. These advances have been made possible by high-throughput genotyping and genome-wide association analysis for identification of genetic variants associated with autism. This approach has revealed single nucleotide polymorphisms (SNPs), copy number variants (CNVs), and microinserts and deletions (InDels) providing insights into the genetic basis of autism. However, the full breadth of the goals of the Autism Genome Project and the emergence of high-throughput genotyping for genome-wide association studies are rapidly running into several bottlenecks in translating genomic findings into clinical practice to improve human health. One of the more significant bottlenecks is the inability to elucidate the effects of genetic variants (SNPs, CNVs and InDels) on protein coding and noncoding genes. While GWAS has powerfully identified genetic variants, majority of these variants (>60%) are located in noncoding and intergenic regions, and much work remains to elucidate their effects on gene function.
Objectives: The objective of this study is to elucidate the effects of genetic variants (SNPs, CNVs, InDels) on protein coding and noncoding genes.

Methods: We have and continue to use the power of computational systems biology framework to (a) create an inventory of the genetic variants that contribute to autism risk and (b) to leverage genotype data with sequence data to elucidate the effects of identified genetic variants on protein coding and noncoding genes.

Results: We have performed computational analysis of the effects of genetic variants on *cis regulatory* elements, regulatory regions and splice sites in 260 autism candidate genes currently in the Autism Candidate Gene Map (ACGMap) Database that we have created. In more than 60% of the genes we have shown that genetic variants, particularly structural variants (CNVs and InDels) can adversely affect or disrupt *cis regulatory* elements, regulatory regions and splicing events. Furthermore, through *ab initio* prediction, we have identified potential regions for targeted sequencing.

Conclusions: We show that the effects of genetic variants on gene function can be elucidated computationally. Given the prevalence of genetic variants in noncoding regions and the significance of these regions with respect to gene regulation, it is imperative that *cis regulatory* elements disrupted by these variants be identified. While experimental methods are essential for validating predicted *cis regulatory* elements, computational prediction provides a quick and cost effective approach.

118.040 40 Exon-Level Expression Profiling: Evaluation of Global Alternative Splicing in Autism, a Proof of Concept Study. R. Aldenderfer*[1], B. Han[2], X. W. Chen[2] and Z. Talebizadeh[1], (1)*Children's Mercy Hospital and University of Missouri-Kansas City*, (2)*The University of Kansas*

Background: Autism is a complex, heterogeneous neurobehavioral disorder with many causes and varying degrees of severity. To date, the main technique used to screen autism candidate genes has been direct sequencing of exons using genomic DNA. It is surprising that for strong candidate genes such as NLGN3 and NLGN4, few functional mutations have been identified in association with autism. This suggests that implications may be at a higher level than their genomic sequence, including alternative splicing. Previously, we reported novel alternative splicing variants in the NLGN3 and NLGN4 genes using RT-PCR and DNA sequencing. Alternative splicing of primary transcripts (pre-mRNAs) is a regulatory mechanism contributing to the increased complexity of higher eukaryotic organisms resulting in exon skipping, alternative splice site usage, and intron retention, thus leading to structurally and functionally distinct transcript isoforms and protein variants. Alternative splicing is a gene expression regulatory process that allows a single gene to generate multiple transcripts increasing protein diversity. The dysregulation of this process has been associated with some cancers and neurological diseases such as Parkinson's and Alzheimer's. Objectives: Here we report the feasibility of exon-level global gene expression profiling in autism using lymphoblastoid cell lines (LCLs). Methods: Global alternative splicing was evaluated using the Affymetrix Human Exon

1.0 ST array in LCLs from five autism subjects and five unrelated, age and gender matched controls obtained from the Autism Genetics Resource Exchange. Exon array data was analyzed using Agilent's GeneSpring GX 10.0. Gene Ontology and pathway analysis were conducted using the functional annotation tool, DAVID. In addition to DAVID, the Pearson correlation coefficient was used to measure gene relations (acquired from the Human Protein Reference Database and TRANSFAC database) in differentially expressed gene list identified by exon array profiling of autism compared to control samples. Results: ANOVA and Bonferroni multi-test correction identified 57 genes that exhibit differential expression at the exon-level, suggesting potentially different alternatively spliced transcripts between the two study groups. This list includes genes associated with neurological diseases such as Alzheimer's (SLC30A7). Several of the genes identified have been linked to nervous system development or autism including CYFIP1, ROBO1, and CDKL5. Biological processes overrepresented in this gene list included nervous system development, post-translational protein modification, neuronal activities, protein modification and amino acid biosynthesis. Upon RT-PCR validation of gene exons identified as differentially expressed between the two groups, we discovered multiple unreported splice variants of a zinc-finger protein, ZMYM6. Each new ZMYM6 spliced isoform has been confirmed using exon-junction-specific PCR primers and DNA sequencing. Conclusions: This is the first study to evaluate global alternative splicing in autism. Our results indicate that changes at the alternative splicing level should be considered in the etiology of autism. This pilot study demonstrates that even though LCLs are not neuronal cells, they are a viable cellular model for human neurological diseases and can provide informative alternative splicing data regarding complex neurodevelopmental disorders such as autism.

118.041 41 Autism Genetic Database (AGD): Using Bioinformatics to Study the Genetics of Autism. Z. Talebizadeh*[1] and G. Matuszek[2], (1)*Children's Mercy Hospital and University of Missouri-Kansas City*, (2)*University of Kansas*

Background: Autism is a neurodevelopmental disorder with onset in early childhood. It belongs to a group of conditions known as autism spectrum disorders (ASD). The complex and heterogeneous clinical manifestation of this genetic disorder requires a multidisciplinary approach to simultaneously investigate the impact of multiple genetic factors. Recently, we have developed the first comprehensive autism repository, Autism Genetic Database (AGD), which comprises a list of reported autism susceptibility genes and copy number variations (CNVs), as well as all known human noncoding RNAs and fragile sites. The ultimate goal of this bioinformatics project is to provide a public repository of autism genetic information for the research community. In the past few years, several studies have generated CNV data on healthy individuals to be used as a baseline for evaluating pathogenic relevance of disease related CNVs. Furthermore, CNVs have been linked to various types of developmental and psychiatric disorders including schizophrenia, bipolar disorder, ADHD, and mental retardation. Clinical and genetic overlap among different neurodevelopmental disorders has indicated the importance of evaluating their common underlying mechanisms. Objectives: The objectives of this study were (1) to update our newly developed AGD database and to expand its scope by adding new features; and (2) to identify testable hypotheses by applying statistical analyses using AGD data. Methods: Susceptibility genes with at least one suggestive autism association were included. CNVs with at least one reported disease association were included and classified based on the association with ASD or other neurodevelopmental disorders. Statistical data analyses were performed using updated information stored in AGD. Results: Since the initial development of AGD, there have been new reports of genes and CNVs associated with autism. The list of autism susceptibility genes and CNVs were updated in our database according to literature searches. CNVs in healthy individuals as well as other neurodevelopmental disorders (i.e., ADHD, schizophrenia, and bipolar disorder) were added and labeled in the AGD database. Statistical data analyses were conducted

using information stored in AGD to evaluate the distribution and potential correlation of different data-points in autism. To further elucidate autism specific profiles, applied analyses were also performed based on the distribution of reported CNVs in other neurodevelopmental disorders and healthy subjects. Conclusions: Our study demonstrates that bioinformatic tools will enable rigorous evaluation of the growing list of autism susceptibility factors. Our comprehensive autism database provides an opportunity to perform initial in silico analyses identifying previously undetected potential association/interaction profiles of these multiple genetic factors. The AGD database not only introduces a new and useful bioinformatics tool to the research community, but also enhances basic molecular genetic research projects by providing models and analytically driven hypotheses to be evaluated in the laboratory.

118.042 42 Comparison of Human Brain Persistent Organic Pollutant Levels with Epigenetic Alterations in DNA Methylation and MeCP2. M. M. Mitchell[1], A. L. George*[2], L. -. H. Chi[3], P. J. Kostynaik[3] and J. M. LaSalle[1], (1)*UC Davis School of Medicine*, (2)*University of California at Davis*, (3)*University at Buffalo*

Background: Epigenetics act at the interface of genetic and environmental factors in autism risk. Several autism-spectrum disorders have genetic mutations in gene or gene loci regulated by epigenetic mechanisms, including X-linked Rett syndrome (RTT, MECP2), and imprinted chromosomal region 15q11-13 disorders Prader-Willi (PWS) and Angelman syndromes (AS). Aberrant DNA methylation has previously been observed at the MECP2 promoter in autism male brain, as well as epigenetic alterations in expression of the 15q11-13 GABAA receptor genes. Persistent organic pollutants (POPs), including polychlorinated biphenyls (PCBs) and polybrominated diphenylethers (PBDEs) bioaccumulate in fat and lipid-rich tissues, and thus are of particular concern for the effects on neurodevelopment. High organic pollutant exposures in Greenlandic Inuits have previously been associated with reduced global DNA methylation. Objectives: Investigate epigenetic alterations in DNA methylation and MeCP2 levels in human cortex samples from control, autism, and other neurodevelopmental disorders to test the hypothesis that exposures to POPs may correlate with epigenetic changes. Methods: PBDEs were analysed by GC/MS using NCI (negative chemical ionization) and PCBs were analysed by GC/uECD (micro electron capture detector) on human post mortem cortex and cerebellum frozen samples. Levels of pollutants were normalized to lipid content in each brain sample. To investigate global DNA methylation, 5-Methyl-Cytosine immunofluorescence was detected by laser scanning cytometry (LSC) and normalized to control mouse IgG staining on each tissue samples arranged on a tissue microarray. Results: Preliminary data on 25 control, 16 autism, and 27 other genetic disorders (combined RTT, PWS, AS, and DS) brain samples show that BDE-47 is the most abundant PBDE congener in all groups included in this study, followed by BDE-99, -153 and -100. PCB congeners as a group were much lower than PBDEs in the same samples. Autism samples showed significantly lower levels of PCB-118, -138, and -153 compared to controls. PBDE levels were not significantly different in autism, but showed a trend towards lower levels of BDE-47, -99, and -183 compared to controls. An additional 32 brain samples are currently being analyzed to test a potential significance of PBDE levels in autism brain samples. Autism samples showed higher levels of global DNA methylation compared to controls both in the MeCP2-hi and total cell populations on the tissue microarray. A correlation analysis of each PBDE congener with DNA methylation levels will be performed. Conclusions: While POPs, particularly PBDE-47, are detectable in human brain samples, autism brain samples show lower levels of several PCBs and a trend for lower levels of PBDEs. Our preliminary data supports other work in blood suggesting an inverse correlation between POP exposure and global DNA methylation levels.

118.043 43 Computational Detection of Homologous Recombination Hotspots in X-Chromosome Autism Associated Genes. A. Ard[1], M. LaMadrid[2], S. Bwabye[2], K. Koyama[2] and T. Deisher*[2], (1)*University of Portland*, (2)*Sound Choice Pharmaceutical Institute*

Background: Autism prevalence rates in the US and UK began increasing temporally close to the time that the MMR vaccine was switched from the type manufactured using animal cells to a type manufactured using human cells. A yet unstudied possible environmental cause for autism is residual human DNA contaminant in the vaccines produced using human cells. Debate about the dangers of residual human DNA in vaccines has been going on for 50 years, mainly related to cancer initiation. Clinical gene therapy (1996) of male infants has induced childhood leukemia due to improper DNA insertion. To minimize the possibility of oncogenic DNA integrating into a vaccine recipient's genome, the WHO and FDA have recommended DNAse treatments to reduce the size of contaminant DNA fragments to less than genic lengths, ~200-1000bp. These recommendations were developed before the sequencing of the human genome. DNA cellular diffusion studies have shown that short DNA fragments (<250bp) have higher probability of entering the nucleus than longer lengths. Gene therapy studies have also demonstrated that naked DNA, injected intramuscularly, can remain intact and be transported to the brain via retrograde axonal transport in motor neurons. Once inside the nucleus, exogenous DNA can integrate via homologous recombination, potentially in genomic regions called 'recombination hotspots'. Intra-species DNA integration, e.g., by homologous recombination, occurs with a probability a billion times greater than inter-species homologous recombination. Integration of short human DNA fragments has the potential to contribute to various human diseases, including autism.

Objectives: To verify the lengths of residual human DNA in vaccines and to determine if recombination hotspots occur near or in X-chromosome genes known to be associated with autism.

Methods: Human DNA from inactivated vaccines was isolated and characterized using standard procedures. A list of recombination hotspots, computationally derived by using Hapmap Phase II data, was downloaded. A list of 238 genes associated with autism (AAGs) was downloaded from the ACGMAP website. Gene coordinates, including transcription start and end sites, were downloaded from the UCSC Human Genome website. Software was written to automate the location of overlaps between autism associated genes and recombination hotspots.

Results: The average human DNA fragment length in rubella vaccine was 220 base pairs. Out of 1145 hotspots in the X-chromosome, 25 hotspots are located in 5 of 15 X-chromosome AAGs, between the transcription start and end sites. These genes are NLGN3 and NLGN4X (neuroligins involved in synapse formation), AFF2 and IL1RAPL1 (involved in X-linked mental retardation), and GRPR (gastrin releasing peptide receptor).

Conclusions: Autism-associated genes in the X-chromosome contain multiple regions where potential insertion of short, non-host homologous DNA can occur. With new knowledge due to the human genome project, particularly in regards to SNPs and epigenetics, further work must be done to understand the implications of integrated residual human DNA to the etiology of autism.

118.044 44 Genes Involved in Neuron Migration and Centromere-Microtubule Interaction Show Enriched Association Signal in Autism: Evidence From the Autism Genome Project. R. J. Anney*[1], E. Heron[1], R. Segurado[1], E. Kenny[1], C. O'Dushlaine[1], M. Gill[1] and L. Gallagher[2], (1)*Trinity College Dublin, Ireland*, (2)*Trinity College Dublin*

Background: Recent genome-wide association (GWA) studies, have implicated a range of genes from discrete biological pathways in the aetiology of autism. However, despite the strong influence of genetic factors autism, linkage studies and association studies have yet to identify robust major effect genes or SNPs. Objectives: It is possible and plausible that real genetic risk exists within the milieu of nominal to strong association signal observed in the GWAS data. One approach to data-mine the GWA data for additional information is to formally test for enrichment of signal in groups of biologically linked genes such as gene pathways. Here we

present a modification to the SNP-ratio test (SRT) methodology described by O'Dushlaine et al., (2009) to apply to family-based designs. Methods: Using the modified family-based SRT, we performed a hypothesis-free analysis of all gene-ontology gene sets and identify four pathways that show enriched signals in a GWAS of a narrow diagnosis of autism from the Autism Genome Project (AGP). Empirical P-values were calculated from 10000 simulation GWAS using affection shuffling between probands and pseudo-probands generated from the non-transmitted chromosomes. Sensitivity to single genes of the top-pathways was examined. Results: Five pathways with multiple genes driving the association were identified. These include gene sets involved in neuron migration, brain development, glial-cell differentiation, neuro-immunological response and fidelity of mitosis. These processes have previously been proposed as important in the aetiology of autism. Conclusions: The application of a pathway approach to the AGP GWAS data has provided additional evidence to support hypothesised biological processes implicated in autism. Further characterisation of these sets of genes may offer additional data from the GWA to understand genetic risk of autism.

118.045 45 Genetic Analysis of Latent Phenotypes in Autism Spectrum Disorders. X. Q. Liu*[1], S. Georgiades[2], E. Duku[2], A. P. Thompson[2], A. D. Paterson[1] and P. Szatmari[2], (1)*The Hospital for Sick Children*, (2)*McMaster University*

Background: A better understanding of the latent phenotype constructs of autism spectrum disorders (ASD) will help us identify the etiological factors of the disorder. To date, even though many studies have been conducted to detect latent constructs of ASD, no study has systematically explored the genetic components of ASD using latent phenotypes derived from factor analysis.

Objectives: 1) To detect latent phenotype constructs underlying ASD; 2) To identify genetic loci that are linked to these latent phenotypes.

Methods: Exploratory factor analyses were applied to two independent datasets using 28 selected ADI-R algorithm items. The first dataset was from the Autism Genome Project (AGP) phase I (1,009 individuals from 618 families); the second was from the AGP phase II (1,034 unrelated individuals). Latent phenotypes derived from the factor analysis were then used in genome-wide multipoint variance components linkage analyses.

Results: Six latent factors which accounted for all the common variance from the 28 ADI-R algorithm items were retained for both datasets. Based on the common characteristics of items in each factor, the factors represent 1) social interaction and communication; 2) joint attention; 3) non-verbal communication; 4) sensory-motor; 5) peer interaction; and 6) insistence on sameness. The factor loading patterns from the two datasets were in high agreement with each other (coefficients of factor congruence from 0.84 to 0.99). All latent phenotypes showed familial aggregation with heritability estimates ranging from 29 to 67% (before adjustment for ascertainment). A strong linkage signal was obtained for the social interaction and communication factor on chromosome 11q23 (logarithm of odds (LOD) score=4.00) which contains candidate genes involved in neural cell adhesion and synapse function. A strong linkage signal was also obtained for the sensory-motor factor on chromosome 19q13.3 (LOD score=4.92).

Conclusions: The top linkage findings from this study do not overlap with the most significant linkage results from the AGP linkage study using ASD diagnosis as a primary outcome (AGP 2007) and another AGP linkage study using either subsets of families or ADI-R domain total scores as traits (Liu et al. 2008). This once again reflects the complexity of gene mapping for ASD. However, this study does demonstrate that the latent constructs of ASD is replicable in different datasets and the derived latent phenotypes are suitable and informative for genetic studies.

118.046 46 Functional Annotation of ASD Susceptibility Loci. S. R. Wadhawan*, B. Georgi, R. Liu, S. Hannenhalli and M. Bucan, *University of Pennsylvania*

Background:

Autism spectrum disorders (ASD) are a heterogeneous group of disorders that are characterized by abnormalities in communication and social behaviors. ASD typically manifest in the first 3 years of life and have a strong heritability showing 2-6% concordance rates in siblings of affected individuals, ~10% in dizygotic twins and over 90% in monozygotic twins. Recent genome wide association studies (GWAS) utilizing high-density single nucleotide polymorphisms (SNPs) have revealed extensive genetic heterogeneity and structural rearrangements across the genomes of affected individuals. A vast majority of the copy number variants (CNVs) occur in the intergenic regions, thereby supporting the notion that most of the functional variation underlying ASD affects gene regulation rather than the protein-encoding sequences. Current findings support a model that common variants with a moderate effect together with rare and de novo mutations in genes involved in neuronal development and signaling underlie ASD susceptibility.

Objectives:

In order to identify these genes and their associated pathways we (I) performed pathway based analysis of genome-wide association signals for ASD subtypes; (II) prioritized ASD-associated loci using pathway-based computational approaches; (III) initiated resequencing of over 100 loci in ASD subjects from the Autism Genetics Research Exchange (AGRE) collection.
Methods:

In order to prioritize candidate ASD loci for resequencing we selected a list of 188 genes (46.55 MB) from the literature. Since a majority of CNVs associated with ASD have been found in the intergenic region, we included the entire flanking region (up to the next gene) for each of the genes in the list (total of 164 MB) constituting 188 genomic regions of interest (GROI). For each gene in the GROI we mapped conserved non-coding regions, small non-coding and alternatively spliced RNAs, and methylation marks in several cell types on CNV - ASD susceptibility regions. These data facilitated refinement of the list of genomic regions associated with ASD. A tiling array with short genomic regions (total 3.5MB) representing these ASD candidate loci will be used to capture DNA for resequencing using Illumina Genome analyzer.
Results:

We identified highly conserved sequences within these GROI and annotated potential enhancers and chromatin modification marks. For example, p300, a trancriptional coactivator is critical for embryonic development. We used p300 ChIP-Seq data and found an excess of forebrain (4%) and midbrain (3%) p300 binding sites compared to limb-bud enhancers (2%) in our GROI. Furthermore, we showed that 20 % of conserved sequences in non-protein coding regions, corresponded to RNA detected in a published RNA-Seq experiment.
Conclusions:

We are nearing completion of the custom array design which will be used to screen 100 affected ASD subjects from AGRE. The resulting sequence data will be comprehensively analyzed for non-synonymous SNPs in exonic regions and their effects on protein structure/function. Furthermore, we expect to identify additional causative variants in potential regulatory elements in non-protein coding regions, and fine map boundaries for previously detected and newly discovered CNVs.

118.047 47 Analysis of Selected mTOR Pathway Genes in ASD Families Reveals a Deletion Event in PTEN. D. Yu*, R. L. Beauchamp, S. Haddad, R. Sasanfar, J. F. Gusella, M. J. Daly, S. L. Santangelo and V. Ramesh, *Massachusetts General Hospital*

Background: The co-occurrence of Autism Spectrum Disorders (ASD) and Tuberous Sclerosis Complex (TSC) has been recognized for many years. TSC involves two genes, *TSC1* and *TSC2*, which function together to inhibit mammalian Target of Rapamycin (mTOR) signaling. mTOR signaling plays an essential role in neural plasticity, and activation of mTOR signaling is known to result in rapid synthesis of a diverse array of neuronal proteins which may have implications for synapse strength. Therefore, aberrant regulation of mTOR

signaling in neurons is a potential common cause for deficits associated with TSC as well as ASD.

Objectives: To investigate whether inherited variations in mTOR pathway genes may also be associated with genetic risk for ASD, we chose a candidate gene approach focusing on 7 genes known or suspected to be involved in aberrant regulation of mTOR signaling: *TSC1, TSC2, FKBP1A, NF1, PTEN, RHEB and MYCBP2.*

Methods: The association study included 3006 individuals from 743 Autism Genetic Resource Exchange (AGRE) families comprising 1177 ASD affected cases, as well as 1385 parents and 444 siblings who were either unaffected or had no phenotypic information. A total of 140 single-nucleotide polymorphisms (SNPs) spanning the candidate genes (including 7 rare variants in *PTEN*) were chosen using pairwise tagging and an R^2 threshold of 0.8 in HAPMAP. SNPs were genotyped with Sequenom, and Transmission Disequilibrium Test (TDT) was carried out using PLINK. The deletion event in *PTEN* was initially detected by specific Mendelian errors in neighboring SNPs, and was later confirmed by real-time quantitative PCR, cloning and sequencing.

Results: Association analysis revealed no significant association of the 7 candidate mTOR pathway genes with ASD. However, an anomalous allele pattern of two adjacent SNPs in intron 1 of *PTEN* was identified in 21 AGRE families, which could be explained with the hypothetical occurrence of a deletion event. Direct sequencing of the two *PTEN* SNPs excluded the possibility of simple genotyping error, and quantitative PCR detected a ~50% decreased allele dosage, further strengthening evidence for the *PTEN* deletion. This is finally confirmed with cloning and sequencing. The *PTEN* deletion spans 898 bp in intron1, ending at 59 bp upstream of exon2.

Conclusions: An identical deletion of 898 bp in intron 1 of PTEN was found in a subset of ASD families. There was no record in these families of Cowden's Syndrome, characterized by hamartomatous growths, or a variety of other cancers in which mutations in the PTEN tumor suppressor are implicated. However exclusion of some clinical records in the dataset cannot be ruled out. In addition to a role as a key regulator of the mTOR signaling pathway, PTEN has been implicated in ASD or autistic-like phenotypes in both humans and mouse models. As a next step, it is critical to investigate whether this deletion is associated with ASD, and whether it affects PTEN mRNA expression or processing. If confirmed, these results will break new ground for understanding the pathogenesis of a subset of ASD.

Sensory Systems, Motor Systems, and Reptetative Behavior Program

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118.048 48 A Comparison of Toddlers with ASD and Typical Development: Relating Repetitive Behaviors, Early Social Communication Symptoms, and Nonverbal Skills. M. V. Pouncey*, A. B. Barber and L. G. Klinger, *University of Alabama*

Background:
While repetitive and stereotyped behaviors (RSB) were once considered to be later developing symptoms of autism spectrum disorder (ASD), more recent research has found that RSB emerges during the toddler years. Research examining the relationship between RSB and other early ASD symptoms (e.g., social communication, symbolic play) is limited, but emerging. More in depth research into this relationship will guide the development of intervention targets appropriate for very young children with ASD, and further the empirical understanding of early ASD symptomology. (Shumway & Wetherby, 2009).
Objectives:
There were three objectives of this study: 1) to compare toddlers with ASD to mental age matched toddlers with typical development on early symptoms measured using the *Communicative and Symbolic Behavior Scales* (CSBS; Wetherby and Prizant, 2002). While previous research with the CSBS has compared toddlers with ASD and typical development matched on chronological age, we were interested in how mental age matched groups compare; 2) to compare how RSB differed across groups and how they relate to other early symptoms; and 3) to examine how early symptoms of ASD relate

to nonverbal ability.
Methods:
Thus far, participants include 7 18-36 month old boys with ASD (diagnosed using the ADOS) and 7 typically developing (TD) boys matched on mental age measured by the Mullen Scales of Early Learning (Mullen, 1992). Participants were administered the CSBS and composite scores were calculated. Additionally, each behavior sample was scored and subsequently coded for RSB using the CSBS RSB Movement Scale (Wetherby and Morgan, 2007). Date collection is ongoing.
Results:
Thus far, toddlers with ASD received lower scores on the Social Composite (i.e., emotion and eye gaze, gestures, and communication rate/function) compared to children with TD, $t(6) = 14.49$, $p < .0001$. Further, they received lower scores on the Symbolic Composite (i.e., use of objects, understanding of words), $t(6) = 3.54$, $p < .01$. While there was a trend for toddlers with ASD to show lower scores on the Speech Composite (use of sounds, use of words), this was not significant in the current small sample, $t(6) = 1.94$, $p < .10$. Further, CSBS scores were related to nonverbal mental age such that toddlers with ASD who had lower nonverbal abilities demonstrated less social, symbolic, and expressive language skills, $r(7) = .98$, $p < .01$. It is predicted that these early symptoms will be related to repetitive behaviors in toddlers with ASD. RSB coding is ongoing and data will be available within a few weeks.
Conclusions:
Thus far, toddlers with ASD showed less social skills, symbolic understanding, and expressive language skills than toddlers with TD matched on mental age. This study represents one of the first studies examining whether the CSBS is appropriate for comparing groups matched on mental rather than chronological age. Further, these preliminary results suggest that nonverbal mental age is related to ASD symptoms, such that those toddlers with higher nonverbal skills showed milder symptoms. Finally, it is hypothesized that early repetitive behaviors will be related to these core symptoms of ASD and data analyses to address this question is ongoing.

118.049 49 Graphomotor Disorders in High-Functioning Children with Autism Spectrum Disorders. T. Hellinckx*, H. Roeyers and H. Van Waelvelde, *Ghent University*

Background: Several studies described motor control disorders in children with Autism Spectrum Disorders (ASD), even in groups of high-functioning children with ASD (HFA). Graphomotor skills have not yet been examined in children with ASD, although they are extremely relevant because they are linked to academic achievement.

Objectives: Firstly, it will be explored if graphomotor disorders are more common in children with HFA than in typically developing (TD) children. Secondly, it will be examined if handwriting legibility or speed differs in both groups. Finally, several components of writing (visual-motor integration skills, visual perception skills, reading skills and manual dexterity) will be compared between the two groups.

Methods: *Participants* 60 children with HFA and 60 TD children between 7 and 12 years old, with an IQ > 80, participated. Groups were matched on age, IQ, gender and hand preference. Children with medical diagnoses interfering with their motor development were excluded.
Materials 'Systematische Opsporing van Schrijfmotorische stoornissen' (SOS-test) (Van Waelvelde, De Mey & Smits-Engelsman, 2008) was used to evaluate graphomotor skills. Handwriting quality is determined by evaluating 6 items, with higher scores indicating poorer performance. Handwriting speed is measured by counting up the letters written in 5 minutes. 'Beery-Buktenica Developmental Test of Visual Motor-Integration test' (VMI) (Beery & Beery, 2005) was used to evaluate visual-motor integration and visual perception abilities. 'One-Minute Reading Test' (EMT) (Brus & Voeten, 1976) was used to assess reading skills. 'Movement-Assessment Battery for Children - 2nd edition' (M-ABC-II) (Henderson & Sugden, 2007) was used to assess manual dexterity.

Results: Preliminary results show that 82.7% of the children with HFA (n=34) fell below or at the 5th percentile regarding HW quality, as opposed to merely 22.5% of TD children.

None of the TD children scored at or below the 5th percentile regarding HW speed as opposed to 22.9% of the children with HFA. A significantly poorer quality was found in children with HFA ($t(54)=-4,81$; $p\leq.001$) due to poor writing fluency ($Z=-2,74$; $p=.006$), dysfluent transitions between letters ($Z=-2,79$; $p=.005$), larger HW ($Z=-3$; $p=.003$), more irregular letter height ($Z=-3,68$; $p\leq.001$) and irregular lines ($Z=-3,45$; $p=.001$). No significant difference in writing speed was found. When comparing components of writing, children with HFA had significantly poorer visual-motor integration skills ($t(55)=3,14$; $p=.003$), reading skills ($t(55)=3,68$; $p=.001$) and manual dexterity ($t(55)=474$; $p\leq.001$) than the TD group. No significant difference in visual perception skills was found.

Conclusions: Preliminary results show that there is a high prevalence of graphomotor disorders in children with HFA. Children with ASD have poorer HW quality compared to a matched control group possibly due to poorer visual-motor integration skills, reading skills and manual dexterity. Results and conclusions for the whole sample will be presented at the IMFAR meeting.

118.050 50 Overt Head Turning During Contingency Learning and Gross Motor Performance of Young Infants at Risk for Autism. 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: Postural control and attentional impairments are common in children with autism (Ozonoff et al., 2008; Zwaigenbaum et al., 2005). Few studies have examined the relationship between postural and attentional impairments in autism. Both these systems develop rapidly within the first year of life and may interact and influence each other. Objectives: In order to better understand such multisystem interactions, we compared overt head turning and gross motor performance in infant siblings of children with autism (AU sibs) and typically developing (TD) infants at 6 months of age. Methods: 25 AU sibs and 25 TD infants were observed in a novel associative learning task at 6 months. The Alberta Infant Motor Scale (AIMS) was also administered at 6 months. Learning task data were coded for frequency of overt head turning while looking to non-social cues such as objects or other and social cues such as the caregiver. A sum of prone and sit scores from the AIMS was used as a postural control measure. Results: AU sibs showed lower total head turn rates as compared to TD infants ($p<0.05$). Specifically, they performed significantly fewer head turns to social as well as non-social cues as compared to TD infants. Lastly, the postural control measure based on AIMS scores was significantly lower in AU sibs than TD infants ($p<0.05$). Conclusions: AU sibs who lacked overt head turning also showed poor postural control as compared to a group of TD infants. Together, these findings suggest that motor constraints such as poor postural control may contribute to the atypical/covert attention patterns of AU sibs. Lastly, these data also suggest that motor as well as attentional impairments may be the earliest markers of developmental disruptions related to autism.

118.051 51 Postural Development in Infants with and without Risk for Autism Spectrum Disorders. L. Nickel*, A. Thatcher and J. M. Iverson, *University of Pittsburgh*

Background: Evidence suggests that motor impairments exist in children and adults diagnosed with autism spectrum disorders (ASD), including difficulties with postural stability. Retrospective video studies of infants later diagnosed with ASD indicate that these atypicalities may be apparent early in development (e.g., Ozonoff, 2007). Delays and/or atypicalities in postural development may thus be potential indicators of risk for an eventual ASD diagnosis.

Objectives: The goal of this study is to investigate early postural development prospectively and longitudinally in infants at heightened risk for ASD and comparison infants in a naturalistic setting.

Methods: Twenty-one infants (6 male) with an older sibling diagnosed with autism (High Risk; HR) and 18 infants (8 male) with a typically-developing older sibling (Low Risk; LR) participated in this research. At 36 months, the ADOS-G (Lord et al., 2000) was administered to all HR infants; three received an autism diagnosis (AD infants). Infants

were videotaped at home for approximately 45 minutes at 6, 9, 12, and 14 months while engaged in everyday activities and play. All postures were coded (i.e., Prone, Supine, Sit Supported), and each posture change was characterized as being initiated by either the child or parent. All supported postures were further classified according to source of sustainment (i.e., child, parent, other).

Results: HR and LR infants exhibited comparable postural behavior. With age, they spent less time in postures involving external sources of support (e.g. Prone) and more time in postures requiring increased strength and balance (e.g. Stand Unsupported). AD infants, however, were observed in a smaller variety of postures, and the emergence of more advanced self-initiated postures was substantially delayed.
At each age point, AD infants had fewer postures in their repertoire. For example, at 9 months, AD infants were only observed in Prone, Supine, and All-4 postures. HR and LR infants exhibited postures similar to the AD infants, but were also observed in Sit Supported, Sit Unsupported, Kneel, and Stand Supported.
AD infants initiated posture changes later than HR and LR infants. For example, HR and LR infants were seen moving themselves into a child-sustained Sit Supported at 6 months. However, AD infants did not initiate this posture change until 12 months. Also, while HR and LR infants were first observed initiating a child-sustained Stand Supported at 9 months, AD infants were not observed initiating this posture until 14 months.
Furthermore, although the frequency of child-initiated posture changes increased in all groups from 6 to 12 months, AD infants initiated fewer posture changes overall than HR and LR infants combined (e.g., at 12 months, M_{AD} =14; $M_{LR/HR}$ = 41.6). At 14 months, however, this difference was no longer apparent.
Conclusions: These results suggest that in the first year of life, ASD infants exhibit delays in postural development. Findings are discussed in terms of the potential cascading effects of such delays on opportunities for infant exploration and learning.

118.052 52 Reduced Sensitivity to Minimum-Jerk Biological Motion in Autism Spectrum Conditions. J. Cook*[1], A. P. Saygin[2], R. Swain[1] and S. J. Blakemore[1], (1)*University College London*, (2)*University of California*

Background:

Previous studies have found a deficit in biological motion perception in participants with autism spectrum condition (ASC). However, the literature is mixed and other studies have found no difference between participants with ASC and controls in the perception of biological motion.

Objectives:

We used a novel paradigm to compare psychophysical thresholds for biological and non-biological motion detection in adult participants with ASC and age-, gender- and IQ-matched control participants.

Methods:

Participants watched pairs of animations that showed a biological object (a hand) or a non-biological object (a tennis ball) moving across the screen. The velocity profile of the movement was either 100% natural motion (minimum jerk (MJ) for the hand and gravitational (G) for the ball) or 100% constant velocity, or some linear combination of the two extremes. On each trial, two animations were shown successively and participants were asked to judge which was 'less natural'. A forced-choice adaptive staircase paradigm was employed to generate separate thresholds for the biological and the non-biological conditions. A low threshold indicates a high sensitivity to perturbations to the natural motion velocity profile.

Results:

There was a significant interaction between group and condition. This was driven by lower discrimination thresholds in the MJ condition than in the G condition for the control group only. There was no difference in the discrimination thresholds of the two conditions for the ASC group.

Conclusions:

Thresholds in the MJ condition were lower than in the G condition for the control group whereas there was no difference between the thresholds in the two conditions for the ASC group. Thus, unlike the controls, the ASC group did not show an increased sensitivity for perturbation to biological over non-biological velocity profiles.

118.053 53 Relationship Between Postural Control and Restricted, Repetitive Behaviors in Autism Spectrum Disorders. K. Radonovich*, K. Fournier, M. Lewis and C. Hass, *University of Florida*

Background: Restricted interests and repetitive stereotyped behaviors (RRBs) are one of the core diagnostic areas of autism spectrum disorders (ASD). Poor motor control has been reported to be predictor of repetitive behavior in individuals with mental retardation; however the relationship between motor control and repetitive behaviors in ASD is not fully defined.
Objectives: We compared the center of pressure (COP) sway area during quiet stance with intensity and frequency scores on the Repetitive Behavior Scale-Revised (RBS-R) in children with ASD and typically developing controls (TD). Our goals were to determine whether subjects with ASD had greater postural sway and whether RBS-R scores were related to the magnitude of postural sway. Further, we want to examine profiles of abilities in the group with ASD.
Methods: We have currently enrolled 18 children (IQ>70) diagnosed with ASD (3.9 to 15.7 yrs) and 28 TD children (3.4 to 15.9 yrs). Parents completed the RBS-R to determine the frequency and intensity of RRBs: Stereotyped Behavior, Self-Injurious Behavior, Compulsive Behavior, Ritualistic Behavior, Sameness Behavior and Restricted Behavior. Subjects also performed four quiet stance trials at a self–selected stance width for 15 seconds. Foot positioning was marked on the initial trial and used for all subsequent trials. Ground reaction forces were recorded (360Hz) from a forceplate (Type 4060–10, Bertec Corp., Columbus, OH) embedded level within the floor to calculate COP.
Results: Subjects with ASD had greater postural sway area compared to controls ($p=0.003$). Not surprisingly, subjects with ASD exhibited greater frequencies and intensities of RRBs overall and on all 6 subscales. Visual analysis of the postural sway area for the ASD group suggests that roughly half scored comparable to TD controls, whereas the other half scored >2 SD outside the TD range. Preliminary analyses found that motor impaired children did not have significantly worse IQ scores, but were younger ($p=0.02$) and had greater frequencies and intensities on the Stereotypies, Compulsive, and Restricted subscales ($p<0.05$).
Overall postural sway area was significantly correlated with the Total RBS-R frequency and intensity scores ($r=.52$, $p<0.001$ and $r=.54$, $p<0.001$), as well as 5 subscale scores (r range of .37 to .65, all $p<0.01$). Sway area was not related to the Self-injurious Behavior subscale. When examining the groups separately, however, these relationships appear to be driven by the strong correlations within the group with ASD; whereas, in controls postural sway was only related to the frequency and intensity of self injurious behavior.
Conclusions: Results support previous findings of relationships between RRBs and postural control. Motor control deficits in ASD continue to be more well-defined. It appears that motor control impairments may characterize a subset of individuals with ASD. Better delineation of function in these individuals will be important. Findings from animal and human neurobiological studies suggest that cortico-striato-thalamo-cortical circuits are involved in RRBs and motor and cognitive functions. These findings support a model relating RRBs in autism to deficits in motor control and cognitive functions (e.g. cognitive flexibility). We are continuing to collect data to examine these relationships.

118.054 54 Repetitive Behaviors and Anxiety in Children with Autism Spectrum Disorder. M. K. DeRamus*[1], L. G. Klinger[1] and H. R. Harwood[2], (1)*University of Alabama*, (2)*University of North Carolina at Chapel Hill*

Background: There has been limited research on repetitive behaviors in ASD and the relation between repetitive behaviors, anxiety, and social impairments in ASD. Baron-Cohen (1989) suggested that social impairments in ASD lead to increased anxiety, which in turn leads to increased repetitive behaviors, but this theory has not

yet been tested. An alternate model drawn from the OCD literature predicts that anxiety leads to repetitive behaviors which lead to social impairments. Additionally, there has been only one study directly comparing repetitive behaviors in children with ASD and children with OCD (Zandt, 2007).

Objectives: This study examined the relation between repetitive behaviors, anxiety, and social problems in ASD. Specifically, two models of repetitive behaviors in ASD were tested: Baron-Cohen's model suggesting that anxiety mediates the relation between social impairments and repetitive behaviors, and an OCD model suggesting that repetitive behaviors mediate the relation between anxiety and social impairments. Further, this study directly compared the pattern of repetitive behaviors in children with ASD and children with OCD.

Methods: Parents of 49 children with high-functioning ASD and 12 children with OCD, ages 7-17, completed interviews and surveys regarding their children's repetitive behaviors (Children's Yale-Brown Obsessive Compulsive Scale; Repetitive Behavior Scale – Revised), anxiety (Spence Children's Anxiety Scale for Parents), and social impairment (Social Responsiveness Scale).

Results: Within the ASD group, approximately half of participants were reported to have clinically significant levels of anxiety. Mediation analyses (i.e., Sobel tests) provided some support for Baron-Cohen's (1989) model suggesting that social difficulties lead to anxiety, producing repetitive behaviors in individuals with ASD (indirect effect = .01). However, there was more support for the model based on theories of repetitive behaviors in OCD, suggesting that anxiety leads to repetitive behaviors, creating social problems (indirect effect = .40). Both models support theories suggesting that anxiety leads to repetitive behaviors in ASD. Multivariate analysis of covariance and qualitative descriptions were used to compare children with ASD and children with OCD. Results indicated that the severity and frequency of most types of repetitive behaviors are similar in children with ASD and children with OCD. However, differences were evident between groups on the number of obsessions (more in OCD) and stereotyped and restricted behavior (more in ASD). The distinction between groups on these symptoms suggests that they may be useful in differentiating ASD from other disorders. A significant number (74%) of children with ASD met criteria for OCD.

Conclusions: The current study provides converging evidence that anxiety is a significant clinical issue for many children with ASD and is related to core social and repetitive behavior symptoms. Further, the relation between anxiety, repetitive behaviors, and social impairments in this ASD sample was similar to the relation suggested in the OCD literature. This research suggests that it may be beneficial to examine the assessment and treatment of OCD when developing appropriate treatments for individuals with high-functioning ASD. The significant number of children with ASD who met criteria for OCD suggests that it may be appropriate to use both diagnoses in the same individual.

118.055 55 Repetitive Behaviors: A Comparison of Obsessive Compulsive Disorder with and without Autism Spectrum Disorder. L. Joseph*[1], P. Grant[1], A. Thurm[2], C. Corbin[1] and S. E. Swedo[2], (1)*National Institute of Mental Health*, (2)*National Institute of Mental Health, National Institutes of Health*

Background: Restricted, repetitive and stereotyped behaviors (RRSB) are among the core symptoms of Autism Spectrum Disorders (ASD) and share features in common with the compulsions of Obsessive-Compulsive disorder (OCD), as well as mental retardation. The behaviors often impede daily functioning for patients. Little research has been done comparing these symptoms, with a single report finding no differences in parent reports (Zandt, Prior, & Kyrios, 2007).
Objectives: This study examined the differences in RRSB in participants with OCD only (OCD) as they compared to participants with a diagnosis of both OCD and an ASD (OCD+ASD). The relationship of RRSB scores to cognitive ability is investigated in both groups.

Methods: 47 participants: 31 OCD (Mean age = 14.40 +/- 2.3 yrs), and 16 OCD+ASD (14.11+/- 2.64 yrs) completed the Repetitive Behavior Scale-Revised (RBS-R, Bodfish, Symons, Parker & Lewis, 2000), a parent rating of repetitive behaviors, consisting of 5 subscales: Stereotypic Behavior , Self-Injurious Behavior , Compulsive Behavior, Rituals/Sameness Behavior, and Restricted Interests. Overall scores as well as subscale scores were analyzed using the Lam scoring system (Lam and Aman, 2007). The Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS, Goodman, 1986) was also used, with compulsions ratings obtained for the whole group and obsessions ratings for 15 of 16 OCD+ASD participants. 44 participants completed a cognitive assessment, Weschler Abbreviated Scale of Intelligence (WASI), (n=41), the Mullen Scales of Early Learning (n=1), and the Differential Abilities Scale (n=2). We examined differences between the two groups on both the RBS-R and CY-BOCS, and on each RBS-R subscale. We also examined correlations between the RBS-R and both the CY-BOCS and scores of cognitive ability.
Results: Preliminary results indicate no significant differences in the overall scores on the RBS-R between the OCD (X=23.00 +/- 17.22) and OCD+ASD groups (X=29.00+/- 13.28; t = -1.32, p=.19). However, the Restricted Interests subscale differed significantly between groups (OCD: 2.06 +/- 2.78; OCD+ASD: 4.75 +/- 1.81; t = -3.99, p < .00). No significant differences were found between groups on either obsessions or compulsion scales of the CY-BOCS. Scores on the RBS-R and CY-BOCS compulsions were positively correlated (r =.316, p = .05). Seven percent (n= 2) of individuals in the OCD and 27% (n = 4) OCD+ASD scored below 70 on a cognitive test. Mean cognitive scores (OCD: 101.90 +/-16.52, OCD+ASD: 80.87 +/-28.35) were negatively correlated with scores on the overall score of the RBS-R and on all of the subscales of the RBS-R with the exception of the Compulsive Behavior subscale.
Conclusions: Analyses indicate no differences between groups on the RBS-R overall score, but the OCD+ASD group had higher scores on the Restricted Interests subscale than the OCD group. The results suggest that the RBS-R is capturing obsessive-compulsive symptoms of both OCD and autism, and individuals with OCD and an ASD appear to have other types of significant repetitive behavior. Since cognitive ability influences these behaviors as well, assessments must be administered in the context of a more complete evaluation.

118.056 56 Specificity of Praxis Impairments in Children with Autism. L. K. MacNeil*[1], L. R. Dowell[1], E. M. Mahone[1], M. B. Denckla[2] and S. H. Mostofsky[2], (1)*Kennedy Krieger Institute*, (2)*Kennedy Krieger Institute, Johns Hopkins University School of Medicine*

Background: Motor impairment is a common finding in children with autism spectrum disorder (ASD). Studies are highly consistent in revealing that children with ASD show difficulties with motor control as well as impaired performance of more complex skilled motor gestures to command, with imitation, and with tool use on praxis examination (Dewey et al., 2007; Dowell et al., 2009; Dziuk et al., 2007; Mostofsky et al., 2006). Additionally, children with Attention-deficit/Hyperactivity Disorder (ADHD) have been shown to exhibit deficits in motor control (Cole et al., 2008; Denckla et al., 1978); however, they do not appear to show impaired praxis (Dewey et al., 2007).

Objectives: To explore the specificity of impaired praxis and postural knowledge (the ability to recognize correct praxis gestures in others) to autism by examining three samples of children, including those with ASD, ADHD, and typically developing (TD) children.

Methods: Twenty-four children with ASD (mean year 9.69; 5 female), 24 children with ADHD (mean year 9.73; 5 female), and 24 TD children (mean year 10.33; 5 female) each completed the Physical and Neurological Exam for Subtle Signs (PANESS) (Denckla et al., 1985) as an assessment of motor skills, a modified version of the Florida Apraxia Battery (Heilman and Rothi, 1993) as an assessment of performance of skilled gestures involving tool use (e.g., combing hair) and social communication (e.g., waving goodbye), and the Postural Knowledge Test (PKT) (Mozaz et al., 2007) as an assessment

of recognition of correct hand postures necessary to perform these skilled gestures.

Results: A 3-way MANOVA revealed a significant multivariate effect of diagnosis for the three motor assessments which was also observed with univariate tests for each of the three motor variables (all with $p<0.01$). Post hoc analyses revealed that children with ASD performed significantly worse than TD children on all three motor assessments (praxis total % correct: $F=31.40$, $p<0.001$; total PANESS: $F=31.60$, $p<0.001$; PKT: $F=9.28$, $p=0.012$). In contrast, children with ADHD performed significantly worse than TD controls on PANESS (total: $F=24.64$, $p<0.001$) but not on praxis (total % correct: $F=4.84$, $p=0.10$) or PKT. Furthermore, comparisons of ASD and ADHD groups revealed that the ASD group performed significantly worse than the ADHD group on the praxis examination (total % correct: $F=13.65$, $p=0.003$) and PKT ($F=6.21$, $p=0.048$) but not on the PANESS. All p-values were Bonferroni corrected.

Conclusions: When compared to TD children, children with ASD show impaired motor control and praxis performance, as well as impaired postural knowledge; furthermore they exhibited impairments in praxis and PKT when compared to children with ADHD. In contrast, children with ADHD show impaired motor control, yet intact praxis performance and postural knowledge compared to TD children. The findings suggest that impaired formation of perceptual-motor action models necessary to development of skilled gestures and other goal directed behavior is specific to autism; whereas, impaired basic motor control may be a more generalized finding.

118.057 57 The Presence of Restricted and Repetitive Behaviors in Infants and Toddlers with Typical Development. J. Richler*[1], R. Luyster[2] and C. Lord[3], (1)*Indiana University*, (2)*Children's Hospital Boston/Harvard Medical School*, (3)*University of Michigan*

Background: Early diagnosis of autism spectrum disorders (ASD) has become increasingly common, due in part to research highlighting the importance of early identification and intervention. If 'red flags' for ASD are to be accurately identified, researchers and clinicians must have a good understanding of the range of behavior that can be expected in very young children with typical development. Yet to date, relatively little is known about the prevalence of restricted and repetitive behaviors (RRBs) and other 'unusual' behaviors in very young children with typical development (TD), despite the fact that these behaviors constitute a core component of the ASD phenotype.

Objectives: The aim of the present study is to learn more about the presence of repetitive and other 'unusual' behaviors in very young typically developing children.

Methods: Data were analyzed for 110 TD children (7-24 months old) who were evaluated as part of the development of the Autism Diagnostic Observation Schedule (ADOS) Toddler Module. Analyses included 4 items that are part of the RRB section of the ADOS Toddler Module (*hand/finger mannerisms, other complex mannerisms, unusual sensory interests, unusually repetitive interests/stereotyped behaviors*); and 5 items in the Communication section that involve unusual and/or repetitive forms of communication (*echolalia, stereotyped speech, frequency of undirected vocalizations, use of other's body to communicate, unusual intonation*).

Results: *Undirected vocalizations* were significantly more common in children under 18 months compared to children over 18 months, $\_^2 = 18.8$, $p < .001$, as were *hand/finger mannerisms*, $\_^2 = 8.8$, $p < .01$. There were no gender differences for any of the behaviors. Nearly all the behaviors analyzed were present in a substantial minority (i.e., between one-third and half) of the participants. Only two behaviors, *unusual sensory interests* and *other complex mannerisms*, were present in less than 25% of children. Although most individual behaviors were relatively common, few children received high total scores across these items, because each behavior they exhibited was relatively infrequent and/or because they tended to exhibit only one or two behaviors.

Conclusions: The present findings are consistent with previous studies of preschool-age children and indicate that so-called

'unusual behaviors' are far from rare in typically developing infants and toddlers. The findings on age differences suggest that some of these behaviors might become less common with age. Although most of the behaviors examined were not uncommon, it was rare for children to exhibit several behaviors and/or to display a given behavior frequently. Thus, although the presence of a single repetitive behavior should not be considered a 'red flag' for ASD, the existence of several or frequent 'unusual' behaviors should be. That being said, the fact that a small subsample of TD children had high total scores suggests that even with a conservative approach to diagnosis, there is still the risk for false positives, particularly if clinicians are swayed by the presence of 'unusual' behaviors. These findings therefore highlight the importance of clinical expertise in the complexities of both typical development and the very early ASD phenotype across several domains of behavior.

118.058 58 A Stimulating Play Situation Designed to Observe Restricted Interests and Repetitive Behaviors in Young Autistic Children. C. Jacques*, S. Mineau, S. Ferguson, D. Cousineau and L. Mottron, *Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*

Background: Restricted interests and repetitive behaviors (RIRBs) in young autistic children have largely been documented through questionnaires and parental reports, a indirect method which limits the scope and usefulness of the results. Although some direct-observation measures of RIRBs have been recently attempted (Baranek & al. 2007; Barrett & al. 2004; Bruckner & Yoder, 2007; Goldman & al. 2008; MacDonald & al, 2007; Ozonoff & al. 2008) their role in standard diagnostic instruments remains limited, with only recent inclusion in the ADOS algorithm and with doubts remain as to their specificity and measurability.

Objectives: a) To develop a stimulation play situation (SPS) which triggers RIRBs in 2 to 5 years old autistic and non-autistic children by exposing children to objects of interest. b) to compare RIRB produced in the ADOS-G and in the proposed SPS.

Methods: The SPS is composed of 35 objects providing specific presses for RIRBs. Children are exposed to items in three different formats: free play, semi-free play and semi-structured play. Frequency and duration of thirty-one behaviours, chosen based on information acquired (questionnaire) from a previous study with 100 autistics experts, are coded: hand flapping, lining-up objects, visual explorations, rotating objects, hopping, searching for the same object, tiptoe-walking, shaking objects, pacing and running, holding objects in hand, talking about the same subject, repeating a sequence of actions, tapping objects, putting fingers or hands in ears, rocking, putting objects in mouth, touching objects, repeating sounds, pressing objects, fingers in mouth, sticking objects on cheeks, hand or finger posturing, smelling objects, placing objects on ears, rubbing hands, fingers in ears, putting part of other's people body in mouth, squinting of eyes, hands on eyes, fingers in nose, put object in movement. Each behavior relies on a reliability superior to 80% between scorers. The frequency, duration, and contextual releasers of these behaviors will be compared in the SPS and in the ADOS-G, (module 1), in a group of 40 typical children and 40 autistics children. The order of passation will be balanced across groups.

Results: Preliminary analyses (6 subjects) in the autism subgroup indicate that the SPS produces more RIRBs (6,17; SD 2,9) than the ADOS-G (2,88; SD 1,3).

Conclusions: These preliminary findings suggest that the SPS is potentially useful to reveal RIRBs in young autistic children. The specificity of these repetitive behaviors to the autism category will be examined through their aggregation with ADOS-G diagnoses.

118.059 59 Catatonia in Autism: A Case Study. H. Bozkurt*, *Istanbul Medical Faculty*

Background: Catatonia is being increasingly reported in individuals with autism. Despite the relative increase in the number of published reports in coexistence of autism and catatonia, still there is a lack of awareness on comorbidity of these two important clinical entities.

Objectives: In this case study we presented clinical features and treatment of a pediatric case with autism and catatonia. Methods: Case: An 11 year-old boy with autism referred to our out-patient unit by his mother due to mutism, slowness in his movements, posturing, toilet refusal because of his immobility and loss of appetite. During his psychiatric evaluation, he was mute, had no interest in surrounding, had no response to questions, showed posturing and waxy flexibility. After clinical evaluation, the diagnosis of autistic disorder was confirmed and he also received additional diagnosis of catatonia. He was given Lorazepam 1 mg / day to test the response. The symptoms of catatonia resolved dramatically within hours; his movements increased and he started talking to his mother and the other people around him. He began to go to toilet and his sleeplessness during this period ameliorated. Therefore, we continued with lorazepam in a dose of 1mg/d. In addition, reviewing his family history proved the presence of depression in his mother. He also had lost his father when he was 8. The bereavement caused him have some crying spells which continued till catatonic symptoms.

Results: The pediatric case with autism represented catatonic symptoms and was treated with Lorazepam successfully. Conclusions: The case reported here shows some differences from previous reported cases in terms of age of onset and showing all characteristics of catatonia as defined in DSM-IV. In addition although it was stated that catatonia in this group is commonly associated with impaired language and social passivity, our case was an active verbal autistic. Moreover it seems that lack of awareness of mental health professionals about life events such as bereavement in autistic individuals have a deep negative influence in their quality of life. Lack of enough support and appropriate treatment for treatable disorders such grief reaction and depression may contribute to life threatening conditions such as catatonia.

118.060 60 Developmental Differences in Movement Planning Among Children with ASD. K. Staples*[1] and G. Reid[2], (1)*University of Regina*, (2)*McGill University*

Background: Children with ASD demonstrate impaired performance of fundamental movement skills early in life, thereby impacting nearly every aspect of subsequent development. These performance differences may be related to factors underlying skill acquisition, such as movement planning.

Objectives: To examine how children with ASD plan and execute fundamental movement skills using a developmental framework.

Methods: Twenty-five children (ages 9 to 12 years) with ASD were individually matched to three groups of typically developing children on developmental variables related to movement behaviour: chronological age (CA), locomotor skill (LOC), and mental age equivalence (MA). Performance on an obstacle course comprised of 8 horizontal barriers (relative to 30, 40, 50, or 60% of each participant's height) was compared to examine how fundamental locomotor skills are planned and executed. Each child moved through the obstacle course four times, twice at each of two speeds (self determined and as fast as possible). Performance was filmed and analyzed at 30 frames per second. Movement planning was inferred from the frequency of acts of hesitation (ACTS) -- an inference in a change from an initial plan. Movement execution was inferred from execution time (EXEC), movement pattern (over/under), and percentage of successful clearance.

Results: Mann-Whitney analyses revealed that when compared to children matched on CA, children with ASD had significantly greater frequency of ACTS at all barriers ($p < .01$) except the one reflecting 60% of their height. When compared to younger children matched on LOC or MA, children with ASD executed significantly more ACTS when all barrier heights were considered together ($p < .01$) and at barrier heights reflecting 40% ($p < .01$) and 50% ($p < .05$) of their height. Based on MANOVA, significant differences in EXEC were found demonstrating that children with ASD moved through the obstacle course significantly slower than children matched on CA ($p < .01$), LOC ($p < .05$), and MA ($p < .01$). Mann-Whitney analyses were also used

to examine the choice of movement pattern and rates of successful clearance. All children tended to move over barriers at 30% and under at 60% and children with ASD chose to move over the barriers at 40 and 50% with similar frequency as the younger children matched on LOC. The children with ASD had similar rates of successful clearance as the younger children matched on LOC or MA.

Conclusions: Despite demonstrating similar movement patterns as younger children matched on LOC or MA, the children with ASD took significantly more time to plan and execute their movements. Collectively, these results suggest children with ASD have difficulty planning their movements beyond what would be expected for their CA, LOC, or MA. To explore trajectories of development, the obstacle course performance of 16 children with ASD and 15 children initially matched on LOC was followed for 3 consecutive years and these results will be discussed.

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118.061 61 Dynamical Systems Analysis of Hand Movement Organization in Autism: Association of Movement Organization with Problem-Solving and Symptom Severity. I. M. Eigsti*, J. A. Dixon, A. B. de Marchena and M. Helt, *University of Connecticut*

Background: Since Asperger's first descriptions, clinicians have reported striking differences in the conversational gestures produced by individuals with autism spectrum disorders (ASD), noting that gestures are "clumsy" and "inappropriate." Currently, gestural quantity, quality, and integration with speech contribute to 1/3 of diagnostic items on the ADOS. The limited empirical literature focuses primarily on declarative (attention-drawing) pointing gestures in preschoolers. Furthermore, work from our lab and elsewhere indicates that individuals with ASD gesture as frequently as their peers. Objectives: Dynamical systems theory indicates that behaviors at multiple timescales (e.g., from milliseconds to minutes) can reliably drive behaviors at other timescales. For example, new cognitive structures emerge as a consequence of multi-scale behaviors. By examining hand movements as participants solve a computer-based "gears" puzzle, we assess (1) the contribution of multi-scale behaviors to solving the puzzles, and (2) group differences in behavior structures. If individuals with ASD show distinctive patterns of organization in their hand movements, this may provide some insight both into cognitive differences and into clinicians' observations of gesture impairments. Methods: Participants were 15 high-functioning adolescents with ASD and 14 TD adolescents matched for age, gender, IQ, and receptive vocabulary (p's > .18). Participants completed a computer-based gears task and were videotaped explaining their reasoning after each trial. The ASD group was as accurate for smaller gear systems, but less accurate for 7-gear systems, p = .006. Hand movements during explanation were tracked and examined to assess relative structure (e.g., organization), and the prediction of structure at one timepoint based on the previous timepoints. Specifically, two-dimensional X,Y hand positions of participants as they explained and gestured about their gear puzzle solutions were coded. X,Y position data were subjected to detrended fluctuation analysis (DFA), which can measure activity in a nested multiscale structure. After dividing the integrated time series into bins, a least-squares line was fitted for each bin. The root mean square error (RMSE) of the time series within the bin is the quantity of interest; this measures the activity of the system at a particular scale (i.e., bin size). This procedure is repeated and RMSE is calculated for multiple bin sizes. The scaling relation between RMSE and bin size typically follows a power-law, indexed by the power-law exponent, H. Results: The structure of hand movements over successive trials of the task, in DFA, showed a significant group by time interaction, p = .03. Unlike controls, the ASD group showed no increase in structure over time. For the ASD group, DFA value across trials was also significantly associated with symptom severity (ADOS repetitive behaviors), r =.63, p = .02. DFA was uncorrelated with age and IQ, p's > .35,

suggesting it was not simply indexing general abilities. Conclusions: Low-level organization of hand movements was related to gears task performance (e.g., the timing of new concept learning; Dixon & Bangert, 2005). These analyses suggest (1) meaningful differences between ASD and control groups in coordinating motor movements, and (2) associations between this coordination and autistic symptomatology.

118.062 62 Longitudinal Study of Repetitive Behavior and Volumes of the Caudate and Thalamus in Children with Autism Spectrum Disorder Between 3 and 9 Years of Age. M. W. Bryan*, A. M. Estes and S. Dager, *University of Washington*

Background: Abnormalities of the caudate and thalami may contribute to symptom expression in autism spectrum disorders (ASD). Cross-sectional studies of older children and adults with ASD report an association between volumetric alterations of these structures and higher levels of repetitive behavior (RB). We are not aware of previous studies investigating developmental changes in young children in terms of caudate and thalami volumes and level of RB.

Objectives: We investigated changes in RB from 3 to 9 years of age in children with ASD. Caudate and thalami volumes were compared in children with ASD, developmental delay (DD) and typical development (TD) at 3, 6 and 9 years. Longitudinal relationships between RB and volumetric measures were examined from 3 to 9 years of age among children with ASD.

Methods: Children were assessed at 3, 6, and 9 years for RB with subscales from the ADI, ADOS and ABC (ASD n=75). A subgroup was also assessed with 3-D MRI (ASD n=45 at age 3) with additional MRI data for DD (n=14 at age 3) and TD groups (n=25 at age 3). Structures assessed include the caudate and thalami as well as total cerebral volume (TCV).

Results: Severity of RB increased between 3 and 9 years of age among children with ASD. This trend persisted after adjusting for differences in cognitive ability. Mean caudate volumes were larger in the ASD group at ages 3, 6 and 9 compared to the TD group. Differences were not significant after scaling for TCV. Thalami volumes did not differ between the ASD and TD groups. The ASD group had larger thalami and caudate compared to the DD group at age 3, 6, and 9. After scaling for TCV, these differences were significant at age 3 for the thalami and age 3 and 6 for the caudate. We will present results on the association between RB and volumetric measures at age 3, 6, and 9.

Conclusions: RB level increased in children with ASD between the ages of 3 and 9. Volumetric measures did not differ between the ASD and TD group after scaling for TCV. Thalami and caudate volumes were decreased in the DD group. Developmental changes in the thalami and caudate will be presented as will potential relations between RB and thalami and caudate volumes.

118.063 63 Profile and Specificity of Motor Deficits in Children with Autism Spectrum Disorder. L. J. Koenig*[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: An increasing number of research studies have pointed to motor control as an area of difficulty in children with autism spectrum disorder (ASD) (e.g., Jansiewicz et al., 2006; Fuentes, Mostofsky, & Bastian, 2009). However, critical questions remain regarding the profile and specificity of motor deficits in ASD.

Objectives: To better characterize the profile of motor difficulties associated with autism using the Movement Assessment Battery for Children, 2nd Edition (Movement ABC-2, Henderson & Sugden, 2007), which assesses three different sub-categories of motor functioning: balance, manual dexterity, and aiming/catching; and, to examine the specificity of motor findings in autism by comparing performance of children with ASD with that of typically developing (TD) children as well as that of another control group with developmental motor difficulties – children with Attention Deficit/Hyperactivity Disorder (ADHD).

Methods: Participants included 52 children, ages 8-12 years: 16 with ASD (4 female), 18 with ADHD (4 female), and 19 TD children (5

female). Groups were matched on age, gender, IQ, and race. ANOVAs were used to examine an effect of diagnosis on total and subtest scores on the Movement ABC-2. The manual dexterity component requires tasks to be timed by the examiner to determine how rapidly the movements can be performed. As the ASD group presented with significantly lower Processing Speed Index (PSI) scores on the Wechsler Intelligence Scale for Children-4th ed. (WISC-IV, Wechsler, 2003) than ADHD and control subjects, analyses for this component were co-varied for PSI.
Results: Three-group ANOVA revealed a significant effect of diagnosis for the components of balance ($F = 3.886$, $p = .027$) and manual dexterity ($F = 5.888$, $p = .005$), but not for aiming/catching. Follow-up two group analyses revealed the ASD group showed poorer balance compared to TD children ($F = 5.982$, $p = .02$) and a trend towards poorer balance compared to ADHD children ($F = 3.919$, $p = .057$), with no significant differences between the ADHD and TD groups. For manual dexterity, the ASD group showed substantially significant poorer performance compared to TD children ($F = 16.059$, $p < .001$), but not those with ADHD; and, there was a trend towards ADHD children showing significantly poorer performance compared to TD children ($F = 3.725$, $p = .063$).
Conclusions: Children with ASD have significant difficulty with both manual dexterity and balance compared to TD children. Comparisons to children with ADHD suggest that impairments in balance, while not as substantial as those in manual dexterity, appear to be more specific to ASD.

118.064 64 Restricted and Repetitive Behaviors in Young Children with ASD: Concurrent Correlates and Predictors of Change Over a One-Year Period. C. E. Ray-Subramanian*[1], S. Ellis Weismer[2] and N. Huai[1], (1)*Waisman Center, University of Wisconsin-Madison*, (2)*University of Wisconsin-Madison*

Background: Restricted and repetitive behaviors (RRBs) are a core feature of autism according to diagnostic criteria. Research has shown that RRBs–specifically, those with a repetitive sensorimotor component as opposed to those characterized by an insistence on sameness–are prevalent among children on the autism spectrum as young as age two and are more common among these children than same-age peers with typical development and those with developmental disabilities who are not on the autism spectrum (Richler, Bishop, Kleinke, & Lord, 2007). The degree of RRBs present at age two has also been shown to predict expressive language level at age four (Paul, Chawarska, Cicchetti, & Volkmar, 2008). However, much of the existing research on RRBs in young children has been based on parent-reported behavior (e.g., Bishop, Richler, & Lord, 2006; Richler et al., 2007) and has not examined change in RRBs over time during early childhood. Examining clinician-observed RRBs and changes in RRBs during early childhood can further enhance our understanding of RRBs in young children on the autism spectrum. Objectives: The objectives of this study were to examine factors associated with (a) clinician-observed RRBs on the ADOS at ages two and three, and (b) changes in the degree of clinician-observed RRBs on the ADOS over this one-year period. Methods: Participants were 102 children (mean age at Visit 1 = 31 months; mean age at Visit 2 = 44 months) on the autism spectrum who are 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. Measures used in the current study (ADOS; Mullen; Vineland-II; and Preschool Language Scale-4th Edition) were administered at Visit 1 and Visit 2. Results: At Visit 1, the degree of RRBs observed was negatively correlated with receptive language skills, as measured by parent report on the Vineland-II ($r = -.26$, $p<.05$) and performance on the PLS ($r = -.39$, $p<.01$). RRBs were also negatively correlated with performance on the Mullen Visual Reception scale ($r = -.34$, $p<.01$). At Visit 2, observed RRBs continued to be negatively correlated with receptive language skills on the Vineland-II ($r = -.33$, $p<.01$) and PLS ($r = -.36$, $p<.01$), but were not significantly associated with performance on the Mullen Visual Reception scale. The degree of RRBs observed at Visit 2 was also negatively correlated with expressive language skills, as

measured by the PLS (r = -.25, p<.05). A regression analysis of standardized residual change scores revealed that growth in receptive language skills over a one-year period, as measured by the PLS, significantly predicted reduction in the degree of observed RRBs, when controlling for changes in expressive language and cognitive skills. Conclusions: RRBs among children on the autism spectrum were found to be negatively associated with receptive language skills at ages two and three. An increase in receptive language skills over this one-year period predicted a decline in observed RRBs. Associations between RRBs and expressive language and cognitive skills were less clear at these young ages.

118.065 65 Special Skills in Autism Spectrum Disorders Are Associated with Unique Phenotypic Characteristics. G. L. Wallace*[1], N. A. Dankner[1] and S. J. Webb[2], (1)*National Institute of Mental Health, National Institutes of Health*, (2)*University of Washington*

Background: Autism spectrum disorders (ASD), more so than other neurodevelopmental disorders, are associated with 'islets of ability' ranging from relative strengths to so-called 'savant' skills (Heaton & Wallace, 2004). In spite of this well-established connection, very little is known about how individuals with ASD may differ from one another based on the presence of special skills, which may constitute an informative phenotype within ASD.

Objectives: Examine basic characteristics (i.e., age, sex ratio, IQ, autism symptomatology) associated with elevated special skills in a large sample of individuals with ASD (n>500).

Methods: Using Autism Diagnostic Interview-Revised parent ratings of special skills from several sites within the Collaborative Programs of Excellence in Autism and Studies to Advance Autism Research and Treatment, we categorized participants into two groups: individuals without a reported special skill (n=245) and individuals with a skill above both their general ability level and population norms, regardless of its functionality (n=274). We assessed whether the presence of special skills is associated with differences in terms of age, sex ratio, IQ, and autism symptomatology. For the sake of comparability across sites and instruments, we restricted our sample to those individuals with available Wechsler IQ data (range=39-150) and participants 60 months and older (range=60-351 months).

Results: Individuals with ASD rated as possessing special skills (Ns: memory=183, reading=102, visual-spatial=75, computational=58, drawing=49, music=45; multiple skills=138) were older (M=140.02+/-53.37 vs. 119.53+/-49.41 months), had a higher male to female ratio (244:30 vs. 184:61), and had a higher mean IQ (M=91.79+/-26.08 vs. 77.52+/-25.10) than those without special skills (*p*s<.001). Importantly, males and females in this sample did not differ in terms of age and IQ (*p*s>.3), ruling out these possibly confounding factors in the observed sex ratio difference. Repetitive behavior symptoms, unlike social and communication symptoms, were elevated in the special skills group (*p*=.004) even though these participants on average had higher IQs and were older. Therefore, controlling for age and IQ only served to enhance the group difference in repetitive behavior symptoms (*p*<.001). Preliminary item analysis within the repetitive behavior domain revealed significantly greater endorsement of circumscribed interests for the special skills group (*p*<.001).

Conclusions: The presence of special skills in the context of ASD is associated with unique phenotypic characteristics. We find that within a sample of children, adolescents and young adults with ASD, individuals rated as possessing special skills were on average older, and consistent with Howlin, Goode, Hutton, and Rutter (2009) had higher mean IQs and a greater male to female ratio. Extending previously documented subclinical associations (Vital, Ronald, Wallace, & Happé, 2009), repetitive behavior was the only symptom cluster to be more elevated among individuals with special skills. Howlin et al. (2009) did not find differences in Autism Diagnostic Interview (ADI) repetitive behavior ratings in their savant group, but the ADI version used in their study did not include assessment of circumscribed

interests, which we have shown to receive greater endorsement in the special skills group.

118.066 66 Specificity of Handwriting Impairments in Children with Autism Spectrum Disorder. M. Adler*[1], L. R. Dowell[1], A. Apostu[1] and S. H. Mostofsky[2], (1)*Kennedy Krieger Institute*, (2)*Kennedy Krieger Institute, Johns Hopkins University School of Medicine*

Background: Handwriting impairments have long been recognized as being common in autism. Numerous studies have revealed difficulties with motor function in children with autism spectrum disorder (ASD) (e.g., Manjiviona et al., 1995; Ghaziuddin et al., 1998; Noterdaeme et al., 2002; Jansiewicz et al., 2006; Mostofsky et al., 2006); however, none included a detailed analysis of handwriting until very recently when we reported that, compared to typically developing (TD) children, children with ASD showed significant difficulty with handwriting (Fuentes et al., 2009). Our findings revealed that children with ASD had particular difficulty with letter formation, but not in their ability to correctly size, align, or space their letters. Whether this pattern of findings is specific to ASD remains unclear. In separate studies, handwriting impairments have been observed in children with Attention Deficit Hyperactivity Disorder (ADHD); these children show particular difficulty with writing legibly and with correctly aligning and spacing letters (Tucha & Lange, 2001). There have been no studies, however, directly comparing handwriting in children with ASD and ADHD.

Objectives: To examine the specificity of handwriting impairments in children with ASD by comparing their performance to children with ADHD as well as TD children.

Methods: Nine children with ASD (mean age 10.35; 3 females), 7 children with ADHD (mean age 10.00; 3 females), and 10 TD children (mean age 10.89; 4 females) completed the Minnesota Handwriting Assessment (MHA) (Reisman et al., 1999); the groups were matched on age, gender, handedness and IQ. Subjects were instructed to use their best handwriting to copy the following words exactly on the provided test sheet: "The brown jumped lazy fox quick dogs over". Each letter was scored individually according to the Minnesota Handwriting Assessment scoring protocol on five categories: Legibility, Form, Alignment, Size and Spacing.

Results: A 3-way MANOVA revealed a significant effect of diagnosis for form ($p=0.02$), alignment ($p=0.05$) and total ($p=0.03$) scores. Further 2-way analyses revealed that children with ASD demonstrated significantly worse form ($F=7.36$, $p=0.02$) and total score ($F=7.98$, $p=0.01$) than TD children. In comparison, children with ADHD demonstrated significant handwriting impairments in legibility ($F=6.47$, $p=0.02$), form ($F=7.81$, $p=0.01$) and alignment ($F=10.01$, $p=0.01$). Comparisons of ASD and ADHD children revealed no significant differences on legibility, form, alignment, size or spacing.

Conclusions: Children with ASD demonstrated an overall impairment in handwriting, specifically seen in the quality of letter formation. In contrast, children with ADHD showed a broader range of impairments, which included difficulties with legibility, form and alignment. The findings suggest that for children with ASD, difficulty with handwriting may be associated with abnormalities in the internal representation of how the letters are formed and/or how those representations are executed. In contrast, handwriting difficulty in children with ADHD appears to be associated with a broader range of difficulties, in particular problems with motor control necessary for proper alignment and legibility.

118.067 67 Visuomotor Skill, Simple Reaction Time and Perceptual Processing Speed in Autism. A. A. Meilleur*[1], E. B. Barbeau[1], L. Mottron[1] and T. A. Zeffiro[2], (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*Neural Systems Group, Massachussetts General Hospital*

Background: Although atypicalities in visuomotor coordination, often generically labelled as "clumsiness", are commonly observed to varying degrees in autistics of all ages, their precise mechanism is poorly understood. The failure to achieve desired spatial and temporal accuracy in a relatively simple task like visually-guided reaching

could arise from a range of sources, including visual analysis of target or hand position, hand/body/target coordinate transformation determination, or movement execution. In addition, while it has been suggested that the Asperger subgroup is particularly likely to exhibit atypical motor behavior, the empirical evidence supporting this assertion has been somewhat inconsistent.

Objectives: To localize the potential sources of atypical visuomotor coordination, we undertook a behavioral analysis of the processes responsible for visually-guided reaching by investigating perceptual analysis, peg moving and simple response generation skills in autistic and Asperger participants.

Methods: We measured perceptual inspection time, peg moving skill and simple manual reaction time in 24 autistic, 22 Asperger and 30 typical participants matched on Wechsler IQ (FSIQ mean=103.20), matrix reasoning skill (Raven Progressive Matrices percentile score mean=69.86,) and age (mean=21.88, range: 14-37). Clinical participants were diagnosed using DSM-IV, ADI-R and ADOS-G standards and none of the subjects were taking medication. Tasks included: (1) Inspection Time (IT), in which two vertical lines of different length were presented for durations of 10-200 ms and then immediately masked by two irregular lines, participants indicated the longer of the two lines, and stimulus duration was adaptively varied in a staircase psychophysical procedure, (2) Purdue Pegboard (PP), which measures finger dexterity and hand-eye coordination while putting small pegs into a pegboard using left, right, or both hands, (3) Annett Peg Moving (APM), which measures the speed at which larger pegs can be moved from one set of holes to another, and (4) visually-triggered simple reaction time (SRT). Manual preference was controlled by classifying responses as dominant (DH) or nondominant hand (NDH).

Results: The Asperger and autistic groups did not differ from typicals on the IT task ($p>0.05$) or the visually-triggered SRT task ($p>0.05$). The Asperger, but not the autistic, group was slower on the PP task (DH: $p=0.007$; NDH: $p=0.023$), but not in the bimanual conditions. On the Annett test, the Asperger and autistic groups had longer completion times than controls (Asperger - DH: $p=0.015$; NDH: $p=0.023$ and autistic - DH: $p=0.038$; NDH: 0.047). Secondary analyses did not identify differences between the Asperger and autistic groups on any of the motor tasks.

Conclusions: We found that both autistic and Asperger participants had atypical performance on two different visuomotor tasks. These differences could not be explained with reference to impairments in either perceptual processing speed or response execution assessed with a simple task. This pattern of findings suggests that the differences observed in the visually-guided reaching tasks cannot be explained by slower sensory information processing or impaired motor execution, but may rather reflect difficulties in integrating dynamically changing sensory guidance information with evolving action plans.

118.068 68 Analysis of Unsupported Gait in Toddlers with Autism.

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Background: A number of studies have suggested the importance of motor development in autism. Motor development has been considered a possible biomarker of autism since it does not depend on either social or linguistic development.

Objectives: Based on the hypothesis that suggests movement as an early indicator of Autistic Disorders (AD), the purpose was to analyze the first unsupported gait at the age when child reach the walking autonomy. Using retrospective video analysis we investigated the first unsupported gait in toddlers with Autism. Our study aims to verify, through observational methods, the possibility of distinguishing toddlers with ASD from toddlers with typical development or with developmental delay by movement.

Methods: Fifty-five toddlers, belonging to three groups were recruited: toddlers with autism (AD, n=20, mean age 14.2mo, sd 1.4mo) and as comparison groups: typically developing toddlers (TD, n=20, mean age

12.9mo, sd 1.1mo) and toddlers with non-autistic developmental delays of mixed aetiology (DD, n=15, mean age 13.1mo, sd 0.8mo).The Walking Observation Scale (WOS) and the Eshkol-Wachman Movement Analysis (EWMN) were used to gather data on the first unsupported gait. The WOS includes 11 items that analyze gait through three axes: foot movements; arm movements; global movements while the EWMN analyses static and dynamical symmetry during gait.

Results: Data shows significant differences in gait patterns among the group of toddlers with autism as opposed to those with typical development or with developmental delay. ANOVA shows significant differences ($p<.01$) between AD group and the two control groups for the total scores of the WOS (the average score among all the 11 items of the WOS). Tukey HSD Post-Hoc indicates that AD group shows higher WOS scores than DD (M difference = 7.62, SE = 2.84, $p\leq.001$) and TD (M difference = 14.32, SE = 2.23, $p\leq.001$); differences were also found between DD and TD (M difference = 9.21, SE = 2.41, $p\leq.001$). Significant differences ($p<.01$) were also found between AD group and the two control groups for the EWMN. Tukey HSD Post-Hoc indicates that AD toddlers show more asymmetry than DD (M difference = 27.05, SE = 3.34, $p\leq.001$) and TD (M difference = 25.75, SE = 3.09, $p\leq.001$); no differences was found between DD and TD (M difference = 1.75, SE = 3.34, ns).

Conclusions: In this study we have identified significant differences in gait patterns among the group of toddlers with autism as opposed to the matching controls. The specificity of disturbances in motor sequence we have identified in autism (more postural asymmetry, more rigidity, also defined upper-body-type "Parkinsonian") is consistent with previous findings that implicated cerebellar involvement in the motor symptoms of autism.

118.069 69 Direct Quantitative Measurement of Motor Coordination in Sibling Pairs Discordant for Autism: New Evidence for Motor Impairment as a Core Component of Autistic Syndromes. C. L. Hilton*, Y. Zhang, M. White, A. Babb and J. N. Constantino, *Washington University School of Medicine*

Background: Studies of unaffected family members of children with Autism Spectrum Disorders (ASD) have revealed an aggregation of sub clinical autistic social impairment among these individuals suggesting the possibility that such impairment constitutes an autism endophenotype. Since previous studies have found children with autism to have a high incidence of motor coordination abnormalities, we conducted an initial exploration of how such abnormalities are distributed in ASD-affected families. Objectives: This study examined the distribution of motor impairment in siblings concordant and discordant for autism. Methods: Sibling pairs discordant (N = 33) and concordant (N = 50) for ASD were assessed using the Bruininks Oseretsky Test of Motor Performance, 2nd Edition (BOT-2), a standardized, comprehensive, direct observational measure of motor coordination. In addition to a total motor composite score, the BOT-2 generates four gender-specific motor area composite scores, scale scores, standard scores and percentile ranks for fine manual control, manual coordination, body coordination, and strength and agility, and is capable of detecting subtle differences between clinical and nonclinical subjects across a wide range of motor abilities.

Results: As predicted, mean scores for motor skills among ASD-affected children were significantly impaired across all domains (effect size = 1.5 to 1.8), however the scores for unaffected siblings in this primarily simplex autism sample were within the normal range. ASD-affected children with phrase speech had significantly better motor skills than those who were non-verbal ($t = 3.22$; $df = 60$; $p = .002$). Total motor coordination scores of at least 1 SD below the general population mean were seen in 84% of the affected group and scores of at least 2 SDs were observed in 46%. Of particular note is that among the ASD-affected children, motor impairment scores were continuously (not dichotomously) distributed, and moderately correlated with degree of social impairment for the affected children ($N = 79$; $r = .366$; $p < .05$).

Conclusions: The current observations—that motor coordination exhibits a pathologically-shifted, continuous distribution in ASD, that the degree of motor impairment is correlated with the degree of social impairment in ASD, but absent among unaffected siblings (in simplex families)—suggest that motor coordination abnormalities, as measured by the BOT-2 constitute core features of the autistic phenotype. Further studies of quantitative impairments of motor coordination among unaffected children in multiplex families (for which the sample size in this study was too small to draw conclusions) are warranted to explore possible endophenotypic characteristics of motor impairments in ASD-affected families. Moreover, pursuit of the genetic and neurobiologic underpinnings of motor coordination abnormalities in ASD may provide critical clues to the pathogenesis of autistic syndromes.

118.070 70 Evidence for Specificity of Anomalous Motor Learning in Autism. S. H. Mostofsky*[1], J. Izawa[2], S. Penky[2], M. Marko[2], L. R. Dowell[3] and R. Shadmehr[2], (1)*Kennedy Krieger Institute, Johns Hopkins University School of Medicine*, (2)*Johns Hopkins University*, (3)*Kennedy Krieger Institute*

Background: Differences in procedural (skill-based) learning appears highly relevant to autism, with several investigators positing that impaired development of social and communicative skills may be linked to anomalous formation of action models beginning early in infancy. Consistent with this idea, there is increasing evidence that autism is associated with anomalous motor development, including impaired imitation and execution of goal-directed actions ("dyspraxia"). One of the crucial steps in motor learning is for the brain to form internal models: a mapping between motor commands and the expected sensory feedback. We recently reported (Haswell et al., 2009) that children with autism spectrum disorder (ASD) show an anomalous pattern of motor learning as compared to typically developing (TD) children, with excessive reliance on proprioceptive, rather than visual, feedback; furthermore, for children with ASD, this bias towards proprioceptive-based formation of action models was strongly correlated with motor, as well as social, skill impairment. Critical questions remain, including whether this anomalous pattern of motor learning is specific to ASD.

Objectives: To explore the specificity of anomalous motor learning in ASD, by comparing formation and generalization of action models in children with ASD to that of another population with developmental motor impairments – children with Attention Deficit/Hyperactivity Disorder (ADHD).

Methods: We quantified the representation of internal models by measuring patterns of generalization in age, gender, and IQ-matched groups of 14 children with ASD (age 10.5±1.7), 10 with ADHD (age 11.0±1.7 years), and 13 TD children (age 10.4±1.8). 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 ("Target 1"). In this task, the brain builds an association between self-generated motor commands and the sensory consequences (visual and proprioceptive). The strength of each association can be inferred by how the brain generalizes the errors from the trained movements to novel movements. As such, we quantified generalization in the right workspace in the intrinsic (proprioceptive) coordinates of the arm (Target 3, identical joint rotations as compared to Target 1) and in the extrinsic (visual) coordinates of the task (Target 2, identical hand motion as compared to Target 1).

Results: Superficially, learning appeared similar across the groups, with 3-group ANOVA revealing no effect of diagnosis on adaption to the force when reaching to Target 1. In contrast, 3-group ANOVA revealed a significant effect of diagnosis on generalization pattern ($F(2,34)=8.89$, $p=0.0008$) with follow-up two-group contrasts revealing that children with ASD showed significantly greater generalization in intrinsic versus extrinsic coordinates compared with ADHD ($F(1,22)=9.99$, $p=0.0045$) as well as TD ($F(1,25)=55.7$, $p<0.0001$ – as reported in Haswell et al., 2009), but that the pattern in TD and ADHD children did not significantly differ ($F(1,21)=0.19$, $p=0.67$).

Conclusions: Children with ASD show an anomalous pattern of generalization compared to children with ADHD, as well as TD children. The findings provide evidence suggesting that the pattern of excessive reliance on proprioceptive, rather than visual, feedback during motor learning is specific to autism.

118.071 71 Individuals with Autism Demonstrate Circumscribed Attention During Passing Viewing of Competing Social and Non-Social Stimuli. G. Dichter*[1], A. Sabatino[2], N. Sasson[3] and J. W. Bodfish[4], (1)*University of North Carolina*, (2)*University of North Carolina at Chapel Hill*, (3)*University of Texas at Dallas*, (4)*University of North Carolina - Chapel Hill*

Background: Individuals with Autism Spectrum Disorders (ASD) are characterized by abnormalities in the processing of social information that contribute to impairments in social functioning. While reductions in social attention have often been conceptualized as resulting from decreased salience of social information, they may also emerge as the result of competing salience of other non-social features in the environment. Previous research has demonstrated that children with autism disproportionately explore and perseverate attention on object types commonly associated with circumscribed interests (Sasson, et al. 2008).

Objectives: We developed a passive viewing task to measure whether the presence of such object types would differentially affect attention to social stimuli in adults with and without ASD.

Methods: Participants with and without ASD completed a paired preference task. Task stimuli included 40 image pairs of social (i.e., neutral Nimstim faces) and non-social images (i.e., "High Autism Interest" (HAI) objects derived from Sasson et al., 2008. Gaze behavior was quantified using eye-tracking technology. To date, we have assessed 15 typically developing individuals [mean age in years= 24.10 ± 3.58] and 4 individuals with Autism [mean age in years= 24.69 ± 12.18].

Results: Preliminary analyses on onscreen fixation time indicated a significant Group by Stimulus type (i.e. object or face) interaction ($F(1, 17) = 6.01$, $p = .025$, $\_2 = .26$). While the control group spent 52% of all onscreen fixation time on faces and just 37% on objects, the ASD group displayed the opposite pattern, spending 49% on objects and only 37% on faces. One way ANOVA results on the 8 categories of objects indicated that the two groups differ significantly on trains ($F(1, 17) = 6.07$, $p = .025$) and planes ($F(1, 17) = 9.74$, $p = .006$), with the ASD group spending nearly 30% more of their fixation time on these objects compared to the control group. Data collection is ongoing, and with the larger ASD sample expected by next spring, we plan to pursue more detailed eye tracking analyses, as well as examine whether attention patterns are associated with repetitive behaviors and restricted interests as measured by the Interview for Repetitive Behaviors and Repetitive Behavior Scale.

Conclusions: Individuals with ASD appear to attend atypically to competing social and non-social information. These processing patterns may reflect a tendency for individuals with ASD to perseverate on objects of high interest rather than concurrently presented social stimuli. Assessment of visual attention may thus be used to quantify discrete aspects of the repetitive behavior phenotype in autism, including the modulating effect of circumscribed interests on social attention.

118.072 72 Insistence On Sameness in Asperger Syndrome Is Related to Cortisol. M. Brosnan*[1], J. Turner-Cobb[1], Z. Munro-Naan[1] and D. Jessop[2], (1)*University of Bath*, (2)*University of Bristol*

Background: Asperger Syndrome (AS) is characterized in part by a dysfunctional ability to adapt to novel experiences and environments, clinically referred to as a 'need for sameness' or 'resistance to change'. The hypothalamic-pituitary-adrenal (HPA) axis modulates our ability to react emotionally and physiologically to change which culminates in the release of cortisol. Whilst individuals with AS have a preserved diurnal decline in cortisol (a decline from morning to evening), the Cortisol Awakening Response (CAR: a two-fold increase in cortisol release in the first 30 minutes after awakening) is

significantly attenuated. The ADI-R is widely regarded as the most comprehensive assessment for AS and has been found to consist of two factors: 'social and communication behaviours' and 'restricted and repetitive behaviours (RRBs)'. Further factor analysis within RRBs has identified two separate RRB factors: Insistence-on-Sameness and repetitive-sensory-motor-actions. Unlike repetitive-sensory-motor-actions, behaviours associated with Insistence-on-Sameness have been found not to be sensitive to developmental level and may be specific to AS.

Objectives: To identify if diurnal cortisol variations, the CAR or diurnal decline, related to RRBs in AS. We specifically examined the relationship between the CAR and the Insistence-on-Sameness factor of the ADI-R as these are the two aspects of HPA functioning and RRBs that may be specific to AS.

Methods: Data from this sample of 24 males (ages ranged from 9 to 16, mean = 12.3 years, sd=2 years) with a clinical diagnosis of AS has previously identified an attenuated CAR in this AS group. This data was combined with an analysis of the RRB subscale of the ADI-R. The researcher was blind to the cortisol level data when rating for current (during the period of saliva sampling) RRB behaviour using the 4 point scale of the ADI-R (current behaviour). To index levels of perceived stress during the period of sampling, participants completed the self-report, 20-item, Daily Hassles Scale.

Results: There was a significant correlation between the CAR and Insistence-on-Sameness (r_{24}=-0.44, p=0.016). The correlation between the CAR and Insistence-on-Sameness remained significant when it was rerun as a partial correlation controlling for both age and hassles (r_{20}=-0.43, p=0.048). The CAR did not correlate with the RRB total (r_{24}=-0.18, ns) nor repetitive-sensory-motor-actions (r_{24}=0.05, ns), although Insistence-on-Sameness did significantly correlate with repetitive-sensory-motor-actions (r_{24}=0.70, p<0.001). The CAR also did not significantly correlate with age nor hassles. Diurnal decline did not significantly correlate with either Insistence-on-Sameness or repetitive-sensory-motor-actions. The mean for Insistence-on-Sameness was significantly higher than the mean for repetitive-sensory-motor-actions (1.99(0.53) vs.1.08(0.50), repeated measures t-test t_{23}=10.93, p<0.001).

Conclusions: Increased severity of Insistence-on-Sameness behaviour (assessed through the ADI-R) was associated with decreased HPA axis activation (assessed through the CAR). This is particularly salient as Insistence-on-Sameness is the factor within restricted and repetitive patterns of behaviour argued to be specific to AS and an impaired CAR is the specific aspect of the diurnal HPA axis pattern impaired in AS. This is pertinent as Insistence-on-Sameness was identified as significantly more severe than repetitive-sensory-motor-actions, highlighting the need to research Insistence-on-Sameness specifically within AS.

118.073 73 Psychomotor Profiles in Autism : a Psychomotor Observation Scale. K. Yvonnet*, C. Chatel, M. Viellard, D. DA Fonseca and F. Poinso, *Centre de Ressources Autisme*

Background: The literature brings heterogeneous elements on the psychomotor development of the autistic children without a real consensus about the psychomotor activity. Most of time the autistic children are assessed with development or behavior scales or functional motor development scales, which do not really let appear the psychomotor domains.

Objectives: First, the objective of this study is to validate a specific scale based on psychomotor concepts, which is created from clinical observations in autistic children. Secondly, the purpose will be to show psychomotor profiles and to analyze their specificities in these children. What are the psychomotor disorders implied in the social interactions impairments in autism?

Methods:

Patients were recruited in « Centre de Ressources Autisme » of Child Psychiatric Unit of Hospital Ste Marguerite in Marseille (France). 19 children with autism (age mean: 4 years two month old) w ere recruited on the

criteria of the DSM-IV-TR and the ADI (Autism Diagnostic Interview).

First, every child is tested with the functional motor development scale of the young children (Vaivre-Douret, 1997) in order to obtain a motor development level. Secondly, children are assessed with a specific scale of the psychomotor skills (a Pervasive Development Disorders Psychomotor Observation Scale: PDDPOS) which is constituted by 4 domains: motor domain, bodily expressiveness, sensory domain and bodily commitment.

Results:

The results on the functional motor development scale show a global motor delay. The data analysis on the PDDPOS reveals psychomotor specificities. The analysis of different domains shows a significant difference between the motor domain and the bodily expressiveness ($p<0.05$), and a significant difference between the bodily expressiveness and the bodily commitment ($p<0.05$). The performances in the others domains are relatively homogeneous.

Conclusions: Preliminary findings reveal that all the assessed children have a motor delay. The PDDPOS shows psychomotor profiles. Indeed, the bodily expressiveness is better protected than the motor domain or the bodily commitment. In spite of social interactions and communicative impairments, the children keep skills in expression by means of the body.

We'll discuss these results according to the perceptive and motor theories. The PDDPOS allows to obtain a more precise analysis of the psychomotor profiles in the autistic children. It brings to light the determinant role which plays the psychomotor examiner in evaluation and in therapy.

118.074 74 Repetitive and Stereotyped Behaviors From Age 2 to Age 4: A Look at the Development of High- and Low-Level Behaviors. K. Knoch*[1], L. E. Herlihy[1], E. Troyb[1], T. Dumont-Mathieu[1], J. Green[1], M. L. Barton[1], D. A. Fein[1] and H. Boorstein[2], (1)*University of Connecticut*, (2)*Children's Mercy Hospital*

Background:

Restricted, repetitive, and stereotyped patterns of behaviors, interests, or activities are core features in autism spectrum disorder (ASD). These patterns of behavior are wide ranging and include motor stereotypies, circumscribed interests, compulsions, and insistence on sameness. Previous literature has subdivided repetitive and stereotyped behaviors (RSB) into two categories: low- and high-level behaviors. Lower-level behaviors are characterized by repetition of movement, such as stereotyped movements, repetitive use of objects, and dyskinesias. Furthermore, this pattern of behavior is hypothesized to be associated with lower developmental levels. Higher-level behaviors are thought to require higher cognitive abilities, and include insistence on sameness, adherence to a routine, and circumscribed interests. There is conflicting evidence regarding the relationship between early RSB and later developmental outcomes.

Objectives:

To examine developmental differences associated with high- and low- level repetitive and stereotyped behaviors in young children diagnosed with an ASD.

Methods:

Participants were evaluated after screening positive on the Modified Checklist for Autism (M-CHAT), a developmental screener designed to identify children at risk for ASD between the ages of 16 and 30 months and receiving a developmental/diagnostic evaluation. Participants then received a follow-up evaluation between the ages of 41 and 69 months. Follow-up data from the ADI-R was used to categorize children as having high- and low-level RSB. Children in the low-level group displayed repetitive motor movements (hand and finger mannerisms or stereotyped body movements) in the absence of any high-level behaviors. Those in the high-level group displayed one or more of the following: unusual preoccupations, circumscribed interests, compulsions or rituals, or difficulty with changes in their routine or environment, without any low-level RSB. Measures of

cognitive functioning and social-communicative development were examined between the two groups at age 2.

Results:

Preliminary analyses yielded significant differences in cognitive functioning, as measured by the Mullen Scales of Early Learning, where individuals with low-level behaviors display lower standard scores on the Early Learning Composite. Significant differences were also obtained when comparing early social skills, with parental report suggesting lower levels of social competence in individuals with low-level behaviors.

Conclusions:

The present study suggests that the development of low-level repetitive behaviors is associated with lower levels of cognitive functioning, which may interfere with social and communicative development in young children with ASD.

118.075 75 Response Inhibition in Manual and Oculomotor Systems in ASD. M. W. Mosconi*, L. Ankeny, M. E. Ragozzino and J. A. Sweeney, *University of Illinois at Chicago*

Background: Studies of response inhibition in ASD have yielded inconsistent findings, although considerable evidence now documents increased error rates on oculomotor inhibition tasks. In particular, inconsistencies in findings with manual and oculomotor paradigms raise questions about the task or neural system specificity of response inhibition deficits in ASD.

Objectives: To examine manual and oculomotor response inhibition in individuals with ASD.

Methods: Thirty-one individuals with ASD and 27 healthy controls matched on age (range 6-38 years) and Performance IQ were administered one manual motor and one oculomotor stop-signal task (SST). During SST's, subjects were instructed to either press a button (manual version) or make a saccade (oculomotor version) when a peripheral target appeared ('go' trials), or inhibit these responses when a central stop signal appeared following the appearance of the peripheral cue ('stop' trials). Subjects' baseline manual and saccade latencies (i.e., reaction times) also were examined.

Results: During the manual ($p=.011$) and oculomotor ($p<.001$) SSTs, individuals with ASD made more errors than controls. For both tasks, adults (≥18 years) with ASD were relatively more impaired than children and adolescents with ASD suggesting diminished improvement in this cognitive ability with age in adult patients. For both tasks, subjects increased their response latencies from the baseline measures to 'go' trials of the SSTs. The amount of slowing in reaction times on the SST task relative to the control task was associated with the percentage of correct 'stop' trials for manual ($r= .71$) and oculomotor ($r= .57$) tasks. This suggests that the more individuals slowed their reaction times, the better they were at suppressing responses when stop signals were presented. Individuals with ASD did not increase their reaction times as much as controls for either the manual ($p=.001$) or oculomotor ($p=.001$) SST.

Conclusions: These results indicate that individuals with ASD show response inhibition deficits that affect both manual and oculomotor systems, and both of these deficits appear to reflect a reduced ability to adaptively and strategically slow reaction times to enhance the ability to suppress responses on stop trials. Individuals with ASD are limited in their ability to utilize this strategic bias and thus are less able to voluntarily suppress reflexive/automatic responses in a context appropriate fashion. Results also indicated that the developmental trajectory of manual and oculomotor inhibitory control may follow distinct developmental time courses in ASD. For both tasks, performance improves beyond early adolescence for healthy individuals but less so for adults with ASD. Studies of SST performance in ASD therefore may offer insight into the timing and nature of atypical brain development affecting the voluntary control of manual and oculo- motor systems. The pathophysiology of these alterations has yet to be elucidated in ASD, but our results indicate that studies of SST

performance may yield important insights into cognitive and neural mechanisms associated with these disorders.

118.076 76 Visual Stereotypies in Young Children with Autism Spectrum Disorders. S. Goldman*, D. J. Meringolo and N. Tarshis, *Albert Einstein College of Medicine*

Background: Repetitive and stereotyped behaviors are one of the diagnostic criteria for Autism Spectrum Disorders (ASD). Visual Stereotypies (VIS) including lateral glances, close inspection and tracing are particularly disruptive to learning activities and social interaction. These visual behaviors are not systematically identified or described, are often grouped with other stereotyped behaviors and are poorly understood.

Objectives: The first goal of this study was to identify, describe, and categorize Visual Stereotypies in young children with ASD. The second goal was to analyze the relationship of VIS to age at referral, cognitive, language and social functioning.

Methods: Based on retrospective chart review and Autism Diagnostic Observation Schedule (ADOS) videos and protocols, 2 groups of ASD children matched on gender and chronological age were included. One group exhibited Visual Stereotypies (VIS) and one group did not (NoVIS). The VIS group was comprised of 10 ASD children: 7 boys, 3 girls; mean age 30 months (range: 20-42). The NoVIS comparison group was comprised of 14 ASD children: 10 boys, 3 girls; mean age 31 months (range: 16-49). Using the total scores from the subscales of the ADOS protocol, we assessed and compared communication, socialization, play and repetitive behaviors. We compared group means for age at referral and IQ levels.

Results: First, we identified five subtypes of VIS. The most frequent was lateral glances; the least frequent was tracing. We found no statistical differences between the groups in regard to language, play, or social interaction, based on the ADOS scores. However, the analysis showed that compared to the NoVIS group, the VIS group presented with significantly earlier age at referral ($p < .04$), higher cognitive scores ($p < .05$), and higher prevalence of stereotyped behaviors and restricted interests ($p < .01$) from the ADOS.

Conclusions: Visual Stereotypies in preschool children with ASD are brief and relatively rare. The identification and characterization of these stereotypical behaviors through videos analysis can be challenging. This preliminary study identified five specific subtypes of VIS. It revealed that children with VIS, despite their higher cognitive functioning, are recognized and, therefore, referred earlier for diagnostic assessment. Limitations of this study included a relatively small sample and variable quality of the video recording. However, these findings highlight the need to examine repetitive behaviors in greater detail and the potential of visual stereotypies as a phenotypical marker for autism. Further analysis will examine the long-range outcomes of this subgroup of children.

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118.077 77 A Preliminary Investigation of the Relationship Between Commitment to Philosophy and Burnout Among Teachers of Preschool Children with Autism Spectrum Disorders. D. C. Coman*[1], A. Gutierrez[1], M. R. Schneider[1], L. Sperry[2], K. Hume[3], M. Alessandri[1], B. Boyd[4] and S. Odom[5], (1)*University of Miami*, (2)*University of Colorado Denver*, (3)*Frank Porter Graham Child Development Institute, University of North Carolina, Chapel Hill*, (4)*University of North Carolina at Chapel Hill*, (5)*University of North Carolina*

Background: The primary source of intervention for most children with autism spectrum disorders (ASD) and their families is provided through the school system. As such, it is critical that there are highly qualified special education teachers implementing these interventions. For more than two decades, special education teacher shortages and attrition have been of concern to policymakers and administrators who work to recruit and retain special educators (Council for Exceptional Children [CEC], 2000; Morsink, 1982; Smith-Davis & Billingsley, 1993; Smith-Davis, Burke, & Noel, 1984). The resulting deficiency has serious and far-reaching consequences for children with disabilities; particularly those with ASD. It is imperative, therefore, to investigate the antecedents that may be at the root cause of the decision by special educators to leave the

field. Although a multiplicity of variables have been shown to be related to teacher attrition, considerable research has shown teacher burnout, a unique type of stress syndrome, to be directly influencing this outcome (Billingsley, 2004; Winiewski & Gargiulo, 1997; [CEC], 1998). Fortunately, there are factors that have been shown to mitigate the onset of this syndrome. Prior research suggests that teachers who endorse the underlying philosophy of their teaching approach are more satisfied with the work they were doing and exhibit less burnout (Jennet, Harris, & Mesibov, 2003).

Objectives: We propose to explore the relationship between teacher commitment to model philosophy and the three domains of teacher burnout Emotional Exhaustion (EE), Depersonalization (DP), and Personal Accomplishment PA, across three widely utilized preschool treatment models for children with ASD: TEACCH (Treatment and Education of Autistic and Related Communication-Handicapped Children), LEAP (Learning Experiences and Alternative Program for Preschoolers and their Parents), and a Business As Usual (BAU) model. It is hypothesized that teachers with a greater commitment to the philosophy underlying their teaching approach will experience less burnout across the year.

Methods: This study was conducted in conjunction with and support from a larger multi-site (CO, NC, FL) treatment comparison project. 22 teachers (9 TEACCH, 5 LEAP, and 8 BAU) were asked to complete the Teacher Philosophy Questionnaire-Adapted Version and a demographic questionnaire at the beginning of the school year. Additionally, the Maslach Burnout Inventory-Educators Survey was administered at 4 different time points across the year.

Results: While controlling for selected variables (e.g., number of years teaching, number of years teaching children with ASD, average classroom size, and number of full time classroom staff), preliminary analyses of hierarchical linear modeling indicated a significant positive relationship between teacher commitment to model philosophy and the average amount of EE experienced throughout the year, $R^2 = .52$, adjusted $R^2 = .36$, $F(5, 15) = 3.212$, $p < .05$. Approximately 16% of the variance of EE was accounted for by its relationship with teacher commitment to philosophy. This is year 1 data of a three year project.

Conclusions: Preliminary analyses suggest that an understanding and commitment to the theoretical underpinnings of particular autism-specific teaching approaches may serve as a buffer for experiencing aspects of teacher burnout across the school year.

118.078 78 An Ecological Approach to the Study of the Service Dog's Effects On the Families of Children with Pervasive Development Disorder. S. Fecteau*, M. Trudel and M. Maurer, *Sherbrooke University*

Background:

Results from several studies have reported that the presence of an autistic child may induce additional stress for the family (Baker-Ericzén *et al*., 2005; Yamada *et al*., 2007). Furthermore, some studies support the notion that parental stress may be influenced by the family functioning (Dyson, 1997). In fact, the evaluation of the family ecology is of particular importance since poor family harmony has been found to be a good predictor of stress (Perry *et al*., 2004). It seems that the exacerbation of the stress level linked with these behaviours is reduced following the introduction of intervention programs which include the parents' collaboration (Wiggs & Stores, 2001). Since one of the symptoms of autism is impaired social functioning and that the presence of a dog seems to help develop these skills (Martin & Farnum, 2002) it is plausible to believe that the integration of a service dog in the family home could be a promising intervention.

Objectives:

The present study will first evaluate how the degree of severity of the autistic symptoms affects the variation of stress levels reported. Secondly, this study aims to estimate in what manner family functioning and parental stress interact with each other. And lastly, the impact of a service dog (provided and trained by the Mira Foundation) on the parental

stress and the family functioning is evaluated both before and after the insertion of the dog within the family.

Methods:

Measurements are taken during home visits one month before the dog's introduction and six months after. The total sample is composed of 38 families who received a service dog and 33 families from a waiting list (control group). The stress level is evaluated using the Parental Stress Index short form (Abidin, 1995). The parent also completed the Family Environment Scale (Moos & Moos, 1981). As for the severity of the autistic symptomology, it is estimated using the Childhood Autism Rating Scale (Schopler *et al*., 1980) and filled out by the evaluator after the home visits.

Results:

The results indicate no difference between the two groups as for age and severity of the diagnosis. They also suggest that the families reported a great amount of stress before the introduction of the service dog. These stress levels are diminished following the integration of the dog. As for the family ecology, a significant difference between the two groups was observed. In fact, the family who received a dog seemed to put more emphasis on expressiveness and independence and have a tendency to encourage achievement following the integration of the animal.

Conclusions:

Our results confirm those found by Dyson (1997) indicating that parents of children with developmental disabilities report a higher level of stress which is influenced by family functioning. The results indicate that the introduction of a trained dog may be a good form of intervention in relieving stress from the parent. Finally, the project reflects a conceptual framework suggesting that the study of the service dog's impact on the autistic child should be addressed from a family-centered perspective.

118.079 79 Evaluation of the York University Asperger Mentorship Program. M. Ames*, C. A. McMorris, L. N. Hancock, J. M. Bebko and Y. U. Asperger Mentorship Program, *York University*

Background: In recent years, the number of students with an autism spectrum disorder (ASD) pursuing post-secondary education has significantly increased. A survey exploring the student population of eighty American universities found that on average, ten students per year identify themselves as having an ASD. Although many students with an ASD are able to excel academically, services provided by most universities do not address the particular social difficulties these students face. The AS Mentorship Program was developed to address these issues and to help students with Asperger syndrome (AS) navigate the social and academic framework of York University's campus life. The AS Mentorship Program is a multifaceted service for students diagnosed with AS. Broadly, the program is comprised of two parts: 1) weekly or bi-weekly, one-to-one meetings with a mentor who provides individualized support; and 2) group meetings/social events which provide students with a safe environment to meet other students with AS, as well as an opportunity to create a peer group within the university setting. Therefore, the AS Mentorship Program aims to: 1) help students build a social network/ peer group within the university community; and 2) provide a supportive environment for university students with AS.

Objectives: The purpose of the present study is to critically evaluate this peer to peer AS Mentorship Program. Through qualitative and quantitative methods, the current study examines the effectiveness of the AS Mentorship Program in meeting the students' needs and if the program is achieving the goals and objectives previously mentioned.

Methods: At the beginning of the academic year (or upon entrance into the program), students complete an initial interview with their individual mentor, as well as three questionnaires (the Social Provisions Scale, the Social Support Questionnaire and the Interpersonal Support Evaluation List). Whereas the interview asks students specifically about their strengths, weaknesses and goals in the AS Mentorship Program, the

questionnaires ask students to quantify their feelings of belonging and acceptance in the university setting. Students are given a similar interview and questionnaires at the end of the academic year. Qualitative analyses are used to assess student satisfaction with the mentorship program, specifically how much the program met their individual needs, as well as some areas of strength and recommended improvements. Analyses also examine potential changes in feelings of belonging, acceptance and support in the university setting at the end of the academic year.

Results: Currently, twelve students diagnosed with an ASD, most commonly Asperger syndrome, are participating in the AS Mentorship Program and have completed the initial interview and questionnaires. Data analysis of interviews and questionnaires will be updated at the end of the academic year.

Conclusions: Results of the present study will inform the future development of the AS Mentorship Program, as well as help to provide quality services to address the needs of students with AS in the university setting.

118.080 80 Examining the Relationship Between Varying Symptom Presentation in Children with Autism Spectrum Disorder and the Adjustment of Their Typically Developing Siblings. K. Greenberg*, A. Lian, R. Hundley and E. Hanson, *Children's Hospital Boston*

Background: Sibling relationships are known to have a significant impact on the process of social and emotional development (Dunn, 2008). A number of studies have focused on potential challenges faced by typically developing (TD) siblings of children who have physical or developmental disability, including autism spectrum disorder (ASD) (Bagenholm & Gillberg, 1991; Knott, Lewis & Williams, 1995; Opperman & Alant, 2003; Hastings, 2007; Barr, McLeod & Daniel, 2008). This study aims to examine how the varying symptom presentation in children with ASD impacts the adjustment of their TD siblings. Objectives: Assess the relationship between the behavioral phenotype and severity of symptoms in children with ASD and the social, emotional and behavioral adjustment of their unaffected siblings. Methods: A convenience sample of 99 families drawn from a larger study who have a child aged 4 to 18, affected with ASD, as well as a TD child aged 6 to 23, have participated in this study. To verify ASD diagnosis in the proband, the Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview-Revised (ADI-R), were performed. In addition, cognitive, adaptive and behavioral measures were administered. Overall severity of symptoms was calculated using the Calibrated Severity Score (CSS) (Gotham, Pickles & Lord, 2009). To confirm neurotypical development in the unaffected child, parents were asked to complete the Social Responsiveness Scale (SRS) and to provide medical and educational information. In addition, parents completed measures to characterize emotional and behavioral development of their TD child, including subdomains of the Child Behavior Checklist (CBCL), and the Maladaptive Behavior Index (MBI) of the Vineland Adaptive Behavioral Scales-II (VABS-II). Results: A regression analysis was used to test for associations between proband behavioral phenotype and TD siblings' emotional, and behavioral development. When compared to the Restricted and Repetitive Behaviors and Interests (RRBI) domain on the ADI-R, ten of the fifteen subdomains in TD siblings tested on the VABS-II MBI and CBCL were found to be statistically significant ($p < .05$): VABS-II Internalizing, CBCL Social Problems, CBCL Aggressive Behavior, CBCL Anxious/Depressed, CBCL Internalizing Problems, CBCL Attention Problems, CBCL Affective Problems, CBCL Somatic Complaints, CBCL Anxiety Problems, CBCL Oppositional Defiant. All other domains on the ADOS and ADI-R, including those assessing social interaction and communication deficits, as well as CSS, were not associated with difficulties in TD siblings. Conclusions: Children with ASD who have an increased presence of RRBIs have siblings with a higher prevalence of social, emotional and behavioral difficulties, when measured using subscales on the CBCL and VABS-II MBI. Social interaction and communication domains on the ADI-R and ADOS, as well as CSS were not significantly correlated with difficulties in the TD sibling. As this study was hypothesis-generating, future studies will be

needed to further clarify the relationship between RRBIs and their effects on TD sibling development.

118.081 81 Family Impact of Raising a Child with Autism Across Different Cultures. N. Luthra* and A. Perry, *York University*

Background:

The diagnosis of any disability in a child has a great impact on the family but families respond differently. Past research has often focused on the negative effects on parents' mental health (Bishop et al., 2007) but recently there has been a shift towards exploring positive effects of raising a child with disabilities (Blacher & Baker, 2007). However, very little research has explored how the family's culture helps, or makes it more difficult for parents to cope with their child's disorder. Cultures vary in their attitudes toward disability, their concepts of what is typical and atypical, the social acceptance or stigma involved and so on (Welterlin & LaRue, 2007). These differences may influence parents' experience of raising a child with autism.

In this study, we used two well researched cultural schemes based on nationality, from the field of social-cultural/organizational psychology: (a) Hofstede's cultural dimensions – *Power Distance*, *Uncertainty Avoidance, Individualism and Masculinity;* and (b) Schwartz's transnational cultural groupings – *Western European countries, English speaking countries, Latin American countries, Eastern European countries, South Asian countries, Confucian influenced countries, and African and Middle Eastern countries.*

Objectives:

The purpose of this study was to examine families' culture in relation to: parenting distress, positive change, knowledge of autism, and perceptions of child progress. There were two research questions: 1. What is the extent of relationship between scores on Hofstede's four cultural dimensions and the dependent variables? and 2. Are there differences in the dependent variables across families grouped according to Schwartz's cultural groups?

Methods:

File review of over 180 participants has been conducted. Toronto, Canada is a multicultural city and we have assessed children of immigrant families from over 25 different countries. Families were grouped based on the parent's country of birth using Hofstede's and Schwartz's methods. Child measures included: cognitive skills (Mullen Scales of Early Learning; Mullen, 1995), adaptive skills (Vineland-II; Sparrow, Cicchetti & Balla, 2005), and severity of autism (CARS; Schopler, Reichler & Renner, 1988). The dependent measures were based on parent questionnaires incorporating measures of stress (the Parental Distress subscale of the Parenting Stress Index- Short Form; Abidin, 1995), positive impact (Scorgie & Sobsey, 2000), knowledge of autism and behavioral intervention (Solish & Perry, 2008), and perception of child progress (Solish & Perry, 2008).

Results:

Data analysis is under way. Correlations will be reported to address Question 1 regarding the relationship between the cultural dimensions and the four dependent variables. To answer Question 2, first child variables and socioeconomic status will be examined to see whether they differ across groups, in which case they will be included as covariates in subsequent analysis. Then, oneway ANOVAs or ANCOVAs will be reported comparing the various subgroups on the same four dependent variables.

Conclusions:

Conclusions will focus on whether the analysis show any relations or differences between cultural groups, and an inference about the possible reasons underlying this. The results may be used to inform changes in training culturally sensitive professionals who deal with families from diverse backgrounds.

118.082 82 Implementation of a Peer-Mentored Program for College Integration of Students with Autism. E. Abrigo*, F. Hurewitz and S. Vass, *Drexel University*

Background:

Adults with autism spectrum disorders who have the academic ability to matriculate into

a full time college environment may still be challenged by the social, self help and advocacy demands of this new environment. These students may benefit from training and support in social skills and in effective self-advocacy specifically geared towards social, academic, and administrative situations in the college environment. Research suggests that peer-mediated intervention (PMI) is a versatile and potentially effective intervention approach for individuals with autism spectrum disorders (Chan, et al., 2009).

Objectives:

Drexel University, under the umbrella of the Eastern Region of the Autism Services, Education, Research and Training (ASERT) has designed a seminar addressing adjustment to college life, self-advocacy, and the development of interpersonal and social skills. The Drexel Autism Support Program (DASP) is geared towards the needs of the burgeoning population of high functioning individuals with autism who are attending college and provides support for college-based trainers. We present pilot results on the feasibility and efficacy of the DASP program.

Methods:

The DASP course meets 1.5 hours once per week for 8 teacher led sessions. The curriculum addresses goal setting, obtaining accommodations, non-verbal communication, conversation, expanding social networks, college coping skills, assessing strengths, and self-advocacy through lecture, discussion, and role-play. We implement a PMI model by incorporating the use of peer mentors (fellow students) who are trained in autism and in mentoring skills. These students are partnered with students with autism for the completion of weekly *in vivo* activities designed to practice skills outside of class. Peer mentors attend class weekly, and an additional 45 minutes of group supervision each week. Students complete a Social Networks Questionnaire and the Friendship Questionnaire (Baron-Cohen & Wheelwright, 2003) pre- and post- seminar. Both students and peer mentors evaluate class activities and assignments weekly. The seminar's first iteration included four students and four peer mentor participants. In Spring 2010 the program will expand to include additional colleges in eastern Pennsylvania.

Results:

Preliminary results indicate student satisfaction with the seminar. Students and mentors rated in-class exercises as applicable and as successfully addressing intended objectives. Role-plays were rated as helpful and as realistic practice for social and academic related exchanges with others. Although students do not receive academic credit for the seminar, there was no attrition. Reported durations of weekly mentor/mentee meetings varied from 15 minutes to one hour depending on individual student needs and the demands of each assignment. Peer mentor ratings of assignments overwhelmingly indicate that students and trainers received adequate training prior to assignments and that students were able to attempt or complete assignments.

Conclusions:

We will discuss the potential to broadly implement PMI programs in college settings. Our initial results suggest that an abundance of students, primarily in social services or educational majors, have an interest in pairing with and helping students with autism as peer mentors. Students with autism appreciate having a social "guide" to college integration. The results of this ongoing study may inform the development of similar programs in post-secondary institutions.

118.083 83 Medical Care Program for Autism Spectrum Disorders Population in Madrid. L. Boada*, J. Romo, C. Moreno, C. Llorente and M. Parellada, *Hospital General Universitario Gregorio Marañón.*

Background: Autism Spectrum Disorders (ASD) individuals have more medical needs than general population. They have more medical pathology and great difficulties in identifying and communicate their symptoms. Medical assisstance to this population is usually poor in our context. To provide access to high quality medical care for individuals

affected with ASD, a comprehensive medical care program has been implemented recently in Madrid (Spain). This program is open to individuals of all ages and serves the whole Madrid´s catchment area (6 million people).

Objectives: ·

. To centralize medical attention and facilitate access to specialized medical care
· To facilitate differential diagnosis of medical problems, including those causing behavioural deterioration.
· To provide access to a Psychiatry Specialized Unit.
· To improve ASD individuals' health, taking care of daily problems as diet, sleep, dental health.
· To provide coordination with different medical services to cover medical needs in an organized fashion (reducing waiting times, adjusting spaces with visual sequences and pictograms, performing several procedures in the same day, etc).
· To enhance knowledge about ASD among health professionals and promote specific adaptation of general medical procedures when treating ASD patients.

Methods:

Population: ASD individuals of all ages throughout all Madrid´s territory (6 million people)

Procedure:

1. Setting up a specialised Psychiatry Unit in a Tertiary Hospital for the treatment of ASD patients.
2. Setting up a case management approach.
3. Meetings with the heads of the most demanded specialities.
4. Development of good practice guidelines for the physical environment, medical procedures and diagnostic techniques.
5. Design and application of questionnaires for the evaluation of the effectiveness and satisfaction with the Program
6. Divulgation of the Program among ASD parent associations and educational services.

Results: During the period 1st April to 1st November 2009, 235 new patients have been attended by this program. There have been 250 follow-up visits. There were 67% children (18 months-16 years) and 33% adults (>16 years). 147 visits have been organised to other medical specialities and 261 have received a medical procedure or a diagnostic technique. The most demanded specialities were Neuropediatrics (27%), Nutrition (13%), Estomatology (9%) Gastroenterology-Digestive (8%), and Dermatology (7%). The most common procedures and diagnostic techniques were blood test (37%), electrocardiogram (22%), and electroencephalography (6%). Preliminary results seem to confirm the presence of more physical pathology in this population.

Conclusions: A nurse case management approach, with emphasis on information and teaching of professionals, support to patients and families, and coordination between and within medical specialties seems appropriate and useful to improve the medical assistance of ASD population. Doctors should centre their activity in improving knowledge and individualizing treatments for this population. A program has been set up to assess the effectiveness of the effect of the Medical Program on the medical assistance of this population.

118.084 84 Autism and the Family in India: An Ethnographic Study. S. Vaidya*, *Indira Gandhi National Open University*

Background: Historically, autism has been a largely unrecognized category in India; people presenting with its symptoms were routinely regarded as mentally retarded or mentally ill. The word "autism" is now increasingly familiar amongst the lay public and professionals alike. However, new avenues for diagnosis and treatment remain largely confined to the educated, urban English speaking sections of the population. The onus for obtaining access to an appropriate diagnosis and intervention is still placed squarely on the family. Parents often have to travel great distances, uproot themselves from the community and undergo great financial and social hardship.

Objectives: This paper seeks to chronicle the lived experiences of families of children with autism by tracing the processes of symptom

recognition, help seeking, and obtaining an appropriate diagnosis and program for action. It attempts to unpack the manner in which families mobilize psychic, interpersonal and cultural resources in order to "make sense" of their child's condition and personhood and interpret it to the wider society.

Methods: Data were gathered in the course of an ethnographic engagement with twenty families based in Delhi, India. The author's position as the mother of a young boy with autism was an integral aspect of the research process, in tune with the reflexive and feminist methodological underpinnings of the work. The study was exploratory, with the aim of opening the area of autism and the family to ethnographic enquiry. Participant observation and extensive unstructured interviews were conducted with parents, siblings, grandparents, domestic helpers and significant others intimately involved with the child.

Results: This study sharply indicated the growing awareness amongst middle-class Indian families about "normal" development and their apprehension about perceived deviance or difference. This is in marked contrast to the more relaxed parenting styles of earlier generations. The impact of western bio-medicine and the pathologizing of difference were also noted. At the same time, cultural explanations with regard to the "divine innocence" of their children and the theory of karma played an important role in helping families come to terms with their child's condition. These apparently contradictory processes mirror the socio-cultural reality in contemporary India.

Conclusions: Autism in India is regarded as a "middle class" disorder precisely because it is only the educated middle class that can undertake the long, frustrating and expensive journey to obtain appropriate interventions for their children. This perception colors disability policy, training of personnel, and outreach. In the absence of a social security net, familial responsibility becomes even more onerous. India is a signatory to multiple international resolutions on disability rights, and has a Constitutional mandate for the protection of the marginalized. However, given the endemic structural problems of the country, actualizing these commitments is very difficult and have yet to translate into action. India's long-standing tradition of communitarian care of the old, sick and disabled needs to be revitalized and reinterpreted within a "rights" framework. The growth of caring communities involving all stakeholders will help ease the burden on the family and integrate affected individuals within meaningful and rewarding community roles.

118.085 85 A Preliminary Study On the Treatment Initiation of Families After Their Child Received An Initial ASD Diagnosis. S. W. Duvall*, B. Lopez, D. Hill and L. Parks, *University of New Mexico*

Background: Given recent advancements in early detection and public awareness, the prevalence of ASD has now reached an unprecedented magnitude. We know that early and intensive intervention can help a child with autism make substantial developmental and adaptive improvements. A major obstacle for children with ASD in obtaining early and efficacious intervention is a family's ability to bridge the gap between initial diagnosis and the initiation of interventions that are consistent with 'best practices'. Unfortunately, to date there has been limited research examining the factors that influence a family's ability to initiate early and efficacious intervention.

Objectives: To describe the rates of treatment initiation and services received in the first six months after initial ASD diagnosis and to preliminarily describe characteristics associated with differential rates of treatment initiation.

Methods: Participants included 17 children and their families who were diagnosed with Autistic Disorder or PDD-NOS for the first time between 18 and 42 months of age. After initial diagnosis parents completed questionnaires selected to assess autism-specific behaviors and adaptive behaviors, family strengths and stressors, perceived strengths and weaknesses in services, and treatment types, hours, and when initiated. Children underwent a developmental and diagnostic evaluation that included the ADOS

and Mullen Scales of Early Learning. At 2, 4, & 6 months following the initial session, parents completed a treatment history questionnaire and at 6 months completed a phone interview.

Results: More than 60% of children in the study received 0-3 hours of treatment per week before being diagnosed. Six months after diagnosis 27.2% of children still received only 0-3 hours. It appears that children receive variable rates of treatment (0-30 hrs/week) at a 6-month follow-up. There was a significant increase in the overall number of treatment (educational/services) hours received per week, $t(14)=-2.95$, $p=.01$, between time of diagnosis and 2 month follow-up. There was a significant increase between the time of diagnosis and the 6 month follow-up in the overall number of treatment (educational/service) hours received per week, $t(14)=-6.18$, $p>.001$.

Conclusions: Determining what influences families' ability to initiate treatment is critical to children with ASD's long-term prognosis. The current study found that families do initiate different rates of treatment for their children. Although the rates of treatment initiation increase over time after first diagnosis, a sizable portion of children are still receiving limited services 6 months after initial diagnosis. Current data suggest identifying the multisystemic issues that affect treatment initiation is complex and may not be tied to any one variable. Attending school appeared to be the one factor that systematically increased a child's use of treatment services. Preliminary survey suggests family stress, acceptance of diagnosis, and financial factors influence treatment rates.

118.086 86 Assessing the Role of Social Work in Interdisciplinary Autism Spectrum Diagnostic Evaluations. M. Pinkett-Davis*, R. Whitney, L. Kalb, C. Foster and B. H. Freedman, *Kennedy Krieger Institute*

Background: Seeking and receiving an Autism Spectrum Disorder (ASD) diagnosis can be an overwhelming and distressing experience for families (Giarelli et al., 2006; Siklos & Kerns, 2007). Previous studies have emphasized the importance of incorporating opportunities post-evaluation to assess for and ensure that families have a strong understanding of the evaluation results and recommendations (Giarelli et al., 2006). It is presently unclear, however, if providers in the typical interdisciplinary model are able to meet this directive. Historically, social work-based intervention directly addresses these challenges. Yet, despite this intuitive fit, little research has examined the role of social work (SW) in interdisciplinary ASD diagnostic teams.

Objectives: This study measures the effect of incorporating a one-time social work intervention on parent's perception of a) their child's evaluation and b) community resources. Secondly, this study seeks to understand if this intervention has a lagged effect on the aforementioned areas.

Methods: Families are assigned to experimental or control conditions based on routine scheduling, at an outpatient autism clinic. Both conditions receive care as usual, including an evaluation with an MD, SLP and OT. However, families in the experimental condition receive an additional 2 hours of social work intervention during evaluation, designed to process and provide psycho-education related to diagnosis and increase parents awareness of community resources.

Outcomes are measured at two points in time, including directly after their child's evaluation and 4-6 weeks post-evaluation. At baseline, both conditions complete a demographic questionnaire, and the "lack of clarity" and "information" subscales of the *Mishel Uncertainty in Illness Scale* (Mishel, 1981). Similar to previous studies (Lipinksi et al., 2006), the items were customized to measure parents perception of their child's autism diagnostic evaluation. Additionally, an original, 11-item likert-type measure was developed to assess parents' knowledge of and willingness to access available community resources. The follow-up questionnaire, comprised of selected items from both scales, is conducted by phone post-evaluation.

Results: Results from the unpaired two-way *t*-test found no differences in means between conditions ($n=7$) for either subscale scores at

baseline (p > .05). When post-test scores are available and the sample size grows, a multiple linear regression model will be employed to analyze differences in baseline and follow-up means while controlling for social economic indicators.

Conclusions: Results from the preliminary analysis found no significant differences between conditions for parents' clarity and comprehension of both the evaluation process and results, or their perception of community resources. However, this null finding is likely due to the very small sample size. Conclusions from our investigation will describe the relative significance of incorporating SW as one component of a comprehensive multidisciplinary evaluation for ASD. Recommendations will be made regarding the importance of attending to family perception of the evaluation process and caregivers' understanding of and likelihood to seek out recommended resources. Each of these has important implications for the creation and delivery of comprehensive evaluations for ASD.

118.087 87 Association Between Caregiver Factors and the Timing of Autism Spectrum Disorders Diagnosis. T. Y. Perryman*[1] and L. Watson[2], (1)*Vanderbilt University*, (2)*University of North Carolina at Chapel Hill*

Background: Past research has documented later ages of diagnosis of Autism Spectrum Disorders (ASD) for children from ethnic minority backgrounds. Conceivably, this discrepancy could result in differences in the utilization of early intervention and other important support services. With advances in our ability to identify autism symptoms earlier than 3 years of age, disparities in children's age at diagnosis warrant attention and further research.

Objectives: In an effort to understand what may lead to differences in age of diagnosis or recognition of symptoms, this study investigated timing of diagnosis for Black and White children with ASD while examining differences among caregiver empowerment levels, magnitude of concerns about early "red flag" behaviors, and attributions of initial symptoms. Additionally, the association between these "internal caregiver factors'" and the age of ASD diagnosis was explored.

Methods: Using survey methods, a total of 168 North Carolina families were recruited and met inclusion criteria for the study. Caregivers reported on diagnostic factors, empowerment, and concerns/beliefs related to initial ASD-related symptoms.

Results: Although, there were no statistically significant group differences found in the age at diagnosis of ASD or among internal factors, caregivers' level of concern about initial ASD symptoms and caregivers' attributions of the symptoms to behavioral problems were related to the age of ASD diagnosis.

Conclusions: This research provides new information about the importance of parental concerns and attributions in the quest to identify children at risk for ASD at younger ages. Although a variety of factors appear to impact the age of diagnosis of ASD, the role of caregivers should not be underestimated, especially in the absence of routine ASD screening by some medical care providers. Furthermore, these findings provide implications for promoting public awareness of symptoms related to ASD.

118.088 88 Bullying in Children with Autism Spectrum Disorders. K. P. Nowell*[1], C. M. Brewton[1], M. W. Lasala[1], S. U. Peters[2] and R. P. Goin-Kochel[1], (1)*Baylor College of Medicine*, (2)*Vanderbilt University*

Background: A defining characteristic of children diagnosed with an Autism Spectrum Disorder (ASD) is a qualitative impairment in social interaction, which is manifested to varying degrees across the spectrum. However, in all cases, the impairment results in these children having difficulties accurately perceiving their social world (e.g., tone of voice, facial expressions), thus placing them at risk for bullying. Much attention has been given to bullying in schools, but minimal research has been completed specifically investigating the prevalence of bullying in children with ASD. Also, there are conflicting findings within the research literature in terms of how educational placement correlates with incidents of bullying. Some literature suggests that placement in special education

classes increases a child's risk of being bullied (Card & Hodges, 2008), while other research suggests that being included with typically developing peers may result in increased victimization (Sigman and Ruskin, 1999).

Objectives: To quantify incidents of bullying within a sample of children with ASD; qualitatively explore children's perceptions of being teased/bullied; and investigate correlations between level of overall functioning, clinical severity, frequency of peer victimization, and classroom setting.

Methods: Data were ascertained from Baylor College of Medicine's local Simon's Simplex Collection (SSC) sample (N=43). Inclusion criteria were that children were between the ages of 6 and 18 years and had been administered a module 3 of the *Autism Diagnostic Observation Schedule* (ADOS). Children were diagnosed with autism (73%), or ASD (i.e. Asperger's Disorder and PDD-NOS) (27%). Data of interest included specific items from the *Child Behavior Checklist* (CBCL) and *Teacher Rating Form* (TRF). Level of functioning was examined using cognitive evaluation (e.g., *The Differential Ability Scales - Second Edition* (DAS-II)) and the *Vineland Adaptive Behavior Scales* (VABS). Information regarding educational placement was gathered from the ADI-R and a treatment history form. Qualitative data regarding probands' experiences were collected via Module 3 of the ADOS (e.g., from the question "Have you ever been teased or bullied").

Results: Preliminary analysis revealed that 74% of parents reported that their child was sometimes or frequently teased or bullied, while 52% of teachers endorsed the corresponding item. Qualitative data from the Module 3 of the ADOS indicated that 66% of probands denied being teased or bullied, 22% provided an inaccurate description of being bullied, and 12% provided an accurate description of being bullied. Logistic regression analysis will be used to determine whether clinical severity (as measured with ADOS), level of social skills (as assessed by the VABS), and/or level of cognitive functioning predicts parental reports of bullying. The chi-square test of homogeneity will be used to determine whether educational placement is associated with endorsement of CBCL/TRF items.

Conclusions: Results indicate a discrepancy between parent and child reports of bullying incidents. Next-step analyses will reveal more about factors potentially related to (a) parental espousal of their children being bullied and (b) both children's denial and admission of being bullied.

118.089 89 College Programs for Students with ASD: Predictors of Successful College Transition. J. Emmons*[1], S. McCurry[1], M. Ellison[2], M. R. Klinger[1] and L. G. Klinger[1], (1)*University of Alabama*, (2)*Marshall University*

Background: There are a substantial number of individuals with autism spectrum disorders (ASD) who possess the cognitive and academic skills to be successful in college. However, outcome data for these high-functioning individuals is disheartening. Howlin and colleagues (2004) reported that of 68 individuals with high-functioning ASD, 58% had "poor" to "very poor" outcomes in adulthood. Further, only 7% of Howlin's adult sample had attended college. College transition programs are starting to proliferate across the country. However, there is little to no data that addresses what factors predict a successful transition to college for students with ASD.

Objectives: This ongoing study examines the predictors of college success for students with ASD. Specifically, we examined factors that predict success during the freshman year of college including grades, level of anxiety and depression, life satisfaction, college adjustment and social functioning.

Methods: Participants included eleven students with high-functioning ASD who were enrolled in their first year in one of two university-based college transition programs. Each student completed measures of social, emotional, and academic functioning at the beginning of their first semester, at the end of their first semester, and at the end of their second semester. Internalizing symptoms (i.e., anxiety and depression) were measured by the Behavioral Assessment Scale for Children College Report Form. College

adjustment was assessed by the Student Adaptation to College Questionnaire. Overall life satisfaction was measured using the Brief Multidimensional Life Satisfaction Scale. Academic outcome was assessed by grade point average (GPA).

Results: Thus far, analyses have been conducted examining the relation between variables at the beginning of the first semester of college. Adjustment to college was negatively correlated with internalizing symptoms, $r(10)=-.83$, $p=.001$, such that students who had higher levels of internalizing reportedly made poorer adjustment to college. Further, students with higher levels of internalizing symptoms also rated themselves lower in terms of life satisfaction, $r(10)=-.66$, $p=.03$. Preliminary outcome data (i.e., mid-semester grades) were available for 4 students. (One university does not have a formal mid-semester grade report.) Students with higher levels of anxiety and depression at the beginning of college had lower mid-term GPAs, $r(3)=-.96$; $p=.04$. Finally, students who reported better adjustment to college had higher midterm GPAs, $r(3)=.96$, $p=.04$. Complete outcome data from the end of the first semester are currently being collected including end-of-term grades, adjustment to college, and internalizing symptoms.

Conclusions: These results have significant implications for college transition programs supporting students with ASD. First, anxiety and depression were highly correlated with a number of negative outcomes such as lower grades, life satisfaction, and social adjustment. This suggests that screening for and targeting symptoms of anxiety and depression through therapeutic interventions is a critical part of working with students with ASD. Second, results suggest that students that struggle in adjusting to college life may experience more difficulties with depression and low grades. Therefore, it is important to provide supports while beginning students are becoming oriented to being on campus and living away from home for the first time.

118.090 90 Differences in Processing Time, Show Rates, and Parent Perception of Autism Related Services Subsequent to Implementation of An in-Person Intake. J. Hutchison*, A. Kinsman, L. Burgin and D. P. Kelly, *Greenville Hospital System Children's Hospital*

Background: The waiting list for diagnostic services related to autism is often very long and there is a challenge to create support and resource services for families while they wait for their child's evaluation. Families also struggle with a loss of time in accessing services while they wait for their initial appointment. Our department developed an in-person intake procedure to determine evaluation needs and identify services that families can access without waiting for the evaluation. The service coordinator also acts in a supportive role for parents to help educate them on the topics surrounding autism and prepare them for the evaluation process. There is a question as to whether the service coordinator role within an autism program can improve the efficiency of the program.

Objectives: The objective in this study was to examine (1) show rates and time from referral to completion of the evaluation and (2) parent perception of support and the evaluation process subsequent to implementing service coordinators to conduct initial intake procedures.

Methods: Rate of completion of the intake packet and length of time from referral to completion of the evaluation was collected for 2008. Parental show rate for the initial interview and length of time from referral to completion of the evaluation were collected subsequent to implementation of in-person initial intake (January 2009). Additionally, families who completed the evaluation process were sent survey designed to assess impression of the evaluation process.

Results: Rates of parent initiation of the evaluation process and length of time until completion of the evaluation will be compared based upon type of intake procedure. Qualitative analysis of parent impressions will examine perceptions of emotional support, access to intervention services, and efficiency of the diagnostic process (effectiveness of the service coordinators, length of wait time for an evaluation) will also be conducted.

Conclusions: The impact of in-person intake on the efficiency of the diagnostic evaluation services will be discussed. Potential reasons for changes in efficiency (e.g., parental ability to complete the intake information, screening out unnecessary evaluations) will be discussed. Parental perceptions of support, resource information, and sense of empowerment gained via meeting with the service coordinators will be examined.

118.091 91 Earliest Intervention for Young Children with Risk for Autism: What Community Providers and Families Value. E. L. Lee*[1], A. Stahmer[2], K. L. Searcy[1] and L. Cervantes[1], (1)*Rady Children's Hospital, San Diego*, (2)*Rady Children's Hospital*

Background: Increasing numbers of children with communication and relationship disorders, including autism, are identified at early ages and represent a significant public health challenge. Few studies of intervention programs exist, however, that address social-communicative issues in infants and toddlers. Additionally, dissemination of existing programs to community settings has been limited.

The Center for Disease Control (CDC) called for early intervention programming directed toward preventing later mental and developmental disorders with an emphasis of the need to develop preventative interventions using comprehensive community models to promote healthy development. The current project involves a consortium of community practitioners, funding agencies, researchers and families of children presenting with risk for autism, working together to select an efficacious preventative intervention that meets the needs of very young children and their families in a Southern Californian community.

Objectives: To obtain community feedback in an effort to select an evidence-based intervention to implement in the community, and examine the perspectives of parents and intervention providers regarding the use of evidence-based, parent-implemented interventions for 12-24 month old children at risk for disorders of relating and communicating, such as autism.

Methods: Ten early intervention providers and 10 parents of children diagnosed with autism in Southern California participated in four focus group meetings to discuss the efficacy of early intervention services for children between 12 and 24 months, issues they consider when choosing specific techniques, obstacles to providing/obtaining early intervention, and philosophies of what an ideal early intervention program would look like. After attending presentations from three intervention developers, participants met in their focus groups to discuss the strengths and weaknesses of each intervention and how each intervention measured up to the factors identified as important for early intervention. Descriptive analysis and the constant comparative method were used to compare themes and perspectives across each intervention discussion.

Results: Preliminary analysis of the first three focus groups show a great deal of overlap between parent and provider perspectives. Both groups believe it is important for intervention to start as early as possible, be individualized for the child/family, but also be comprehensive. Both stated that interventions must be evidence-based; however they were more influenced by the intervention presenters' method of presenting evidence than the scientific strength of the evidence given. Parents and providers did have some areas where their focus was different. Parents wanted more flexibility in choosing their provider, wanted opportunities to include siblings in the intervention, and wanted more support in understanding and navigating potential diagnoses and services. Providers wanted comprehensive training, on-going supervision, and use of coaching and video feedback techniques as part of training. Additional data from the third intervention and methods for choosing the appropriate intervention will be completed in December, 2009.

Conclusions: Participants are open and willing to discuss their beliefs and address the strengths and weaknesses of parent-implemented intervention. Additionally, there were many areas of congruence

between providers, parents and research findings. Implications for community collaborative research and implementation of evidence-based practice are discussed.

118.092 92 Immunization Beliefs and Practices Among Autism Families. P. Law[1], J. K. Law*[1], R. E. Rosenberg[1], C. Anderson[1] and C. Samango-Sprouse[2], (1)*Kennedy Krieger Institute*, (2)*George Washington University*

Background: There is public concern about a link between routine childhood vaccines and adverse neurological outcomes, specifically the autism spectrum disorders (ASD), focusing on vaccine thimerosal content; measles-mumps-rubella (MMR) vaccine and intestinal disease; and perceived immunologic burden of vaccines. Direct quantitative impact of this controversy on families with ASD-affected children has not been extensively evaluated.

Objectives: The objective of this study was to survey and analyze vaccination beliefs and practices among families who have at least one child with an autism spectrum disorder (ASD).

Methods: Data on 2090 children with ASD and 1151 unaffected siblings provided by 1974 families was used to examine individual, family, and secular factors associated with vaccine-related beliefs about ASD and immunization practices among affected individuals and younger siblings, using ordinal and multinomial logistic regression.

Results: Roughly half of families believed that there "may be" (29.9%) or "definitely is" (15.3%) a link between a child's ASD and immunizations. Odds of increasing belief were associated with increasing severity of a child's skill loss (OR range, 2.2 - 4.9; $p<.001$) and lower maternal education status (graduate degree, OR .48, $p<.05$). Overall proportion of families omitting or delaying vaccination of initial childhood series was higher among siblings born after older siblings first showed developmental signs (24.5%), especially in the case of measles-mump-rubella vaccine (19.6%). Degree of belief, higher maternal education, and younger cohort were significantly correlated with delaying and/or omitting vaccines in younger siblings in the multinomial logistic regression model. Maternal education was also correlated with changing providers.

Conclusions: Belief in a vaccine-autism link and vaccination practices vary widely among families of children with ASD. Pediatricians should be prepared to explore vaccine-autism beliefs and provide in-depth guidance regarding vaccinations for such families; further research focusing on the experiences and concerns of these families is needed.

118.093 93 A Program Evaluation of a Social Interaction and Education Group for Youth with Asperger Syndrome. M. A. Viecili*[1], Y. Lunsky[2] and J. A. Weiss[1], (1)*York University*, (2)*Centre for Addiction and Mental Health*

Background:

Youth with Asperger Syndrome (AS) have severe deficits in sociocommunicative competence, which can lead to mental health problems and difficulties in school and social environments (Little, 2001), and it is critical that we evaluate programs that purport to improve this competence (Rao et al., 2008). The Centre for Addiction and Mental Health (CAMH) in Toronto offers a social skills program to youth with AS. This 10 week program aims to reduce the social skills deficits, anxiety and problem behaviors in youth with AS, and to train parents on how to generalize these skills to alternate environments and improve the parent-child relationship.

Objectives: This poster will examine whether the intervention leads to (a) reductions in anxiety, depression, oppositionality and aggressive behavior, and (b) improved social skills in youth. The poster will also present on the relationship between maladaptive behavior and social competence.

Methods: Twenty-seven children (22 males and 5 females, 7-14 years of age) are currently participating in the 10-week manualized social skills group. Pre-post data will be collected from both youth and parents on measures of social skills, internalizing and externalizing behaviors using the Social Skills Improvement System (SSIS; Gresham, & Elliott, 2008). Youth will also self-report their perceptions of self-concept as measured by

the Self Perceptions Profile For Children (SPPC; Harter, 1985).

Results: Prior to the intervention, 95% of youth had clinically significant deficiencies according to the social skills subscale of the SSIS (*M* = 72.1, *SD* = 8.4), with 81% having below average communication and cooperation skills, and 90% having below average empathy and engagement skills. Seventy five percent of youth had clinically significant problem behaviors (*M* = 127.1, *SD* = 15.9), with above average levels for 62% on externalizing behaviors, and 75% for internalizing behaviors. With regards to youth self-perceptions, 44% reported Low perceived levels of social acceptance with peers. We will present changes in specific SSIS and SPPC scales and on the correlation between change in social skills and in maladaptive behaviour.

Conclusions: There is evidence that social skills groups can be a useful mode of intervention for helping children with AS. Further research is needed to evaluate existing programs so that we can achieve the capacity to meet the needs of this underserved group, and develop evidence-based practices.

118.094 94 A Systematic Review of the Disparities in Health Care Utilization, Expenditures, and Access for Individuals with Autism Spectrum Disorders. M. K. Tregnago*, *University of Missouri*

Background: Individuals with autism spectrum disorders (ASD) are provided with a variety of interventions and services for treatment of a range of medical, behavioral, and psychological symptoms (Myers & Plauché Johnson, 2007). It is for this reason that it is hypothesized that children with ASD utilize more healthcare services and therefore have higher healthcare expenditures than children without ASD.
Objectives: The objective of this research was to conduct a systematic review of the literature to determine whether differences exist for children with ASD versus children without ASD with respect to the use of, the amount of money spent on, and access to health care services; and access to medical home components.
Methods: Medline and PsycInfo databases were searched for studies that were published between 1999 and August 1, 2009, written in the English language, and conducted with a sample in the United States. Studies included in the review had to incorporate an ASD-only group and compare it with other groups of children without ASD. Search terms included population variables (e.g. "autism spectrum disorders" or "pervasive developmental disorders") and outcome variables of interest (e.g. "disparities," "health care costs," "health care accessibility," etc.).
Results: A total of 301 unique articles were located. From the results, 10 articles were selected based upon the inclusion criteria. One additional study was selected from the references of these ten. Resulting articles compared individuals under the age of 21 with an ASD diagnosis to children without autism and/or to children with other special health care needs (OSHCN). Eligible articles were separated into three distinct categories. Six studies addressed health care utilization, eight addressed health care expenditures, and three addressed service access issues and medical homeness.
Conclusions: The results of this review support the hypothesis that there are disparities between children with ASD and children without ASD or with OSHCN in the following areas: access to and utilization of healthcare, healthcare costs, and the tendency to have a medical home.
Compared to children without autism, children with ASD tend to have higher utilization rates of pharmaceuticals as well as inpatient, outpatient, emergency, and special services. Children with ASD also tend to have higher health care costs than children without autism or with OSHCN, especially for outpatient visits, pharmaceuticals, and special services. Families of children with ASD were more likely to report having trouble accessing care, especially subspecialty care, and were less likely to report having components of a medical home. These results have vast implications for autism research and insurance policy, as they show that children with autism appear to utilize additional medical services and have higher costs in some areas relative to other children. Future research should examine child and family characteristics to determine

which variables correlate with higher utilization rates and expenditures.

118.095 95 Bullying Experiences Among Children and Youth with Autism Spectrum Disorders. M. C. Cappadocia*, J. A. Weiss, D. Pepler and J. M. Lyons, *York University*

Background: There is a dearth of research on bullying experiences among children diagnosed with autism spectrum disorders (ASD). Preliminary research suggests that these children are at higher risk for being bullied than typically developing peers; however, researchers have not yet explored the nature of these bullying experiences (Little, 2002; Wainscot et al., 2008). Research within the general population suggests that bullying experiences are common among Canadian children (35% report victimization) and associated with mental health problems (Molcho et al., 2009; Nansel et al., 2001). Thus far, the impact of victimization on mental health has not been studied among children and youth with ASD.

Objectives: The current study is the first to examine rates of various forms of bullying (physical, verbal, and social) experienced by children and youth with ASD, as well as the impact of victimization on mental health. It is hypothesized that social and verbal forms of bullying will be reported more often than physical forms and that victimization will be associated with internalizing and externalizing mental health problems.

Methods: Participants include 268 parents of children diagnosed with ASD aged 6-18 years old from across Canada (85% boys and 15% girls; mean age = 12.03, SD = 4.64). Participants completed the PREVNet assessment tool (PREVNet Assessment Working Group, 2008) to assess bullying experiences and the Nisonger Child Behaviour Rating Form - Parent Form (NCBRF; Aman, Tasse, Rojahn, & Hammer, 1996) to assess mental health problems among their children.

Results: Roughly 75% of parents reported that their child was bullied at school within the last month, with 45% reporting that bullying has persisted for over one year. Verbal and social bullying were most common; 66% of parents reported one or both of these forms of victimization at least once in the last month and 27% reported occurrence 2-3 times per week. Fewer parents (38%) reported physical victimization at least once in the last month. MANOVA analyses suggest that children with ASD who were bullied in the last month have poorer mental health compared to those who were not bullied [$F(7, 208) = 5.130$, $p < .001$], with the dependent variables including NCBRF overall and subscale scores. Children who were bullied, compared to those who were not, exhibited higher scores on the overall NCBRF ($p < .001$), as well as conduct problems ($p < .05$), insecure/anxious ($p < .001$), hyperactive ($p < .01$), and overly sensitive ($p < .001$) subscales.

Conclusions: As expected, victimization occurred at higher rates among children with ASD when compared to the general population and was most often verbal or social in nature. Further analyses will explore age and gender differences. As predicted, bullying experiences were related to both internalizing and externalizing mental health problems among children and youth with ASD. Further analyses will explore the relative contributions of additional factors (e.g., parent mental health, ASD symptom severity) to mental health problems among children with ASD who are bullied. The results of this research will inform school-based bullying prevention and intervention programs.

118.096 96 Creating Structured Teaching Classrooms: Preliminary Evaluation of a 5 Day Training Model. J. Salt*[1], C. Flint[1], K. Johnsen[1], M. Winnega[2] and B. Leventhal[3], (1)*HAVE Dreams*, (2)*University of Illinois at Chicago*, (3)*New York University & Nathan Kline Institute for Psychiatric Research*

Background:

Teachers who are certified in special education rarely receive specialized training in autism. Our training program is a state-wide, intensive training based on structured teaching principles. It was originally established with consultation from Dr Lee Marcus of TEACCH. Structured teaching is a specific instructional strategy designed to accommodate the characteristic strengths and neuropsychological differences of those with autism.

Our week long, interactive training provides an opportunity to receive in-vivo supervision and feedback from experienced trainers. Through lectures, hands-on construction of visual supports and materials, participants create a classroom and work with children with ASD based on the pyramid model of physical structure, individual schedules, independent work systems, routines and strategies, and visual organization.

Objectives:
This study investigated the preliminary effectiveness of the training model for instructing teachers to set up structured teaching classrooms. The study addressed (i) knowledge of structured teaching gained across the 5 day training period and (ii) the implementation of specific structured teaching strategies following training.
Methods:

(i) Participating teachers and educators (n= 90) who attended the hands on 5 day training workshop completed a structured questionnaire pre and post training.

The questionnaire was developed and piloted by the lead trainers to assess key aspects of structured teaching practice and principles. Answer responses were mixed between fill-in-the blank, open ended and forced choice responses. The final questionnaire had 16 questions, with a maximum total score of 48.

(ii) 3 months into the school year following training, participants were contacted by email and asked to return a survey of structured teaching strategies they implemented in their schools.

Results:

i) T-test revealed that there was a significant ($p<.05$) increase in knowledge of structured teaching scores pre and post training.

2 questions were focused on a re-structure of a visual task and were double scored for accuracy. For these tasks, inter-rater reliability was excellent (96%) as measured by the proportion of agreement between scorers.

ii) A response rate of n= 40 (44%) was achieved for the follow up survey.

Follow up questions indicated that physical structure, visual schedules, work systems and visual tasks were universally implemented by responders. Follow up consultation, directly following training, was requested by 39/40 responders. Direct observation of a small number of classrooms was achieved at follow up (n=5). Self report and direct observation of implemented strategies was 100%, indicating that self report was accurate in a small sample.

Conclusions:

These results indicate the preliminary effectiveness of our training program. Participants significantly increased their knowledge of structured teaching practices by attending our training. Furthermore, once they returned to their home schools they implemented a multitude of structured teaching techniques. Although satisfaction of training was very high, desire for ongoing consultation at follow up is an issue that could be addressed. A more rigorous methodology is needed to extend confidence in these evaluation results.

118.097 97 Evaluation of Autism Ontario's Realize Community Potential Program: Short-Term and Longer-Term Stress in Parents of Individuals with An ASD. K. McFee*[1], J. H. Schroeder[1], J. M. Bebko[1], M. Thompson[2], M. Spolestra[2], K. Stoner[2] and L. Verbeek[2], (1)*York University*, (2)*Autism Ontario*

Background:
Since 1973, Autism Ontario has worked with government leaders towards a vision of "acceptance and opportunities for all individuals with ASD". The Realize Community Potential Project (RCP) was funded by the Province of Ontario beginning in 2006, to directly support parents of children with Autism Spectrum Disorders (ASD). Major goals of the program include: helping reduce stress in the families, and providing long-term support and resources for families. A program evaluation component was also funded to evaluate effectiveness and identify strengths and improvements needed in the program.

Objectives:
One goal of the program evaluation team was to determine if reductions of reported parent stress had occurred in areas where the RCP program has been implemented.

Methods:
Two tools were developed to assess short-term and longer-term stress in parents. The short-term measure quickly evaluates perceived parent stress levels (using a 5-point Likert scale). It was completed by the RCP Coordinator at the beginning and end of a contact. A longer-term stress measure incorporated modifications of existing measures (the Childhood Autism Rating Scales-Parent version and the Family Empowerment Scale). It evaluated parent perceived self-efficacy, perceived ability to navigate the system and act as a child's advocate, severity of child symptoms and stress associated with those symptoms. This survey was given to families during the first contact with an Autism Ontario local chapter. Twelve to eighteen month follow-up is now occurring, with re-administration of the measure. Results will be compared with families from other local chapters where no RCP program is available.

Results:
Short-term Stress -- Parents seeking general information on Autism Ontario, ASDs, or available services in the community showed a reduction in perceived short-term stress ranging from .12 to .93 points on the 5-point scale. Families contacting the RCP coordinator while in crisis showed the greatest reduction in rated stress, from a mean of 4.0 at the start of contact down to a mean of 2.73 (1.27 mean reduction).
Longer-term Stress -- The first round of data summarized are from parents at their initial contact with the RCP chapter. Data after 12-18 months of contact with the RCP chapter, as well as control data from non-RCP chapters are currently being collected. The majority of families rated their child's symptoms as "a little bit" to "quite a bit" stressful. Intellectual impairment and deficits in verbal communication were the symptoms of autism that were associated with the highest stress ratings. The majority of families rated themselves as feeling empowered. The item that was the most endorsed was "I have the right to approve all services my child receives." In a general quality of life question, 64% of families rated themselves as having a positive quality of life, and 14% of families rated themselves negatively.

Conclusions:
Evaluation of funded programs is ultimately a highly cost-effective way to enhance public accountability, by identifying the effective components of programs such as RCP, to guide future program development and to inform future allocation of limited funding resources.

118.098 98 Facilitating Caregiver Adaptation to Autism Spectrum Disorders: The Role of Perceived Control. K. Voss*[1], L. C. Lee[2] and B. Biesecker[3], (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins Bloomberg School of Public Health*, (3)*National Institutes of Health*

Background: Caregivers of children with Autism Spectrum Disorders (ASDs) must confront different struggles as they adapt to having a child with ASD, including finding a diagnosis and proper treatment, and making long-term care decisions [Sicile-Kira, 2004]. This process of adaptation is influenced by several well-studied factors, such as perceived severity, coping strategies, and the age of the child, as well as many less-well-understood factors including perceived personal control (PPC). Currently, most clinical interventions aimed at facilitating adaptation focus on information giving or encouraging the use of problem-focused coping strategies, such as planning for the future. However, for conditions that have unclear causes, prognoses, and recurrence risks, such as ASD, the level of uncertainty surrounding the condition may impact the utility or availability of some of these traditional interventions. Therefore, interest in developing interventions targeted at other factors involved in adaptation, such as perceived personal control, is growing [Berkenstadt, et al., 1999]. A better understanding of how perceived personal control relates to adaptation is needed in order to identify whether and how to target control perceptions through new clinical

interventions aimed at enhancing adaptation.

Objectives: This study aimed to 1) describe the control beliefs of caregivers of children with ASD and 2) determine how those beliefs relate to adaptation.

Methods: Caregivers (N=324) were recruited through support groups and websites. Caregivers rated the amount of control they had over five domains of their child's ASD (daily symptoms, long-term course, medical care and treatment, general, and control by others), and answered open-ended questions about control. Participants also completed the Mishel Uncertainty in Illness Scale, the Ways of Coping Checklist, and a newly-developed measure of adaptation.

Results: Caregivers in our study reported having moderate amounts of control over each domain, with significantly higher control perceptions in medical care and treatment ($p<0.05$). Multiple regression analyses suggested that control in general and over the long-term course were predictive of a caregiver's overall adaptation ($p<0.01$ for both), as were the time since a child's diagnosis, caregiver's sense of self-efficacy, household income, and child's age at first symptoms ($p<0.01$ for all).

Conclusions: Overall, our results support the importance of control in the process of caregiver adaptation, and suggest possible targets for interventions. In particular, they suggest that the relationships of caregivers with providers may play a critical role in the amount of control they believe that others have over their child's ASD (so-called participatory control), which may facilitate the process of adaptation. Our results also suggest the need to focus on facilitating gains in long-term control, and provide support for Shelley Taylor's Cognitive Theory of Adaptation (Taylor, 1983), which suggests that control beliefs need not be consistent with actual control in order to be adaptive. In particular, the data suggests that long-term control beliefs are strongest in caregivers who believe that the treatments and therapies that they are doing on a daily basis will give their child the best long-term outcomes.

Further studies are needed to develop and test interventions that target PPC.

118.099 99 Parent-Teacher Concordance On the Social Responsiveness Scale for Children with a Putative Diagnosis of ASD. E. M. Reisinger*[1], M. Xie[2], D. S. Mandell[2], S. Shin[1], A. D. Sherman[2] and C. M. Harker[2], (1)*University of Pennsylvania*, (2)*University of Pennsylvania School of Medicine*

Background: The Social Responsiveness Scale (SRS) was developed as a screener and diagnostic aid for individuals on the autism spectrum. While it was originally developed as a parent-report instrument, Constantino et al. (2007) published a study confirming its validity as a teacher report measure. This validation study included a sample of 577 children recruited from the Washington University School of Medicine and the Autism Genetic Resource Exchange. Parent-teacher responses were highly concordant ($r=0.72$); high scores by both teacher and parent increased the diagnostic accuracy of the SRS (Constantino et al., 2007). Generalizability of the findings may be limited, however, due to the lack of socio-economic diversity in their sample and the need for replication.

Objectives: To examine parent-teacher concordance on the SRS with a racially and economically diverse sample of children in autism support classrooms in a large, urban setting, and child and family characteristics associated with concordance.

Methods: The sample included 120 students enrolled in 38 kindergarten-second grade autism support classrooms in a large, urban school district. All subjects received a primary diagnosis of autism and an autism support placement from a school district psychologist prior to enrollment in this study. Subjects were administered the Autism Diagnosis Observation Schedule (ADOS) as a confirmatory measure. The Social Responsiveness Scale (SRS) was completed by parents and teachers at two points during the school year.

Results: Data analyses are ongoing.Preliminary results suggest no significant correlation between teacher and parent report on the SRS raw scores ($r=0.29$, $p=0.01$).Further analysis suggests that 15%

of the sample does not meet research criteria for an ASD. For children meeting criteria, the correlation between parent and teacher scores is moderate, but highly significant (r=0.34, p=0.008).For children not meeting criteria, the correlation between the two ratings were very strong, although not statistically significant (r=0.84, p=0.81). In this group, parents consistently rated their children as more impaired than teachers did. Analyses to be presented will further address factors associated with parent-teacher agreement.

Conclusions: Among children meeting research criteria for ASD, there was good parent-teacher agreement on the SRS in this diverse, primarily low SES group, suggesting the broad utility of the SRS. Among children not meeting research criteria for ASD, agreement was poor, with parents consistently making more severe ratings. Among other reasons, discordance may be due to parents' concerns about loss of services or misattribution of symptoms.

Invited Educational Symposium Program

119 Future Approaches to the Psychopharmacology of Autism

Moderator: E. Anagnostou *Bloorview Research Institute*

Current approaches to pharmacological research of ASD have included exploring phenotypic similarities between autism and other neurodevelopmental/ neuropsychiatric disorders and testing medications effective in such disorders in individuals with ASD. The approach has achieved some success, especially regarding reduction of interfering behaviors. It has also faced some limitations; most notably, it has not produced significant results in treatment of core symptom domains; not generated data to support the use of medications for skill acquisition; nor contributed to our understanding of the disorder. This IES will discuss alternative approaches to neuropsychopharmacology research based on the fact that new advances in basic science provide a series of molecular targets that link to the pathophysiology of autism. The three talks will introduce the concepts of translation and back translation as they relate to clinical trials, illustrate such translation using the Fragile X story, and expand the concept of back-translation using the oxidative stress theory of autism.

119.001 Approaches to the Neuropsychopharmacology of Autism. E. Anagnostou*, *Bloorview Research Institute, Bloorview Kids Rehab*

The goal for this talk is to discuss the translation potential in psychopharmacology research. The speaker will start by reviewing current evidence for use of different classes of psychopharmacologic agents in autism. She will then review basic science data that may in fact support the use of some of these compounds in autism and highlight that although we did not get to such medications through a translational route, translational evidence may exist to support their use and may suggest alternative symptom targets to be tested. She will then explore the potential that by studying the mechanism of treatment response and side effect generation, we have the potential of elucidating the neurobiology of autism (introduce the concept of back-translation)

119.002 Translation in psychopharmacology research: from animal model to clinical trials; the FMR1 story. R. Carpenter*, *Seaside Therapeutics*

To date, translational drug discovery for autism has been unproductive largely due to the lack of mechanistic understanding as well as the absence of predictive animal models. Translational research focused on single gene disorders, such as Fragile X Syndrome, is changing this paradigm through scientific exploration focused on identifying the fundamental pathophysiology and application of this knowledge to develop targeted therapeutics. This talk will demonstrate this point by using Fragile X as an example of the potential for translational research in ASD. Recent discoveries have revealed that a molecular pathway, the mGluR5 signaling cascade, is dysregulated in a specific disorder of brain development – Fragile X syndrome. With this knowledge, further research has provided insights for translating these discoveries into novel medications designed to normalize the function of this pathway. This approach holds promise for developing disease modifying therapeutics that target the fundamental pathophysiology of autism

119.003 Back-translating from clinical trials to neurobiology of disease. A. Y. Hardan*, *Stanford*

Causes of autism remain elusive yet clearly combine genetic, developmental, and environmental factors. A pathway that has received little attention is the anti-oxidative

system which plays a key role in cell metabolism. This talk will focus on the concept of back-translation and will use the oxidative stress hypothesis as a model. Specifically, the speaker will use data from a double-blind, randomized, placebo-controlled trial of oral N-acetylcysteine (NAC), a potent glutathione prodrug, to explore its mechanism of response, and as such attempt to contribute to our understanding of the relationship between oxidative stress and neurobiology of autism.

Clinical Phenotype Program
120 Clinical Phenotype 1

120.001 Trajectory of Early Development: ASD, Broader Phenotype, Typical Development. R. Landa[1], A. Gross*[2], E. Stuart[3] and A. Faherty[1], (1)*Kennedy Krieger Institute*, (2)*The Johns Hopkins Bloomberg School of Public Health*, (3)*Johns Hopkins Univ. School of Public Health*

Background: Prospective and retrospective studies indicate that language development is an area of vulnerability in children with autism, with trajectories characterized by regression in 30-50% of cases. Also, there is evidence for an intermediate phenotype associated with autism, where trajectory of language and social development appears slower than in typical development, but more robust than in children with autism (Landa et al., 2006).

Objectives: To examine latent trajectories across multiple developmental systems in order to identify patterns of growth in children with and without autism.

Methods: Participants were assessed with the Mullen Scales of Early Learning at 6, 14, 18, 24, 30, and 36 months of age. Dependent variables: Visual Reception, Fine and Gross Motor, Receptive and Expressive Language standard scores (Gross Motor norms not available at 36 months). Outcome classifications at 36 months of age included: Autism Spectrum Disorder (ASD; n=59); Intermediate Phenotype (IP, involving language or social delay; n=36); Non-IP (n=121 siblings of children with autism; n=49 low risk controls).

Latent growth curve models were used to study child-specific patterns of performance. A 3-class model was favored. Latent class membership was then related to clinical outcomes through regressions of latent classes on indicators for clinical diagnoses. The most likely latent class membership for an individual is based on posterior probabilities of being in a certain latent class, which suggested good separation between the classes.

Results: Class 1 consisted of an expected proportion of 60% of the sample, and was characterized by stable and normal development in all domains until 18 months of age, after which there was substantial acceleration in all areas except motor (which decreased by .5 standard deviations). This class was comprised of 60% of the non-IP group, 75% of the IP group, and 52% of the ASD group.

Class 2 consisted of another 28% of children; it was characterized by rapid development in all domains through 18 months, followed by stabilization of growth rate relative to gain in age (except motor, which showed disproportionate slowing in relative to age gain). This class consisted of 40% of the non-IP group, 17% of the IP group, and one child with ASD.

Class 3 was characterized by slowed development in all domains, and consisted of 0 children from the Non-IP group, 8% of the IP group, and 46% of the ASD group).

ASD diagnosis increased the odds of assignment to class 3 relative to class 1 (OR=40, $p<0.001$) or class 2 (OR=43, $p<0.001$). Outcome classification of 'Intermediate Phenotype' did not influence odds of assignment to class 2 versus class 1 (OR=-0.76, $p=0.33$).

Conclusions: About half of children with ASD are likely to have slowing in development beginning during infancy and continuing through the third birthday. Children with an Intermediate Phenotype involving language and/or social delays are likely to show a burst in language and cognitive development beginning at 24 months. The common practice of combining Visual Reception and Fine Motor scores to estimate Nonverbal

Developmental Quotient is not supported by the trajectories identified herein.

120.002 A Scale to Assist the Diagnosis of Autism Spectrum Disorders in Adults: (RAADS-R) An International Multi-Center Standardization Study. R. A. Ritvo*[1], E. R. Ritvo[2], M. J. Ritvo[3] and D. Guthrie[4], (1)*Yale University School of Medicine*, (2)*UCLA School of Medicine, Professor Emeritus*, (3)*Yale University*, (4)*UCLA School of Medicine*

Background: The initial version of the Ritvo Autism Asperger Diagnostic Scale (RAADS), designed to assist the diagnosis of Autism Spectrum Disorders (ASD) in adults (18 years and older), contained 78 questions. Published data (1,2) demonstrated it to be reliable, sensitive, and specific in a limited number of subjects. Questions assessed developmental pathology in three symptom areas: language, relatedness, and sensory-motor (following DSM IV-TR criteria). After critical review, a new 80-item version was developed (RAADS-R) with the addition of two questions, several word clarifications and the addition of a circumscribed interests question domain.

Objectives: To present the results of the international multi-center standardization study of the new 80-item version, the RAADS-R.

Methods: 200 ASD subjects were diagnosed at nine medical centers, in four countries, by these research criteria: 1) A clinical interview (must meet each center's criteria). 2) ADI/ADOS or at least ADOS module 4 to assess validity. 3) Standardized IQ test. 4) Constantino SRS-A in a subset of subjects to assess validity. 5) Repeat testing in 50 subjects, a mean of 15 months later, to assess reliability. Comparison subjects: 1) 285 Volunteers without a DSM IV diagnosis. 2) 302 Volunteers with current DSM IV TR diagnosis other than ASD.

Results: The RAADS –R is highly valid, reliable, sensitive (.98), and specific (1). Statistical analysis revealed no significant difference between Autistic and Asperger subjects' mean RAADS-R scores. Test-retest results showed no significant differences in scores in both groups. Cronbach's alpha coefficients were computed for each of the question domains and were satisfactory. Factor analysis and Ancova results will be reported.

Conclusions: The RAADS-R is a highly valid and reliable instrument used to assist clinicians diagnosing adults 18 and older with ASD. The RAADS-R demonstrates higher sensitivity with individuals who have insight. It is less sensitive in younger subjects, 18-21 year-olds who show a tendency to deny symptoms. Also, it appears that more affected individuals are less likely to be accurate reporters. This needs to be studied further. Translations of the RAADS-R into Swedish and Japanese are completed and standardization studies are nearing completion. Translations into Hindi and French are in early stages.

Participating centers are: Yale, USA; Mt. Sinai, USA; University of Utah, USA; Monash University, Australia; UCLA, USA; Griffith University, Australia; ASPECT, Australia; Geneva Center, Canada; King's College, England; Karolinska Institute, Sweden; Hamamatsu University, Japan.

References: 1) A Scale to Assist the Diagnosis of Autism and Asperger Disorder in Adults (RAADS): A Pilot Study. Ritvo RA, Ritvo ER, Guthrie D, Yuwiler A, Ritvo MJ, Weisbender J. Autism Dev Discord (2008) 38: 213-223. 2) Clinical Evidence That Asperger Disorder is a Mild Form of Autism. Riva Ariella Ritvo, Edward R. Ritvo, Donald Guthrie, Max J. Ritvo Comprehensive Psychiatry, (2008) Volume 49, Issue 1, January-February.

120.003 Combining Information From Multiple Sources in the Diagnosis of Autism Spectrum Disorders Using the New ADI-R Algorithms for Toddlers From 12 to 47 Months of Age. S. H. Kim*[1] and C. Lord[2], (1)*University of Michigan Autism and Communication Disorders Center (UMACC)*, (2)*University of Michigan*

Background: Diagnostic instruments such as the Autism Diagnostic Interview-Revised (ADI-R) and Autism Diagnostic Observation Schedule (ADOS) are intended to be used together, and researchers have made a systematic attempt to evaluate how information from those two instruments should be combined together (Risi et al., 2006). However, the ADI-R algorithm used in the previous study was a "*2 years to 3 years*

and 11 months algorithm" and previous studies have shown that this algorithm resulted in relatively poor sensitivity and specificity for the comparison between toddlers and preschoolers with Autism Spectrum Disorders (ASD) and those with nonspectrum disorders (NS) (Lord, Storoschuk, Rutter, & Pickles, 1993; Ventola et al., 2006). Thus, in this study, we used newly developed ADI-R algorithms that have shown better predictive validity than the preexisting algorithm (Kim & Lord, in prep).

Objectives: The purpose of this study is to propose standard criteria for the combined use of the ADI-R and ADOS to diagnose cases of ASD for toddlers from 12 to 47 months of age.

Methods: Analyses were conducted using a dataset of the ADI-R and ADOS psychometric scores for 731 children aged from 12 to 47 months (515 cases with ASD; 142 with NS; 74 from children with typical development). Since the new algorithms were developed separately for different groups of children divided by their chronological age and language level, the cases were divided into three groups to examine different standard criteria using information from the ADI-R and/or ADOS. The three groups were: all children from 12 to 20 months of age and nonverbal children from 21 to 47 months; children with single words from 21 to 47 months; and children with phrase speech from 21 to 47 months. The criteria tested in this study were: meeting the cutoff scores for ASD on 1) *both* the ADOS *and* ADI-R; 2) *either* the ADOS *or* ADI-R; 3) the ADOS *alone*; 4) the ADI-R *alone*.

Results: For all three groups of children, the first criteria of meeting the cutoffs for *both* the ADOS *and* ADI-R resulted in well balanced, high sensitivity and specificity (ranging from 71-88% sensitivity and 70-92% specificity by developmental cells). When the second criteria (meeting the cutoffs on *either* the ADOS *or* ADI-R) was used, sensitivity was very high (ranging from 96-98%) but specificity was relatively poor (48-73%). Similarly, when the ADOS was used alone, sensitivity was very high (ranging from 94-98%) but specificity was poor (59-79%). When the ADI-R was used alone, sensitivity and specificity were well balanced but both were lower than those of the first criteria.

Conclusions: ASD diagnostic criteria using combined information from *both* the ADI-R *and* ADOS better reflect clinical judgments of ASD than any single instrument for toddlers under 4 years of age.

120.004 Diagnostic Features at Time of First Diagnosis in Young Toddlers with Autism Spectrum Disorder: Clinical Observations and Parent Report. V. P. Reinhardt* and A. M. Wetherby, *Florida State University*

Background:

Children are receiving diagnoses of autism spectrum disorder (ASD) at earlier ages and the American Academy of Pediatrics recommends that all children be screened for ASD at 18 and 24 months. Therefore, research about the early diagnostic features of ASD is increasingly important. Since DSM-IV-TR criteria were developed before the diagnosis of toddlers was common, it is important to examine the utility of DSM-IV-TR criteria with a young sample of toddlers with ASD.

Objectives:

The purpose of this study was 1) to describe the diagnostic features of a sample of 18-24 month old toddlers with ASD using DSM-IV-TR criteria, and 2) to compare clinical observation and parent report of core diagnostic features of ASD.

Methods:

Children were recruited by the FIRST WORDS® Project from a general population sample using a broadband screener for communication delays followed by an autism-specific screener. Children participating in this study were diagnosed with ASD (n=60) before 24 months of age. Measures of early diagnostic features of ASD were derived from each child's initial diagnostic assessment which included a clinical observation using the *Autism Diagnostic Observation Schedule*-Toddler Module (ADOS-T: Luyster et al., 2009) and parent report of symptoms using the *Early Screening for Autism and Communication*

Disorders (ESAC; Wetherby, Woods, & Lord). Items from the ADOS-T and ESAC were delineated by DSM-IV-TR domains and diagnostic features.

Results:

A preliminary analysis was completed on 47 children between 15-24 months (*M*=19.3, *SD*=1.76). The majority of children showed three of the diagnostic features in the DSM Social Interaction domain— shared enjoyment (95%), social-emotional reciprocity (95%), and multiple nonverbal behaviors (94%), but difficulty with peer relationships was infrequent (13%). In the Communication domain, the majority of children showed all four diagnostic features-spoken language (98%), symbolic play (98%), reciprocal communication (92%) and repetitive language (83%). In the Repetitive Behavior domain, restricted interests (95%), rituals and routines (78%) and preoccupation with parts of objects (70%) were common while stereotyped mannerisms (43%) were less frequent. Agreement between parent and clinical observations for diagnostic features was examined by DSM domain. Preliminary results suggest fair to moderate agreement between parent and clinician reports in the Social and Communication domains. Agreement between parent and clinician report was weaker in the Repetitive Behavior domain.

Conclusions:

Preliminary analyses indicate that these toddlers with ASD exhibited diagnostic features in all three DSM-IV-TR domains. Features in Social Interaction and Communication domains were most common while Repetitive Behavior features were less frequent but present in most of these toddlers. As expected, difficulty with peer relationships was not a common feature in toddlers with ASD. These findings add to existing research examining the early ASD phenotype and document the utility of DSM-IV-TR criteria for very young toddlers. Further research is needed to examine the frequency of these diagnostic features in toddlers without ASD to ensure specificity of diagnostic criteria. These results provide important information for consideration in the upcoming revision of diagnostic criteria for the DSM-V.

120.005 Evaluation of the DISCO-11: Comparison to ADOS, SCQ, and Clinical Classification in Young and Low Functioning Children.

J. P. W. Maljaars*[1], I. L. J. Noens[2], E. M. Scholte[3] and I. A. van Berckelaer-Onnes[1], (1)*Leiden University*, (2)*Katholieke Universiteit Leuven*, (3)*Universiteit Leiden*

Background: The Diagnostic Interview for Social and Communication Disorders – version 11 (Wing, 2003) is a standardized, semi-structured and interviewer-based schedule. The DISCO can be used to collect information about developmental history and description of skills and behavior and provides a classification based on different classification systems (e.g. ICD-10/DSM-IV). Inter-rater reliability of the DISCO-10 proved to be high (Leekam et al., 2002; Wing et al. 2002) and classification on ICD-10 algorithm is significantly related to clinical diagnosis (Leekam et al., 2002).

Objectives:
1) To explore the sensitivity and specificity of DISCO-11 classifications in differentiating children with a clinical ASD classification from children with intellectual disability (non-ASD) and young, typically developing children;
2) To compare DISCO-11 results with Autism Diagnostic Observation Schedule (ADOS) and Social Communication Questionnaire (SCQ) results;
3) To determine the influence of age, non-verbal intelligence and level of language development on DISCO-11 results.

Methods: The DISCO-11, ADOS (module 1 or 2, revised algorithms) and SCQ were administered from a Dutch sample of 100 children comprising 45 children who had received an independent clinical AD or ASD diagnosis before participation in this study (mainly children with an official AD classification, both with and without intellectual disability; age: 2-12yrs), 20 children with intellectual disability (ID) (non-ASD; age: 5-12yrs) and 35 children with typical development (TD) (age: 2-5yrs). The developmental level of all children ranges from 2 to 6 years.

Results: Preliminary results *(n*=75: 45 ASD, 15 ID, and 15 TD*)* indicate high sensitivity

and specificity for DISCO-11 classifications based on ICD-10 algorithms in differentiating ASD from non-ASD conform the clinical classification. The specificity in relation to the ID group was somewhat lower than in relation to the TD group. The agreement between DISCO-11 and ADOS classifications was substantial (_=.83, p<.001). However, the agreement with the SCQ classifications was only moderate (_=.46, p<.001). The correlations between raw total scores of the DISCO algorithm, ADOS algorithm and SCQ are high (ADOS: r=.90, p<.001; SCQ: r=.85, p<.001). The relation between DISCO and ADOS social/communication domain scores is much higher than between the repetitive behavior domain scores, but are both significant (r=.91, p<.001; r=.61, p<.001). Age, non-verbal intelligence and level of language development are not related to total scores of the DISCO algorithm and DISCO classifications (p>.05). Within the ASD group, chronological age has a significantly negative correlation with the DISCO social domain score (r=-.50; p=.001).

Conclusions: Based on preliminary results the DISCO-11 seems to make an accurate differentiation of AD from non-ASD and is not sensitive to variability in age, non-verbal intelligence and language ability. Although, the interviewers and raters were blind to the previous diagnosis before the DISCO-interview, some parents can have referred to the diagnosis during the conversation. If so, this can have biased the outcomes. The results support the utility of the DISCO-11 as an effective diagnostic tool for young and low functioning children. However, more research to determine the accurateness for the broader autism spectrum is necessary.

120.006 Onset Patterns Prior to 36 Months in Autism Spectrum Disorders. L. Kalb* and R. Landa, *Kennedy Krieger Institute*

Background: Observational data from the past several decades suggest variation in the onset of autism symptomatology. At present, the relationship between symptom onset pattern and outcome in children with an Autism Spectrum Disorder (ASD) remains unclear.

Objectives: The overarching goal of the present study was to investigate differences in current functioning among children with three different autism onset patterns: plateau, regressed, and those without regression or plateau. More specifically, we examined present group differences in parental report of milestone achievement, autism symptom severity, autism diagnosis, presence or absence of cognitive impairment and phrase speech, and behavioral-educational outcomes.

Methods: Cross-sectional data were collected from parents of children aged 3–17 years with an ASD who were recruited through a U.S-based online research database. Parental report of developmental characteristics was assessed through a parent questionnaire and autism symptoms were measured via the *Social Responsiveness Scale* (Constantino et al., 2003) and *Social Communication Questionnaire* (SCQ; Western Psychological Services, Los Angeles). Exclusion criteria for this study included parent report of developmental concerns or loss of skills after their child reached 3 years of age, children that did not meet a cutoff score of ≥15 on the SCQ (to screen for an ASD), or those with a previous diagnosis of tuberous sclerosis and/or Fragile X. The final study sample totaled 2,720 participants. Multiple Linear and logistic regression models were then built to examine outcomes while controlling for demographic variables.

Results: Children of parents who reported a loss of skills were found to have later parental concerns, earlier first words and steps, delayed phrase speech and toilet training compared to children without regression or plateau (p<.001). Children with a developmental plateau had later parental concerns (p<.001). Both children with regression (39%) and plateau (17%) demonstrated elevated autism symptom scores, earlier age at diagnosis, and an increased risk for currently being non-verbal (OR 1.92; OR 1.55), diagnosed with autistic disorder (OR 2.23; OR 1.35), in a supportive academic setting (OR 1.85; OR 1.41) and having a 1:1 classroom aide within that setting (OR 1.63; OR 1.44) compared to children without regression or plateau (all p<.05).

Conclusions: Results from the multivariate analyses indicated that children with regression have a distinct developmental pattern marked by less delayed early development; however, following regression, these children evidenced elevated autism symptom scores and an increased risk for poorer outcomes when compared with their affected peers. These findings were particularly robust for the children of parents who reported the regression as severe. For children with a plateau or developmental halt, a very under researched group, several alarming outcomes emerged from the data. These findings hold important implications to theory, policy, and practice.

120.007 Parental Depression Appears to Influence Reporting of Offspring ASD Symptoms. T. A. Bennett*[1], P. Szatmari[2], S. Georgiades[2], A. P. Thompson[2], E. Duku[2], S. E. Bryson[3], E. Fombonne[4], P. Mirenda[5], W. Roberts[6], I. M. Smith[7], T. Vaillancourt[8], J. Volden[9], C. Waddell[10] and L. Zwaigenbaum[9], (1)*Offord Centre for Child Studies, McMaster University*, (2)*McMaster University*, (3)*Dalhousie University/IWK Health Centre*, (4)*Montreal Children's Hospital*, (5)*University of British Columbia*, (6)*University of Toronto*, (7)*Dalhousie University & IWK Health Centre*, (8)*University of Ottawa*, (9)*University of Alberta*, (10)*Simon Fraser University*

Background: Maximizing measurement validity is an important aim in research. Parents play an essential role as informants in the diagnostic process and it is possible that certain parental characteristics may influence measurement error. Several studies have found parental depression to bias reports of child behavior problems however to date there have been no studies of this issue in autism spectrum disorders (ASD).

Objectives: This study aimed to compare associations between parental depression and measures of autistic symptoms in preschoolers with ASD. Hypotheses: 1) Parental depression symptoms will be more strongly associated with parent-report questionnaire of offspring ASD symptoms than with scores on parent interview, and least strongly with researcher observation; 2) Parental depression symptoms will be positively associated with measurement error on the parent-report questionnaire of offspring ASD symptoms.

Methods: Time 1 data were obtained from a longitudinal study of preschoolers aged 2-4 newly diagnosed with ASD. Participants who completed ADOS Module 1 and for whom data were available for all relevant measures were included (n=224). Child ASD symptoms were assessed using the Social Responsiveness Scale (SRS), a parent-report questionnaire, the Autism Diagnostic Interview-Revised (ADI-R), a semi-structured parent interview and the Autism Diagnostic Observation Schedule, a semi-structured assessment. Parents also completed the Symptoms Checklist-90.

Results: Two sets of structural equation models were developed. In Model 1: parent depression, SRS, ADI-R and ADOS were each represented by a latent variable. The gradient of strength of association between parental depression and each measure was assessed by comparing the size of the regression weight for paths between parent depression and each measure, and the changes in goodness of fit when the paths were constrained to equal each other. Model 2 comprised a latent variable representing parental depression and another one representing ASD symptoms with SRS, ADI-R and ADOS totals as indicators. Parental depression was correlated with the error term for the SRS as well as with the child ASD symptom latent variable. Model 1 demonstrated a gradient of strength of association; the regression coefficient for the path from parent depression to the SRS variable (_=0.35; $p < 0.001$) was twice as large as that to the ADI-R (_ = 0.15, $p>0.05$) and the path from depression to ADOS was not significantly different from zero (_ = 0.08; n.s.). The model demonstrated an excellent fit to the data (CFI = 0.95, RMSEA = 0.06; fit worsened significantly when all paths were constrained to equal each other (__2=17.2(2), $p < 0.01$). In Model 2, the correlation between parental depression and the error term for the SRS ($r= 0.29$, $p < 0.001$) was statistically significant and larger than that between parental depression and child ASD symptoms ($r=0.16$,$p < 0.07$); fit worsened significantly when it was constrained to equal zero (__2=17.1 (1), $p < 0.01$).

Conclusions: Parental depression may significantly influence reporting of severity of autistic symptoms in their children. This study reinforces the importance of obtaining multiple-informant reports of ASD symptoms.

120.008 Using the Childhood Autism Rating Scale (CARS) to Diagnose Autism Spectrum Disorders. C. Chlebowski*, J. Green, M. L. Barton and D. A. Fein, *University of Connecticut*

Background: The Childhood Autism Rating Scale (CARS) is a widely used rating scale for the detection and diagnosis of autism. Although it is highly sensitive, the CARS may over-diagnose young intellectually disabled children as having autism (Lord, 1995). Another limitation of the CARS is the lack of an empirically based Autism Spectrum Disorder (ASD) cutoff. A cutoff of 30 is recommended for Autistic Disorder, but there is no generally accepted or validated cutoff for ASD. Although significant group differences on CARS total scores have been reported among clinical groups (Perry, Condillac, Freeman, Dunn-Geier, & Belair, 2005) the CARS is not designed to distinguish PDD-NOS from Autistic Disorder, or the ASD spectrum from non-spectrum (Perry et al., 2005). Identifying an ASD cutoff on the CARS that would include children with PDD-NOS may make the measure more useful.

Objectives: To investigate the ideal CARS cutoff for a diagnosis of Autistic Disorder and to investigate the utility of the CARS as a tool for ASD diagnoses in samples of 2-year-old and 4-year-old children referred for possible autism.
Methods: Participants were 376 two-year-old and 230 four-year-old children who were screened with the M-CHAT (Robins, et al., 2001), and evaluated at age 2 (mean age=26 months) and/or age 4 (mean age=54 months) using the ADI-R, ADOS, and the CARS, and were given diagnoses from clinical judgment based on DSM-IV criteria. Sensitivity, specificity, and positive and negative predictive values were calculated to determine optimal CARS cutoff scores for a diagnosis of Autistic Disorder as well as for an ASD diagnosis as compared to a gold standard diagnosis based on clinical judgment.

Results: Consistent with Lord (1995), the optimal cut-off score to distinguish Autistic Disorder from PDD-NOS in the two-year-old sample was 32, with a sensitivity (relative to Clinical Best Estimate diagnosis) of 0.79 and a specificity of .81. The optimal cut-off score to distinguish Autistic Disorder from PDD-NOS in the four-year-old sample was 30 with sensitivity of .86 and a specificity of .80. The optimal cut-off score to distinguish ASD from non-ASD in both samples was 25.5, with a sensitivity of .92 and a specificity of .89 in the two-year-old sample and a sensitivity of .82 and a specificity of .95 in the four-year-old sample.
Conclusions: Results suggest that, in a two-year-old sample, a cutoff of score of 32 more accurately distinguishes Autistic Disorder from PDD-NOS than the current cutoff of 30. Findings confirm the utility of the CARS in distinguishing Autistic Disorder from PDD-NOS, and distinguishing ASD from other developmental disorders and typical development and suggest that an ASD cutoff around 25, which is in common clinical use, is valid.

Epidemiology Program
121 Epidemiology 2

121.001 Racial Disparities in Community Identification of Autism Spectrum Disorder Overtime; Metropolitan Atlanta 2000-2006. V. G. Jarquin*[1], L. D. Wiggins[2], L. A. Schieve[2] and K. Van Naarden Braun[2], (1)*CDC*, (2)*Centers for Disease Control and Prevention*

Background:

Past research indicates Non-Hispanic black (NHB) children are less likely than Non-Hispanic white (NHW) children to have an autism spectrum disorder (ASD) diagnosis, even if they appear to meet the DSM-IV criteria for the disorder.

Objectives:

This study examined differences between NHB and NHW children according to ASD diagnoses and ASD educational eligibility noted in health and educational records.

Methods:

Participants were 1273 8-year-old children included in the Metropolitan Atlanta Developmental Disabilities Surveillance Program (MADDSP) who were classified as an ASD surveillance case based on standardized record-review of health and education records during four surveillance years (2000, 2002, 2004, and 2006). Children were placed in one of six mutually exclusive categories based on specificity of diagnoses and placements noted in health and educational records: (1) children with autistic disorder, (2) children with Asperger's disorder without autistic disorder, (3) children with Pervasive Developmental Disorder- Not Otherwise Specified (PDD-NOS) without autistic or Asperger's disorder, (4) children with non-specific ASD only (5) children with ASD educational eligibility without documented ASD diagnosis, and (6) children without any of the aforementioned ASD diagnoses/eligibilities specified in surveillance records, but with enough documented ASD behavioral symptoms to warrant inclusion as an ASD surveillance case.

Results:

Total ASD prevalence was higher for NHW than NHB children each surveillance year (12 and 9.5 per 1,000 in 2006, respectively). NHB children were more likely than NHW children to have autistic disorder documented in a record ($p<.05$ in 2002, 2004, and 2006) and to have met public school criteria for autism eligibility ($p<0.05$ in 2002 and 2006). NHB children were consistently less likely than NHW children to have the more general ASDs – PDD-NOS ($p<0.05$ in 2002 and 2006) and Asperger's disorder ($p<0.05$ in all years) – documented in surveillance records. In all years, NHB children with an ASD were significantly more likely than NHW children to have co-occurring intellectual disability (ID). From 2000-2006, the percentage of children with documented autism eligibility decreased significantly for NHW children (from 26%-14%) and diagnosis of autistic disorder increased for NHB children (23%-35%). Documented Asperger's disorder consistently increased for NHW (from 8%-11%) only, although this was not significant in all years. The proportions of NHW and NHB children without documented ASD classification in their records were similar; while there was an overall decrease from 2000-2002, from 2002 onward the proportions overall and by racial/ethnic subgroups were stable (22% and 20% for NHW and NHB, respectively).

Conclusions:

While cases of ASD are increasing for both NHW and NHB children, the types of ASD classifications received by NHW and NHW are consistently different with NHB children less likely to receive an ASD clinical diagnosis on the milder end of the spectrum. Consequently, lack of recognition and diagnosis of ASD symptoms in NHB children with milder ASD could prevent or delay enrollment into intervention services designed to meet the needs of children with ASD. This study illustrates the need for continued professional education on the presentation of milder forms of ASD, especially as it pertains to minority groups.

121.002 Relationship Status Among Parents of Children with Autism Spectrum Disorders: A Population-Based Study. B. H. Freedman*[1], L. Kalb[1], B. Zablotsky[2] and E. Stuart[3], (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins University, School of Public Health*, (3)*Johns Hopkins Univ. School of Public Health*

Background: A large body of research suggests that raising a child with an Autism Spectrum Disorder (ASD) is a uniquely stressful experience for parents (Fisman et al., 1989; Konstantareas & Homatidis, 1989). The demanding nature of parenting a child with ASD can be particularly deleterious to the parents' relationship, causing a significant decrease in marital satisfaction (Bristol et al., 1988). However, it is presently unclear if having a child with an ASD increases the risk for separation among biological parents. While speculation abounds in the mainstream media about increases in separation and divorce for this population, very little empirical and no epidemiological research has addressed either this claim or the unique factors that may contribute to separation of these parents.

Objectives:

1. Examine the association between having a child with a current ASD diagnosis and the relationship status of their parents.

2. Identify factors that contribute to a greater likelihood of a child with ASD living with two biological or adoptive parents.

Methods: Data used for this study were taken from the 2007 National Survey for Child Health (Blumberg et al., 2009). Using children ages 3 to 17 years, our final sample size was 77,911. Survey weights allow the results to generalize to the noninstitutionalized US population of children. The outcome variable of family structure was dichotomized as being either traditional (two parent household, either biological or adoptive) or non-traditional (a two parent household with step-parents, a single mother or father, other relatives, or other family types). A four-stage sequence of survey weighted logistic regression models were developed to examine the association between having a child with a current ASD diagnosis and living in a traditional family, while controlling for potential confounders. Model 1 controlled for basic demographic confounders; Model 2 added maternal characteristics; Model 3 included additional socioeconomic indicators; and Model 4 included co-occurring psychiatric diagnoses in the child (Externalizing, Internalizing, and ADHD).

Results: No association between a child having a current ASD diagnosis and their family structure was identified in the first three logistic models (OR range .98 - 1.06, all $p>.05$). However, this association reached marginal significance when concurrent psychiatric diagnoses were included (OR 1.66, 95% CI (1.03-2.67), $p=.04$).

Conclusions: Results from the analysis found no consistent evidence of an association between a child having an ASD diagnosis and that child living in a traditional versus nontraditional family. Once we control for co-occurring psychiatric disorders, our results show that a child with an ASD is slightly more likely than those without ASD to live in a traditional household. This somewhat counter-intuitive result is likely due to particularly low probabilities of living in traditional households for children with those other disorders, regardless of whether or not they have ASD. In fact, exploratory analyses suggest that having ADHD, Externalizing, and Internalizing disorders are more strongly related to the probability of not living in a traditional household than is ASD. Findings from this study hold important implications to both research and intervention for families of children with ASDs.

121.003 Diagnostic Practices and Awareness of Autism Among Indian Pediatricians: A Decade of Data. T. C. Daley*, *Westat*

Background: As in many countries, pediatricians in India are an early point of contact for families of young children with autism. Due to the relatively small number of psychologists and child psychiatrists, pediatricians represent a critically important source for obtaining a diagnosis. Correspondingly, their practices may be directly associated with the increase in children who have received a diagnosis in recent years. In the absence of epidemiological studies in India, reported beliefs and practices from professionals can illustrate trends in the diagnosis of autism.

Objectives: This study examined beliefs about autism and characteristics considered in making a diagnosis among a national sample of pediatricians in India, drawing comparisons to a similar sample from 1998.

Methods: All members of the Indian Academy of Pediatrics were invited to receive free informational materials (posters, brochures, and a book of frequently asked questions) and were requested to complete a survey. Participants were asked about their location and years of practice; number of cases seen and diagnosed; recommendations upon diagnosis; opinions about 26 statements about autism; and were asked to indicate which characteristics they considered necessary, helpful but not necessary, and not helpful in making a diagnosis of autism. Responses were received from 584 pediatricians.

Results: Participants had an average of 16.7 years of experience (SD = 10.6). They reported seeing a mean of 23.8 cases during

their career (*SD* = 43.9) and diagnosing a mean of 12.8 (*SD* = 24.4) cases. This is approximately three times the number of cases seen and twice the number of cases reportedly diagnosed by pediatricians in 1998 ($p < .0001$ for both). Among pediatricians who have diagnosed at least one child, significantly more recommend special education (66%; $\chi^2=4.188$, $p < .05$) and significantly fewer recommend medication (23%; $\chi^2=5.269$, $p < .05$) as compared to a decade ago. Pediatricians reported an average of 8 characteristics they considered necessary to make a diagnosis; lack of eye contact, lack of social responsiveness and rigid or stereotyped play activities were the three most endorsed items. However, a sizeable percentage of pediatricians also endorsed other characteristics as necessary, such as attention deficits (46%), mutism (33%) and sudden, unexplained mood changes (25%). In addition, a portion of pediatricians agreed with statements such as "emotional factors play a major role in the etiology of autism," (50%), "Autistic children's withdrawal is mostly due to cold, rejecting parents" (30%) and "Autistic children do not show social attachments, even to parents" (70%). Nearly the entire sample (96%) agreed that autism is under-recognized and often missed in general practice and that "there is a lack of awareness regarding Autism among professionals in this country" (97%).

Conclusions: Awareness of autism among pediatricians in India has improved considerably over the past decade; physicians report significantly more direct experience with children with autism than in the past. Preliminary descriptive results suggest that many beliefs considered outdated in the West are also on the decline in India, although others persist. These data suggest critical areas to target in order to improve diagnostic practices.

121.004 Features of Autism Spectrum Disorders Vary by Race and Ethnicity. U. Obi*[1], L. C. Lee[1], K. Van Naarden Braun[2], L. D. Wiggins[2], C. E. Rice[3], C. DiGuiseppi[4], J. Nicholas[5], F. J. Meaney[6], L. King[5], J. Charles[5], E. Giarelli[7] and M. Yeargin-Allsopp[2], (1)*Johns Hopkins Bloomberg School of Public Health*, (2)*Centers for Disease Control and Prevention*, (3)*National Center on Birth Defects and Developmental Disabilities*, (4)*University of Colorado, Denver*, (5)*Medical University of South Carolina*, (6)*The University of Arizona Health Sciences Center*, (7)*University of Pennsylvania*

Background: One of the most challenging aspects in diagnosing Autism Spectrum Disorders (ASD) is the wide heterogeneity of features in individual children. Some features such as inattention/hyperactivity or intellectual disability that are associated with the ASDs are not included in current diagnostic algorithms. These ASD-associated features (AAF) are rarely studied and their distribution in ASD cases is therefore poorly understood. These features may differ across characteristics such as race/ethnicity, socioeconomic status, gender, or cognitive functioning. Examining the distribution of AAF associated with ASD among racial/ethnic groups may further our understanding of the differences among children with ASD and improve community identification of this disorder. Objectives: To examine differences in ASD associated features according to racial/ethnic sub-populations using a population-based surveillance system. Methods: Utilizing data from the Autism and Developmental Disabilities Monitoring (ADDM) network, we analyzed AAF among 4325 eight-year-old children, born between 1992 and 1998, who met the ASD case definition used by the ADDM network. Outcomes included 12 documented AAF, including behavioral, mood, and developmental characteristics. Race/ethnicity was the independent variable of interest. We analyzed data using logistic regression stratified by level of cognitive functioning to determine whether race/ethnicity predicted the presence of each of the 12 AAF. Results: Of the 4325 ASD children, 81.5% were male, 57.6% were White non-Hispanic, 23.2% were Black non Hispanic, and 9.9% were Hispanic. Additionally, 43.1% had IQs >70, 31.3% had IQs ≤ 70 and 25.7% were missing IQ scores in their records. Data on AAF were > 98% complete except for abnormalities in eating/drinking/sleeping (EDS) which rate is lower. For IQ > 70: compared to non-Hispanic White (NHW), Black non-Hispanic children had a significantly higher occurrence of six of twelve AAF: 1) abnormalities in EDS; 2) argumentative, oppositional, defiant, destructive features; 3) delayed motor

milestones; 4) odd responses to sensory stimuli; 5) self-injurious behavior; and 6) temper tantrums. However, they had a significantly lower occurrence in two AAF: 1) uneven cognitive development or cognitive scatter; and 2) staring spells and seizure-like activity. Hispanic children were significantly more likely than NHW children to have an increase in odd sensory responses. For children with IQ ≤ 70, Black non-Hispanic, compared to NHW, had a significantly higher rate of: 1) abnormalities in EDS; 2) delayed motor milestones; and 3) odd responses to sensory stimuli. Compared to NHW children, Hispanic children had a greater occurrence of: 1) abnormalities in EDS; 2) uneven cognitive development or cognitive scatter; 3) aggression; 4) odd responses to sensory stimuli; and 5) self-injurious behavior.
Conclusions: These preliminary analyses indicate that distribution of AAF varies by race/ethnicity, depending upon level of cognitive functioning (i.e. IQ). However, certain AAF were more common among both minority groups compared to NHW children regardless of IQ level: abnormalities in EDS, delayed motor milestones, and odd responses to sensory stimuli. Inclusion of other factors, such as SES, and timing of ASD diagnosis is needed for further analysis.

121.005 Autism and Distribution of Hazardous Air Pollutants at Birth in Southern California. G. Windham*[1], G. King[2], E. Roberts[3] and J. K. Grether[3], (1)*CA Department of Public Health*, (2)*Public Health Institute*, (3)*California Department of Public Health*

Background: The dramatic increase in the number of children reported with autistic spectrum disorders (ASD) has re-focused the search for causes and preventive measures. Non-genetic factors likely explain some of the increase, leading to an interest in environmental exposures. In a previous study, we linked our autism surveillance system for 1994 births in the San Francisco Bay Area to estimated hazardous air pollutant (HAP) concentrations compiled by the U.S. EPA. We found elevated adjusted odds ratios between ASD and higher concentrations at the birth address of several HAPs, including metals and chlorinated solvents.
Objectives: Investigate environmental risk factors for ASD by substantiating prior results in another geographic area of California and another time period.
Methods: Our target population was the nearly 700,000 singleton births occurring during 1996-98 in the South Coast Air Basin, in which we ascertained 3,386 ASD cases from the statewide Developmental Disabilities Services (DDS) agency. A 5% sample of non-case births that survived to age one were selected as controls (n=30,906), frequency-matched to cases by date of last menstrual period (LMP). The residence at birth was geo-coded and the census tract assigned for linkage to the U.S. EPA 1996 HAPs database. We identified 24 chemicals as potential neurotoxicants, developmental toxicants, and/or endocrine disruptors, as well as focusing on the six prior associated HAPs. Because concentrations of many HAPs were highly correlated, we also combined the chemicals into mechanistic and structural groups, calculating summary index scores. These group scores or individual chemical concentrations were categorized as quartiles and odds ratios (OR) calculated for ASD, adjusting for demographic factors from the birth certificate.
Results: Comparing mean concentrations, cases had slightly higher means than controls for mercury, most aromatic solvents, vinyl chloride, diesel PM, hexane, PAHs and a few other compounds, but lower mean cadmium and manganese means. Focusing on the six compounds of primary interest, most quartile ORs were significantly elevated (1.4-2.1) compared to the lowest quartile, except for cadmium. However, there was little dose-response pattern by quartile. Adjustment for demographics had little effect on the ORs, but including the regional center of case ascertainment reduced them (1.1-1.3), although still significant. Examining the chemical groups, metals showed little association with ASD, whereas the quartile ORs were slightly elevated for aromatic solvents.
Conclusions: Examining HAPs in another region of California with higher concentrations and larger numbers did not replicate the original results. Metals as a group were not associated, but instead aromatic solvents yielded the highest risks. Specific chemicals, including mercury and nickel, were associated

with increased risk of ASD in a threshold type pattern. The magnitude of the associations were reduced when controlling for regional center, a proxy for likelihood of inclusion in DDS, but also geographically based. Examination of HAPs and autism in other areas of the country and with more recent births may shed further light on the potential associations. Studies with biomarkers of environmental exposure would be ideal, but are difficult to conduct unless peri-natal specimens are archived.

121.006 Familial Aggregation of Regression Status and ADOS Parameters Among Individuals with ASD From the AGRE Collection. R. P. Goin-Kochel*[1], A. Abbacchi[2], E. Duku[3] and J. N. Constantino[2], (1)*Baylor College of Medicine*, (2)*Washington University School of Medicine*, (3)*McMaster University*

Background: It is well established that autism is one of the most heritable among behaviorally defined disorders, with concordance rates in monozygotic twins (MZ) ranging from 60—90%, when the criteria are more narrowly or broadly defined, and the rate in dizygotic twins (DZ) at approximately 10%. Concordance rates in non-twin siblings vary between 5—8%. Despite these numbers, identification of etiologically relevant genes in autism spectrum disorders (ASD) has progressed slowly, which has prompted attempts to identify more phenotypically homogeneous subgroups of affected individuals for molecular-genetic analyses. Yet it is not clear whether select grouping variables (e.g., presence of a language delay, regressive onset of the disorder) are influenced more by genetic or environmental factors. Various investigators have discovered familial aggregation among children with ASD for traits such as nonverbal communication per the *Autism Diagnostic Interview—Revised* (ADI-R; Silverman et al., 2002, MacLean et al., 1999), reciprocal social interaction (Mazefsky et al., 2008), and indices of verbal/nonverbal IQ and adaptive functioning (Goin-Kochel et al., 2008). However, heritability for other important parameters, including regression status and core-deficit scores per the *Autism Diagnostic Observation Schedule* (ADOS), are unknown among this population and could prove equally enlightening.
Objectives: To explore familial aggregation of developmental regression, communication skills, social interaction, and stereotyped behaviors/restricted interests among siblings with ASD.
Methods: Data from the Autism Genetic Resource Exchange (AGRE) were analyzed for full, biological siblings who met criteria for an ASD per the ADOS and ADI-R (N = 1358, 78.4% male; M age = 8.0 years, SD = 4.5; 81.7% white). Frequencies of skill loss (regression) were calculated by type of loss (e.g., language, social, fine/gross motor, self-help, play), and twin correlations were computed for all MZ (n = 38) and DZ (n = 37) twin pairs to assess the potential for heritability of regression in ASD per type of loss. Subsequent Intraclass Correlation Coefficients (ICCs) were computed to make full use of this large sample and account for differences in the numbers of affected siblings per family (range = 2—5). Current analyses focus on twin correlations for the ADOS subscale-domain scores for communication skills, reciprocal social interaction, and stereotyped behaviors/restricted interests.
Results: Among this sample, 33.4% had experienced some form of skill regression; the most common losses were for language and social-engagement, experienced by 22.5% and 22.0% of the sample, respectively. Tetrachoric twin correlations for language loss were .85 (MZ) and .17 (DZ) and for social-engagement loss, .80 (MZ) and .67 (DZ); however, the ICC for language loss was .11 and that for social-engagement loss, .16. Comparable results for the ADOS subscale domains are forthcoming, as are heritability estimates for all parameters.
Conclusions: Results from the twin correlations and ICCs for regression items were inconsistent, which may indicate that the genetic mechanisms that were represented in this small DZ twin sample were not representative of the usual mix of genetic mechanisms in the AGRE population. Differences in assisted-reproduction rates between twin and nontwin siblings are currently being explored as one possible explanation.

121.007 Prevalence of Autism Spectrum Disorder in Venezuelan Children Attending An Outpatient Facility. A Preliminary

Analysis. C. Montiel-Nava*, J. Pena, J. A. Chacin, Z. Gonzalez and V. Toledo, *La Universidad del Zulia*

Background: Although the history of autism is short, the universality of this disorder was established very early in the road. However, little is known about autism in Latin American countries. Most Latin American countries lack the epidemiological indicators of child psychopathology. This scarcity of information has as direct consequences the absence or inadequacy of diagnostic and therapeutic services for children with Autism Spectrum Disorders (ASD) Objectives: to determine the prevalence of ASD for children between 5 and 7 years of age attending an outpatient pediatric facility in Maracaibo , Venezuela. Methods: All schools and health services in Maracaibo County (public and private clinics, pediatric hospitals, health centers, and treatment facilities) were contacted to ask for referral of all children with a diagnosis or a probable diagnosis of an ASD. SCQ was used as screening instrument, and positive children underwent a complete assessment that included ADI-R, ADOS-G, PPTV, and Raven. The denominator for calculation of the prevalence was estimated by using the 2005 Venezuelan national census for children born between 2001 and 2003 residents of Maracaibo County (122877 children) . Results: A total of 132 children were identified as having a probable ASD diagnosis. From those children, only 128 completed the assessment. 65% received a diagnosis of autism (n=83), 21% of PDD-NOS (n=27), and 14% (n=18) did not meet the criteria for any of the ASD. The overall rate for all ASD was 6.75 per 10.000 children aged 5 through 7 years. The prevalence for autistic disorder was 6.76. per 10.000 children; while the prevalence rate for PDD-NOS and Asperger´s Syndrome combined was 2.19 per 10.000 children. The autism group had a mean age of 4.78 years (SD 1.94 years) 83% (n=69) boys and 17% girls (n=14); while the PDD-NOS were 77% (n= 21) boys and 23% girls (n=6), with a mean age of 4.43 years (SD 1.80 years) Conclusions: As we the previous Venezuelan study, the prevalence of ASD in Maracaibo County is similar to most other epidemiological studies, although it is in the lower end of such band. Although a clinical sample, this study provides more evidence of the presence of the ASD in Latin American children. This rate might be an underestimation, and a function of the ascertainment process used in this study.

121.008 Autism in a Psychiatric Inpatient Population. L. J. Lawer*[1], K. S. Branch[1], E. S. Brodkin[1], R. Gur[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, many of whom received their diagnoses prior to the changing conceptualization and increased awareness of ASD, may have undiagnosed ASD. 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. Instead, they were most commonly diagnosed with schizophrenia.

Objectives: The objective of this study was two-fold: to validate the previous prevalence estimates of ASD among psychiatric inpatients and to identify characteristics that discriminate between severely impaired adults with ASD and other psychiatric disorders.

Methods: The sample included 322 civilly-committed patients in one state psychiatric hospital in Pennsylvania. Nursing staff completed the Social Responsiveness Scale (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. Data on medications, self-injurious behaviors, and physical/mechanical restraints were collected for each consented patient. 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 were held for all patients.

Results: Eighteen percent of patients received a SRS score ≥100. ADI-R administration and case conferences are ongoing. Of the patients with completed case conferences (n=108), 9% meet criteria for certain or highly probable ASD. Formal analysis of characteristics that discriminate between severely impaired adults with ASD and other psychiatric disorders is ongoing. Preliminary results indicate that unresponsiveness to medications, lack of recreational drug use, and documentation in charts indicating that the patient "responds to internal stimuli" but no clear documentation of hallucinations/delusions discriminate between the presence of ASD and other psychiatric disorders.

Conclusions: Almost one in 10 adults in this state psychiatric hospital met criteria for ASD, a much larger proportion than has been found in most previous studies. Previously validated screening and diagnostic instruments 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.

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122.001 Pressence of Quality Indicators On Autism Websites. B. Reichow*[1], J. Halpern[2] and F. R. Volkmar[3], (1)*Yale Child Study Center*, (2)*Fordham University*, (3)*Yale School of Medicine*

Background:

The number of websites with information on autism is growing. In October of 2009, entering the term "autism" in a Google search resulted in 16,100,000 results. In comparison, conducting a similar search in 1999 would yield 104,950 (Charman, 1999). Research also suggests an increasing number of consumers are obtaining health related information from the internet. Although there are a vast number of autism related websites, little research has been conducted regarding quality of their content, or how the information is used.

Objectives:

The first objective was to develop a tool, the Website Characterization and Quality Indicator Assessment, to accurately assess the presence of quality indicators and key characteristics of websites on autism. The second objective was to use the tool to assess and analyze the presence of the quality indicators on the most popular autism websites.

Methods:

The sample of interest for this study was the top 100 websites returned when the word "autism" was entered into the search engines of Google, Yahoo, and Bing. To conduct the searches, the term "autism" was entered into the search box on each site's homepage and the first 100 websites (not including sponsored links) were entered into a database. There was much overlap between search engines, and website often appeared on one, two, or all three search engine results. Because of the overlap within and between search engine queries, a master list was created with distinct entries for each website domain, which reduced the final sample from 300 websites to 164 distinct website results. The Website Characterization

and Quality Indicator Assessment tool, which contains eight quality indicators (author's identity, references, not offering a commercial product or service, not promoting a miracle cure, updated within the last 6 months, personal information did not have to be provided, a contact information or a feedback mechanism was provided, and the site contained a medically oriented disclaimer) was used to determine the presence or absence of quality indicators on the 164 autism websites.

Results:

On average, the 164 websites analyzed for this study suggested autism related websites contained less than 6 of 8 quality indicators. Nearly 1 in 5 websites offered a product or service for purchase, and/or promoted a miracle cure. These websites were also, on average, some of the least likely websites to contain the quality indicators.

Conclusions:

These findings suggest consumers must be cautious when obtaining information regarding autism from the internet. Specifically, the finding that websites offering a product or service for purchase and/or promoting a miracle cure contained, on average, a lower proportion of total quality indicators suggest that individuals encountering websites containing these aspects must exercise extra cautions. Additionally, the results of this study do not provide data that can be used to reach conclusions about the quality of the information on autism websites. Further research addressing this issue is needed.

122.002 The Impact of the Popular Media On Awareness: *Aap Ki Antara*. N. Singhal*, *Action For Autism National Research Centre for Advocacy, Research, Rehabilitation and Training (AFANCARRT)*

Background: In June 2009, an Indian television network with a global reach of more than 120 countries and 500 million viewers launched a nightly soap opera called *Aap Ki Antara* (*"My Name is Antara"*). The plot centered on a five-year old girl with autism, and each episode concluded with a three minute "testimonial" from a family member of a person with autism, followed by the number of a telephone helpline and address for website of the national autism organization, Action for Autism.

Objectives: To demonstrate the dramatic impact that a mass media outlet can have on awareness of autism, we present summative data on the calls received on the *Aap Ki Antara* national hotline information number. We also present data documenting website traffic prior to and after the launch of the show.

Methods: Basic caller information (location of the caller, sex and age of the person of concern) was documented on all calls. To obtain in-depth information from callers, a five-week sample period was selected. During this time, additional information was recorded, including the relationship of the caller to a person with a disability, the purpose of the call, whether the caller knew about autism prior to the serial, and nature of services the person with a disability currently received.

Results: During the initial months of the hotline, more than 50 calls per day were received. During the five week sample period, the hotline averaged approximately 15 calls per day with a total of 336 calls documented. Geographically, calls were received from 25 states across India as well as from Indians in five other countries. Most calls (69%) were made by a parent; 18% were made by a relative including, siblings, grandparents, aunts and uncles. Thirty five percent of the callers had a child who already had a diagnosis of autism. In general, callers largely indicated they wanted information about autism-related services in their area (48%), with an additional 28% of the callers wanting to know more about autism specifically and 8% asking about both. An unexpected number of callers had children identified with other conditions and requested information related to these issues. Among callers who had a child with an ASD diagnosis,

48% of these children were attending no school at all.

Of particular note, 65% of all callers reported that they heard and became aware about autism only through watching *Aap Ki Antara*.

Data from website traffic during the selected time period showed 7,781 visitors from 129 countries and territories. Compared to a five-week period prior to the onset of the show, this represents an increase of 35% of total visitors and 30% first time visitors.

Conclusions: *Aap Ki Antara* is the first prime-time drama in a developing country, and perhaps any country, to focus on a character with autism. Calls to the national helpline suggest the potential power of a prime-time show to impact awareness of autism among the general public and particularly among families of children with disabilities. Implications for public awareness programs will be discussed.

122.003 Implementation of the Autism Diagnostic Observation Schedule by School Assessment Professionals. N. Akshoomoff*[1], C. Corsello[2] and L. A. Palinkas[3], (1)*University of California, San Diego*, (2)*Rady Children's Hospital - San Diego*, (3)*University of Southern California*

Background: While many children with ASD are identified before entering a school program, a significant number are not identified until they are assessed for special education services. . Often school-based professionals are making a determination regarding eligibility for services under the educational category of autism. School districts often encourage the use of a standardized instrument when evaluating a child for autism but limited information is available about implementation.

Objectives: This exploratory study was designed to identify factors contributing to short-term implementation of the research based diagnostic measure, the Autism Diagnostic Observation Schedule (ADOS) by school assessment professionals. The potential added benefit of individualized feedback following the two-day workshop was also examined.

Methods: Participants were 46 school assessment professionals (30 school psychologists and 16 speech-language pathologists; 89% female) who attended an ADOS two-day workshop and agreed to participate in this follow-up study. A subset (N =15) provided videos of their ADOS testing and attended feedback meetings with the trainers. An average of 5 months later, participants completed a questionnaire about their experience using the ADOS and participated in a small group discussion meeting.

Results: Participants who provided videos of their ADOS administration following a feedback session showed great improvement in administration and coding. Across all participants, the number of assessments conducted with a child with possible or known ASD since the time of the ADOS workshop ranged from 0 to 40 (M = 10.9, SD=9.9) and the total number of ADOS administrations ranged from 0 to 15 (M = 3.3, SD=3.9). In the time following the ADOS workshop participants thus included the ADOS less than half the time they assessed a child for ASD (M = 37.8%). Regarding future use, 47% indicated they would "definitely" use the ADOS and 53% indicated they "may" use the ADOS. Among those who met with a trainer regarding their ADOS administration and coding, 78% indicated they would definitely use the ADOS while only 37% of those who did not meet with a trainer indicated this. Noted barriers to implementation were related to equipment, time, and difficulty with ADOS coding. Participants noted that an advantage of the ADOS was characterizing specific symptoms instead of relying solely on parent report.

Conclusions: ADOS training guidelines indicate practice and support are needed for new users, factors that are often overlooked by school district officials and assessment professionals when considering adoption of the ADOS. The results from this study indicate that without added support, targeted feedback, and opportunities for practice it may be difficult for school teams to effectively implement the ADOS in their autism evaluations.

122.004 Effective Disclosure and Parent Reaction to ASD Diagnosis. Z. Warren*[1], J. L. Taylor[2] and J. L. Cordle[1], (1)*Vanderbilt University*, (2)*Vanderbilt Kennedy Center*

Background: The diagnostic assessment experience itself often represents a pointed stressor for families of young children with ASD and as such holds great potential for readily applicable clinical research. The formal diagnosis of ASD, even when suspected for lengthy intervals of time, contributes to an array of reactions in caregiving systems both in the short- and long-term. Unfortunately, to date very little empirical work has been conducted regarding effective disclosure of diagnoses of ASD, child functioning, associated parenting stress/engagement, and involvement in clinically indicated interventions.
Objectives: In this study we explored parent perceptions of effective characteristics of diagnostic disclosure as well as emotions and thoughts surrounding disclosure.

Methods: All families coming through a university affiliated ASD clinic and receiving a diagnosis of ASD were asked to complete a survey - The Diagnostic Process Questionnaire [DPQ] - regarding characteristics of diagnostic process, questions about what they wished had been a part of the diagnostic event, perceptions of support surrounding the diagnostic event, as well as thoughts and feelings at the time of diagnosis.
Results: 76 families completed the DPQ survey. Families frequently endorsed long-waits (54%> 6 months; 41% > 1 year) and visiting numerous service providers (61% ≥ 3 ; 22% > 5) from the initial time of mentioning concerns to a professional to receiving a formal diagnosis. When asked to reflect on ideal characteristics of evaluation and feedback an overwhelming majority of parents (96%) reported they would want to receive diagnostic feedback the day of the child's assessment. Although a majority of caregivers had support persons present on the day of the diagnosis (88%), those who did not frequently endorsed wishing another support person was present (67%). Of those parents whose child was in fact present in the room for the ASD diagnosis (65%) most noted that they would still want this to be the case (82%).
Parents generally reported positive support from their family concerning the ASD diagnosis (76%); however, they frequently endorsed that specific members of their family/support system (i.e., spouse, parents, in-laws) were not supportive of the ASD diagnosis itself. 45% of parents did not report strong support from their pediatrician about their child's ASD diagnosis.
When inquiring of feeling and thoughts at the time of ASD diagnosis, many parents reported feeling prepared and indicated that the diagnosis was not surprising or shocking, yet at the same time extreme feelings of distress were often reported.
Conclusions: Research examining reactions to the diagnostic assessment process itself in association with clinical characteristics of the child and other family process factors could potentially provide information that clinicians could utilize in adapting the assessment process and recommendations to promote family specific engagement in intervention best practices.

122.005 An Examination of the Support Needs Experienced by Families of School-Aged Children with An Autism Spectrum Disorder. H. K. Brown*, H. Ouellette-Kuntz, D. Hunter and E. A. Kelley, *Queen's University*

Background: The recent increase in demand for autism services has resulted in a strain on the service system in terms of the provision and organization of supports for children with an autism spectrum disorder (ASD), and parents report difficulty navigating the service system. This problem has gained attention in Canada, the United States, and elsewhere and necessitates an examination of the unmet needs of children with ASD and their families. Because, in many jurisdictions, ASD services are significantly cut back after the preschool years, an examination of unmet needs among school-aged children is particularly warranted.

Objectives: The objectives of this research were: (1) to describe areas of unmet need reported by parents of school-aged children with ASD and (2) to examine these unmet needs in relation to the level of functional independence of the child.

Methods: A cross-sectional survey was conducted, which included parents of children who: (1) had an ASD, (2) were between the ages of 6 and 13 years, and (3) were residing in one of the study regions. Parents responded to a written questionnaire (Family Needs Questionnaire; demographic questions) and a telephone interview (Scales of Independent Behaviour-Revised [Short Form]; service use questions). Data collection is in progress; at this time, data are available for 42 of 100 expected participants. The children were diagnosed as having autistic disorder (50.0%), pervasive developmental disorder-not otherwise specified (9.5%), Asperger's disorder (14.3%), and autism spectrum disorder (26.2%). The average age was 9.5 years (SD = 2.3), and 81.0% were male.

Results: Functional independence was measured by the child's adaptive and problem behaviours and was categorized as low (26.2%), moderate (54.8%), or high (19.0%). Needs were ranked first according to importance and then according to whether or not they had been met. In order to compare the types of needs experienced by children in each functional independence category, the top five important needs were selected and the proportions of these which were unmet were reported for each group. Preliminary results indicate that for the low functional independence group, the most commonly reported unmet need was the need for respite for the parent (100.0% unmet). For moderate functional independence, the most commonly endorsed unmet need was the need for financial support to fund therapies (73.7% unmet). For high functional independence, the most commonly reported unmet need was the need for information about available programs (75.0% unmet).

Conclusions: As expected, the types of needs ranked as important and unmet differed according to the functional independence category. Examining unmet needs in this way provides insight into characteristics which may predict families who are at greater risk for having needs which have not been recognized and met by the service system. Information about the unmet needs of children with ASD and their families will help policymakers and service-providers to rethink eligibility criteria and the process of accessing care and will enable them to develop resources and services that are responsive to the needs of their client group.

122.006 Efficacy of the Early Start Denver Model Parent Intervention for Toddlers with ASD Delivered Via Internet Technology. L. A. Vismara* and S. J. Rogers, *M.I.N.D. Institute, University of California at Davis*

Background: There are various challenges to delivering health care to families with Autism Spectrum Disorder (ASD) with long waiting lists and few specialist services. Barriers to service delivery and utilization are even more exacerbated for families living in rural or remote areas, often resulting in limited access to preventative mental health services in general and parenting ASD interventions in particular. Telecommunication technology can support long-distance clinical health care; however there is little information as to how this resource may translate into practice for families with ASD.

Objectives: The current pilot study examined the use of telemedicine technology to deliver a manualized, parent-implemented intervention for families of children with ASD, ages 12-36 months. It was hypothesized that telemedicine technology as a teaching modality would optimize parenting intervention strategies for supporting children's social, affective, communicative, and play development.

Methods: Families received 12 weekly one-hour sessions of direct coaching and instruction of the Early Start Denver Model (ESDM) Parent Delivery Model through an Internet-based video conferencing program. Each week parents were coached on a specific aspect of the intervention through video conferencing program and webcam, allowing parent and therapist to see, hear, and communicate with one another. Parents were taught how to integrate the ESDM into natural, developmentally and age-appropriate play activities and caretaking routines in their homes. Video data were recorded from 10 minutes of parent-child interaction at the start of each session and coded by two independent raters blind to the

order of sessions and hypotheses of the study.

Results: Findings suggested that integrating telemedicine as a teaching modality enabled: (a) parents to implement the ESDM more skillfully after coaching; and (b) increase in children's number of spontaneous words, gestures, and imitative behaviors used.

Conclusions: The current findings support the efficacy and cost-effectiveness of using telemedicine to transfer a developmentally based, relationship focused, and behaviorally informed intervention (i.e., the ESDM) into parents' homes to be delivered within typical parent-child activities. Additional research is needed to confirm the promise and utility of telemedicine for transporting services to families with limited access.

122.007 Changes in Educational Placements for Children with Autism Spectrum Disorders (ASDs) in a Population-Based Sample in a US Metropolitan Area. M. J. Morrier*[1], C. E. Rice[2], J. Baio[2], S. J. Wagner[1] and J. Nicholas[3], (1)*Emory Autism Center, Emory University School of Medicine*, (2)*National Center on Birth Defects and Developmental Disabilities*, (3)*Medical University of South Carolina*

Background: ASDs affect about 1% of children (CDC, 2009) which challenges school systems to meet these students' educational needs. Federal mandates require students with disabilities to be educated in the least restrictive environment to the maximum extent possible (IDEA, 2004).
Objectives: To document changes in educational placements for students with an ASD over four time periods from a population-based ASD surveillance system.
Methods: Children with ASD were identified through record abstraction at multiple health and education sources within a US metropolitan area. Case status based on the DSMIVTR criteria was determined by clinician reviewers. Educational placement was obtained from the child's Individualized Educational Plan (IEP) at age eight, while intellectual level was based on the most recent IQ score on record. Socioeconomic status was coded from Census 2000 indicators based on the child's residence.
Results: A total of 1,497 8-year-old children with an ASD were identified for the study years 2000, 2002, 2004, or 2006. Of these, 141 had no IEP on record and were presumed to be in general education (GenEd). The remaining 1356 children were receiving special education services; however, 50 (3.3%) children with an unknown educational placement were excluded from the analysis. Placements were categorized as (a) Less Restrictive, comprised of 141 (9.7%) in GenEd and 195 (13.5%) outside GenEd < 21% of the time; or (b) More Restrictive, comprised of 214 (14.8%) children outside GenEd 21-60% of the time, 882 (61%) outside GenEd > 60% of the time, and 15 (1%) in separate facilities.
During all four years combined, 336 (23.2%) students with ASD were educated in Less Restrictive environments while 1111 (76.8%) had More Restrictive placements. The proportion of children in Less Restrictive environments increased each year from 2000 to 2006, with children in 2006 significantly more likely to be in Less Restrictive placements (OR = 1.3, 95% CI = 1.0-1.7; p = .03). Overall, children with IQ >70 were significantly more likely to be in Less Restrictive placements (OR = 5.4, 95% CI = 3.8-7.6; p < .001). Children in the lowest SES tertile were significantly more likely to be in More Restrictive placements than those from the middle and higher SES tertiles (OR = 2.5, 95% CI = 1.6-3.8; p < .001). White non-Hispanic race was associated with placement in a Less Restrictive environment (p < .001).
Conclusions: The majority of special education students with ASD were being educated outside of GenEd, and this appears to be decreasing slightly over time. However, some children with mild ASD may not have been identified by the case identification process. Placements were primarily influenced by IQ level. Race/ethnicity and SES were also associated with placement in more restrictive setting, however, an interaction was observed between these factors. Although educational mandates emphasize the least restrictive environment, educational placement in the GenEd is not common for students with ASD.
The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

122.008 Education Placement of Preschool-Aged Children with Autism Spectrum Disorders. W. Jenner*, L. Carpenter, J. Charles, L. King and J. Nicholas, *Medical University of South Carolina*

Background: Much of the existing prevalence data regarding children with Autism Spectrum Disorders (ASD) involves school aged children. Little population-based autism surveillance has been completed involving preschool children despite the fact that many professionals believe that early identification and early intervention is essential for children with ASD. The current study used the same active population-based, multiple source public health surveillance methodology used by the Centers for Disease Control and Prevention's (CDC) Autism and Developmental Disabilities Monitoring Network (ADDM) to determine prevalence and characteristics of 4 year old children with ASD.

Objectives: The purpose of this study was to examine educational placement among 4 year old children with ASD.

Methods: The CDC's ADDM methodology, used for 8 year old children, was applied to 4 year old children in a select region of South Carolina (SC). Additional surveillance sites were added to include preschool programs in early intervention, O-3 year old programs, public school preschool programs (3 and 4 year olds), as well as private and nonprofit programs for preschool children. The surveillance area was narrowed to a 3-county sub region of the larger SC-ADDM surveillance area.

Results: In 2006, in a 3-county sub region of the SC ADDM surveillance area, the total prevalence of ASD in children aged 4 years was 8.0 per 1000 (1:125), higher than for 8 year olds in the same region for each of the previous ADDM study years (2000, 2002, and 2004, respectively). 77% of the 4 year olds with ASD identified by this study had received special education services through the public schools; however only 20 % of these had an educational eligibility of Autism, while 74% of these were identified in the more general category "preschool child with a disability" and hence were not receiving ASD-specific services. Children with documentation in their records of a previous ASD diagnosis (60% of cases) were more likely to receive special education services than those without a community diagnosis. Over half the children with an ASD (54%) had previously been served in an early intervention program (i.e. a state or federally funded program for children under 3 years of age).

Conclusions: Findings suggest that while the prevalence of ASD in 4-year-olds is higher than previous estimates of ASD among school aged children, many of the children in this study were not receiving special education services at all, or were not receiving specialized educational services for children with ASD. Only half of children identified with an ASD in this study had received any state or federally funded services prior to three years of age, suggesting that delays in service provision continue to be common. The surveillance of ASD at an earlier age provides valuable information for the subsequent planning, implementation, and evaluation of resources and interventions for preschool children with ASD. Finally, this study demonstrates that the ADDM methodology can be successfully applied to a younger population.

Funding for this study was provided by Autism Speaks. Methodology for the study was created by the CDC's ADDM network.

123 Developmental Trajectories of Children with Autism Spectrum Disorder

Organizer: S. Georgiades *McMaster University*

Many longitudinal studies in ASD have documented considerable variation in outcome, ranging from remarkable improvement in some children to a decline in others. However, these results are limited by issues such as employment of convenience sampling frames, data collection from few time points, and use of small sample sizes. More recent data suggest a new way of thinking about the developmental course of ASD, in which children are described using distinct homogeneous trajectories, rather than a single heterogeneous group. This panel presents findings from two new longitudinal studies that benefit from large sample sizes, ascertainment of inception cohorts, data acquisition at multiple time-points, use of several outcomes including social-communication symptoms and functioning and problem behaviors, and novel statistical techniques. The findings emphasize that children with ASD follow distinct trajectories both over the short and long term and that this

heterogeneity in developmental course needs to be taken into account in treatment planning.

123.001 Developmental Course of Social Communication Symptoms and Functioning in Young Children with ASD. P. Szatmari*[1], T. A. Bennett[2], S. Georgiades[1], E. Duku[1], S. E. Bryson[3], E. Fombonne[4], P. Mirenda[5], W. Roberts[6], I. M. Smith[7], T. Vaillancourt[8], J. Volden[9], C. Waddell[10], L. Zwaigenbaum[9] and A. P. Thompson[1], (1)*McMaster University*, (2)*Offord Centre for Child Studies, McMaster University*, (3)*Dalhousie University/IWK Health Centre*, (4)*McGill University*, (5)*University of British Columbia*, (6)*University of Toronto*, (7)*Dalhousie University & IWK Health Centre*, (8)*University of Ottawa*, (9)*University of Alberta*, (10)*Simon Fraser University*

Background: Children with Autism Spectrum Disorder (ASD) present symptoms of social-communication impairment (e.g. difficulty reading social cues or facial expressions) and are also faced with more non-specific difficulties related to everyday social-communication functioning (e.g. social conversation, non-verbal communication and forming friendships). Whether or not these indicators are distinct or overlapping constructs within ASD is a question which warrants close investigation. In addition, the possibility that children with ASD follow different developmental trajectories along these outcomes has not been systematically investigated using appropriate statistical techniques.

Objectives: The main objectives of this study were to (a) develop a measurement model of indicators reflecting social- communication symptoms and functioning in children with ASD; and (b) examine the developmental course over 12 months of these empirically derived factors.

Methods: The sample consisted of 273 newly-diagnosed preschool children (mean age: 40.11; SD = 8.82; 233 males) with ASD participating in a longitudinal study. A total of 12 indicators from three instruments: Vineland Adaptive Behaviours Scale (VABS II), Preschool Language Scale (PLS-4), and Social Responsiveness Scale (SRS), were used in exploratory factor analysis. Then, the empirically derived factor scores were used in trajectory analysis to identify distinct mixtures of trajectories within the sample over 12 months.

Results: The structure of social-communication in this sample is best represented using a two-factor solution, explaining 72.45% of the variance. Factor I, Social-Communication Functioning, includes indicators from the VABS II and the PLS-4. Factor II, Social- Communication Symptoms, includes indicators from the SRS. Both factors have acceptable internal consistency. Results indicate that there are three distinct *functioning* trajectory groups, all of which have statistically significant inclining trajectories ($p<0.05$) suggesting all children are improving in their social-communication functioning, but at very different rates. Furthermore, there are statistically significant differences in developmental level between children across the three groups. In the case of social-communication *symptoms*, results also show that there are three distinct trajectory groups (high, low, and intermediate symptoms). The intermediate group has a statistically significant declining trajectory ($p<0.05$) while the end groups (i.e., high and low) have flat trajectories. In the case of the Social-Communication Symptoms, there are no differences in developmental level between children across the three groups.

Conclusions: Findings from this study suggest that (a) social- communication functioning and symptoms are independent dimensions in ASD; (b) trajectory models of social- communication over 12 months reveal 3 groups of preschoolers with ASD who "start off" at different levels of functioning and symptoms; and (c) social-communication functioning improves over time in the first 12 months after diagnosis, with the greatest improvement in those with higher initial functioning. Social-communication symptoms remain relatively unchanged, with some improvement only in the intermediate-severity group. These findings have important implications for informing parents and front-line clinicians about change in ASD children over the first 12 months post-diagnosis in the pre-school years.

123.002 Developmental Trajectories of Internalizing and Externalizing Behaviours in Young Children with ASD. T. Vaillancourt*[1], P. Szatmari[2], S. Georgiades[2], E. Duku[2], S. E. Bryson[3], E. Fombonne[4], P. Mirenda[5], W. Roberts[6], I. M. Smith[7], J. Volden[8], C. Waddell[9], L. Zwaigenbaum[8] and A. P.

Thompson[2], (1)*University of Ottawa*, (2)*McMaster University*, (3)*Dalhousie University/IWK Health Centre*, (4)*McGill University*, (5)*University of British Columbia*, (6)*University of Toronto*, (7)*Dalhousie University & IWK Health Centre*, (8)*University of Alberta*, (9)*Simon Fraser University*

Background: The lack of longitudinal studies examining internalizing and externalizing problems among children with Autism Spectrum Disorder (ASD) is notable given that these behaviours are common in this population. Mapping of the developmental course as well as the potential inter-relationships (i.e., covariation) of these behaviours could add to our understanding of the clinical presentation of children with ASD.

Objectives: The main objectives of this study were to (a) model distinct developmental trajectories of internalizing and externalizing behaviours among preschool children with ASD; and (b) examine the covarying pattern over time of these behavioural problems.

Methods: The sample consisted of 343 newly-diagnosed preschool children (mean age: 38.29; SD = 8.66; 290 boys) with ASD participating in a longitudinal multi-site study. Following diagnosis, the children were assessed three times at 6-month intervals using the Child Behavior Checklist (CBCL 1.5-5; Achenbach & Rescorla, 2000).

Results: Wave-to-wave correlations were first computed to examine the stability of problem behaviour and the co-occurrence of symptoms over time. Results indicated high stability for internalizing (T1 and T2 r=.67; T1 and T3 r=.62) and externalizing behaviours (T1 and T2 r=.64; T1 and T3 r=.64) and a high degree of concurrent co-occurrence (T1 r=.67, T2 r=.66 and T3 r=.77) which increased over time (Fisher z-tests=2.36; T3 >T1 and T2). Next, because correlations can mask distinct developmental patterns of behaviour, CBCL internalizing and externalizing *total* scores were also examined using a semi-parametric, group-based approach (PROC TRAJ). For internalizing problem behaviours, two distinct developmental trajectories were identified: a "decreasing low" trajectory consisting of 82.2% of children, and a "high" trajectory comprising 17.8% of children. For externalizing problem behaviours, two distinct developmental trajectories were again identified: a "decreasing low" trajectory comprised of 68.3% of the children, and a "decreasing high" trajectory comprising 31.7% of the children. Joint trajectory analyses indicated that children following a "high" internalizing trajectory were almost invariably represented on the "decreasing high" externalizing trajectory (87%). Conversely, children on a "decreasing high" externalizing trajectory were equally represented on the "decreasing low" (52.5%) and "high" (47.5%) internalizing trajectories.

Conclusions: Findings from this study suggest that (a) there are distinct developmental patterns of internalizing and externalizing problems among children with ASD; and (b) high severity of internalizing symptoms tends to be accompanied by high severity of externalizing problems. There also exists a relatively "pure" sub-group of children with ASD with high externalizing problems but low internalizing problems. The extent to which these groups differ on other variables (e.g., language, level of impairment, etc.) will be examined, as will the association of certain family variables (e.g., parental stress) with the intercepts and slopes of these trajectories.

123.003 Longitudinal Change in Social Affect and Restricted and Repetitive Behavior Severity Using the ADOS. V. Hus*[1], K. Gotham[1], A. Pickles[2] and C. Lord[3], (1)*University of Michigan Autism & Communication Disorders Center*, (2)*University of Manchester*, (3)*University of Michigan*

Background: The development of a standardized ADOS severity metric (Gotham, Pickles, & Lord, 2009) provides an overall index to measure change in intervention research and will facilitate investigations of developmental trajectories of autism over time. Separate calibration of the Social Affect (SA) and Restricted and Repetitive Behavior (RRB) domains will further promote these efforts by allowing separate examination of these behaviors, which may have distinct trajectories.

Objectives: To standardize ADOS SA and RRB domain scores, and then plot longitudinal trajectories of ASD severity separately for each standardized domain.

Methods: Standardized ADOS severity scores were calibrated separately for the SA and RRB domains using data from 1,807 cases. Mixed effects modeling was then used to identify separate domain severity trajectories for 345 individuals (total of 1,026 longitudinal cases).

Results: For some individuals, there is a discrepancy between SA and RRB severity scores, suggesting more severe symptoms in one domain compared to the other. Separate scores also allowed trajectories of severity to be analyzed for each domain. Several distinct patterns were identified. In general, SA and RRB severity show approximately consistent trajectories, with severity in both domains increasing or decreasing with time. However, in some cases, SA severity appears to decrease over time, whereas RRB severity remains relatively stable. In a few cases, SA and RRB trajectories are apparently opposite - i.e. as one increases, the other decreases.

Conclusions: If replicated, separately calibrated SA and RRB severity scores, as well as the identified trajectories of severity for each domain may be useful for stratifying samples in genetic and neurobiological studies. These scores may also inform clinical recommendations and intervention efforts. For individuals with uneven profiles (i.e. higher severity in one domain compared to the other), more targeted intervention programs may be identified. Using separate calibrated scores may also provide a more sensitive measure of intervention response, enabling change in one domain to be detected, even when behaviors in the second domain persist.

123.004 Growth Trajectories of Problem Behaviors Utilizing the Aberrant Behavior Checklist. M. Maye*[1], D. K. Anderson[1] and C. Lord[2], (1)*University of Michigan Autism & Communication Disorders Center*, (2)*University of Michigan*

Background: Recently there has been an increase in interest in behavioral difficulties that co-occur with Autism Spectrum Disorders (ASD). The majority of longitudinal studies report improvements in behaviors as youths with ASD get older, but there are also repeated references to individuals who experience extreme changes in behavior and sometimes marked deteriorations.

Objectives: To examine predictors of growth trajectories in problem behaviors (lethargy/social isolation, irritability, and hyperactivity) from mid-childhood to late-adolescence.

Methods: The sample (n=120) is comprised of individuals with consecutive referrals for possible autism at age 2 to clinics in North Carolina and Chicago and nonspectrum individuals recruited from North Carolina, Chicago and Michigan with some degree of mental retardation, language delay, or with other disabilities. Growth curve analyses were utilized to determine significant changes in lethargy, irritability and hyperactivity, measured by the Aberrant Behavior Checklist (ABC).

Results: Total scores for the three ABC subscales ranged from 0 to 111 out of a possible 141, with higher scores indicating more problematic behaviors. At both the first and last measurements, the autism group exhibited significantly more problem behaviors overall compared with children with PDD-NOS and nonspectrum delays. However, the autism group also improved the most on average. The overall trend from age 9 to 18 was one of decreases in problem behaviors. About half of the autism group (49%) showed decreases in problem behaviors of at least one standard deviation (S.D.=12.7), while a smaller proportion of the PDD-NOS and nonspectrum groups underwent similar decreases (24% and 38% respectively). The hyperactivity subscale accounted for the largest decrease in problem behaviors. Problem behaviors worsened substantially for a small but significant minority of children with ASD (9-10%). Predictors of outcome and longitudinal "growth" trends were examined separately for the three subscales. For all three subscales, the pattern of change for the autism group alone was one of an accelerated decrease in problem behaviors between ages 9 and 11 (i.e., a significant positive quadratic slope), after which the decline in problem behaviors continued at a slower rate. Verbal IQ predicted fewer problem behaviors for all three subscales,

but did not affect the rate of change over time. Greater lethargy/social isolation at age 9 was reported for children who had one or more seizures in their lifetime, however, the rate of decrease in lethargy over time was also greater compared with those who had never seized. Various other factors were not significant predictors of outcome, including race, gender, caregiver's education, hours of treatment, and pubertal development.

Conclusions: Findings from this study suggest that problem behaviors such as hyperactivity, lethargy/social isolation, and irritability tend to decrease over time for children with ASD and nonspectrum delays but outcome differs according to diagnosis, IQ, and seizure activity. In the final analyses, we will examine additional factors likely to influence outcome such as classroom placement and medication usage. Closer examination of those whose problem behaviors increased over time is needed as well. The clinical implications will be discussed.

124 Earlier Is Better and More Difficult: Opportunities and Challenges in Screening Children for An Autism Spectrum Disorder (ASD) in the General Population During the Second Year of Life

Moderator: C. E. Rice *National Center on Birth Defects and Developmental Disabilities*

Organizer: C. E. Rice *National Center on Birth Defects and Developmental Disabilities*

Recently, there have been advances in understanding the early signs of ASDs with increased public health focus on early developmental screening. The American Academy of Pediatrics now recommends that all children be screened for developmental disabilities throughout the first few years of life and for ASDs at 18 and 24 months. Despite wide consensus that "earlier is better," knowledge gaps exist in what "early" means and how this is successfully implemented in general population settings. Although several screening instruments have been developed for use in the 2nd year of life, data on their utility in general population settings are limited. Unlike families in clinically-referred or sibling research projects who may have heightened concern, families in the general population may be confronted with positive screening results before they have raised concern themselves. This panel presents the latest data on early ASD screening tools used in general population settings and explores opportunities and challenges in the during the 2nd year of life.

124.001 Identifying Young Children with Autism Spectrum Disorder through General Population Screening. A. M. Wetherby*, *Florida State University*

Background: The American Academy of Pediatrics recommends screening for 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 for use in the general population.

Objectives: The major objective of this ongoing study of the FIRST WORDS® Project is to implement a developmental surveillance system to estimate the prevalence of ASD in toddlers using a community-based screening of a general population sample. Methods: Children were first screened with a broadband parent-report surveillance checklist, the *Infant-Toddler Checklist* (ITC), through healthcare providers between 9 and 18 months of age. Two autism-specific screening tools were used for children with a positive broadband screen— the *Early Screening for Autism and Communication Disorders* (ESAC) based on parent report and the Systematic Observation of Red Flags of ASD (SORF) based on an interactive videotaped behavior sample. A diagnostic evaluation to confirm or rule out ASD was completed at 18-24 and 30-36 months of age.

Results: Based on screening of 4,186 children, 49 children have been diagnosed with ASD at 18-24 months of age. We anticipate that this is a conservative estimate because more children may be diagnosed with ASD at 30-36 months of age or older. The accuracy of the broadband and autism-specific screeners will be reported in relation to parent concern. Stability of diagnosis from the 2nd to the 3rd year will be reported for children who reach 30-36 months of age.

Conclusions: These findings document the effectiveness of a developmental surveillance system to screen for ASD in a general population sample of toddlers using a broadband screener followed by two autism-specific screeners. Barriers that impede and strategies that improve parent participation and follow-up in screening and diagnosis of ASD at 18-24 months of age will be discussed.

Funding Sources: CDC, NIH/NIDCD, USDOE

124.002 M-CHAT Best7: A New Scoring Algorithm Improves Positive Predictive Power of the M-CHAT. D. L. Robins*[1], J. Pandey[2], C. Chlebowski[3], K. Carr[3], J. L. Zaj[4], M. Arroyo[1], M. L. Barton[3], J. Green[3] and D. A. Fein[3], (1)*Georgia State University*, (2)*Children's Hospital of Philadelphia*, (3)*University of Connecticut*, (4)*Radford University*

Background: The American Academy of Pediatrics recommends screening for autism spectrum disorders (ASD) at 18- and 24-month well-child visits. Although sensitivity and specificity are important psychometric properties to evaluate for screening measures, positive predictive value (PPV) calculates the confidence that a screen positive result indicates risk for ASD. The Modified Checklist for Autism in Toddlers (M-CHAT; Robins et al., 1999, 2001, 2008) is a validated screening tool; sensitivity is estimated at .8-.9 and specificity is estimated >.90. However, PPV of the M-CHAT is .05-.11 in low-risk samples; adding the M-CHAT Follow-up Interview increases PPV to .57-.65, but requires additional resources.

Objectives: To identify a new scoring algorithm for the M-CHAT maintaining high sensitivity and improving PPV by reducing false positives and reducing the number of Follow-up Interviews needed.

Methods: The sample included 15,650 toddlers screened during checkups (mean age=20.6 months, SD=3.1, range=14-30 months; 7804 males). Potential scoring algorithms were developed based on item analysis, M-CHAT-to-Interview change scores, and discriminant function analysis, and examined for psychometric properties. The new scoring algorithm, called M-CHAT Best7, consists of interest in peers, pretend play, protodeclarative point, shows objects, responds to name, follows point, and wondered if deaf.

Results: Using the original M-CHAT scoring (screen positive=2/6 critical or 3/23 total items), 8.7% (1359/15,650) of the sample screened positive. Of those reached for interview, 13.1% (141/1074) screened positive and were offered an evaluation. Of those children evaluated, 51.8% (58/112) were diagnosed with an ASD. An additional 29 cases were evaluated based on physician or parent concerns, leading to a total of 64 ASD and 77 nonASD cases. Thus, PPV based on M-CHAT+Interview is .52, and PPV for M-CHAT alone is .04. The upper bound of sensitivity, considering ASD cases flagged by physician or parent, is .91, and specificity is .99.

Using the M-CHAT Best7, 1.9% (304/15,650) screened positive, and 42.5% (90/212) screened positive on the Best7 Follow-up Interview. Had we used Best7 initially, 55 ASD cases would have been identified, leading to an upper bound of sensitivity of .86, specificity of .99, PPV of .61 for M-CHAT+Interview, and PPV of .18 for M-CHAT only. For children whose Best7 score was _4, the likelihood of reversing a screen positive score on Interview was small (22.4%), in contrast to the likelihood of reversing scores of 2 (81.4%) or 3 (43.1%).

Conclusions: Although the M-CHAT Follow-up Interview is still needed, the new Best7 scoring reduces the false positive rate fourfold, with only minimal decrease in sensitivity. On initial screening, Best7 scores 0-2 indicate low risk and no follow-up is necessary unless surveillance or other procedures suggest risk for ASD. The M-CHAT Follow-up Interview should be administered for Best7 scores of 2-3, and cases who screen positive on the Interview should be referred for diagnostic evaluations and early intervention. For cases whose Best7 score is >3, the Interview can be bypassed and referrals for evaluation and intervention made immediately. This recommended protocol retains high sensitivity and significantly reduces the false positive rate, making the best use of professional resources.

124.003 Population Screening for ASD: a Comparison of M-CHAT and ESAT. J. Buitelaar*, *Karakter Child and Adolescent Psychiatry University Center*

Background: ESAT and M-CHAT are instruments designed for the screening of ASD in very young children in the general population.

Objectives: To describe the response to the ESAT and M-CHAT and explore overlap and

difference in screen-positive children identified with ESAT and M-CHAT. Further, to examine external validity of ESAT and M-CHAT, by exploring relationships with proxy-measures of clinical caseness.

Methods: The data were collected in the context of the Autism Birth Cohort Study, an ongoing, prospective birth cohort study in Norway. Mothers of 12,948 18 months old children completed a questionnaire which included items from the ESAT, M-CHAT and other items about their child's social and emotional development and behavior.

Results: The percentages screen-positive children on the ESAT (0.5%) and M-CHAT (5.4%) differed significantly from each other ($p<.01$). Among all children, 94% was screen-negative on both questionnaires, 0.33 % was screen-positive on both, 0.2% was only screen-positive on the ESAT, and 5% was only screen-positive on the M-CHAT. Exploration of the ESAT and M-CHAT in relation to proxy-measures revealed the highest percentage of clinical and developmental concerns for children who were screen-positive on both questionnaires. ESAT only screen-positive children scored relatively high on items of behavioral and temperamental problems. For the M-CHAT only screen positive group there were more concerns about motor development.

Conclusions: Results of this study demonstrated that the ESAT and M-CHAT have different profiles in terms of the number and kind of children which are screen positive. Based on the relationship with proxy-measures, the ESAT tends to pick up children with more serious language and behavioral problems whereas the M-CHAT picks up children with more mild and general developmental delays. In addition to presenting comparative data of the ESAT and M-CHAT, issues related to the age at screening and the relationship to caregiver follow-up on results will also be discussed.

125 The Autism Instructional Methods Study: Opportunities, Outcomes and Challenges From Moving Evidence-Based Intervention Into Community Settings

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

In the past few decades, >20 randomized controlled trials have shown the efficacy of behavioral interventions for young children with autism. While findings are promising, little attention has been given as to how interventions might be moved successfully to community settings so that they are effective and sustain. Efforts to transport interventions are hampered by lack of knowledge of real-world context, including teachers' training and resources, their ability and willingness to implement complex programs with fidelity, the school climate for embracing new interventions, and the heterogeneity of the children they serve. The Autism Instructional Methods Study (AIMS) is a four-year, large-scale randomized field trial designed to examine factors associated with the effective implementation and student outcomes of two evidence-based interventions – Strategies for Teaching based on Autism Research (STAR) and Structured Teaching – for students in kindergarten-through-second-grade autism support classrooms in an urban setting. This panel presents early results of the trial, including: the ability and willingness of education staff to implement these programs with fidelity (Stahmer), first-year student outcomes and moderators of outcome (Shin), the role of classroom climate in program fidelity (Dingfelder), and lessons learned in conducting research in partnership with a large school district (Mandell).

125.001 The Autism Instructional Methods Study: What We Planned and Why We Were Wrong. D. S. Mandell*[1], S. Shin[2], A. Stahmer[3] and S. C. Marcus[4], (1)*University of Pennsylvania School of Medicine*, (2)*University of Pennsylvania*, (3)*Rady Children's Hospital*, (4)*University of Pennsylvania School of Social Policy and Practice*

Background:

Many advantages exist in partnering with school districts to evaluate autism interventions. For example, studying subgroup variation will require large samples. Testing interventions in real-world settings determines effectiveness, rather than efficacy. Observations of how interventions are implemented in schools allows for meaningful changes to program manuals. If interventions are shown to be effective in these (rather than university-based) settings, it will increase the probability of uptake in community settings.

There also are challenges: Districts have strongly entrenched, difficult-to-change values and practices. Ethical and practical considerations limit acceptable research designs. Districts have limited resources for

teacher training and program implementation. Classroom staff may have limited ability or willingness to implement interventions with fidelity. Finally, educators may be suspicious of researchers' motivation.

Objectives: to present the strategies and experiences of the Autism Instructional Methods Study (AIMS) in partnering with a large school district to implement a randomized field trial of two classroom-based interventions for children with autism

Methods:

The study was planned in close collaboration with district administrators over a 2-year period. Early planning centered solely on issues important to district personnel. District personnel led efforts to evaluate and choose intervention programs for implementation. A test of two interventions (rather than a "teaching as usual" control group) was conceived based on practical and research considerations. To recruit teachers, letters were sent from the district and the PI visited schools. Union officials were involved in approving data collection, especially videotaping.

Compensation for teachers and parents was high. Parent burden was minimized by conducting assessments at schools. Student recruitment was done through teachers and early intervention transition teams. Passive consent was used for nonparticipating students so videotaping could occur.

Results:

To date, 370 students have been consented, comprising >60% of eligible students. Education staff in 54 of 66 classrooms received training in Years 1 and/or 2 of the study, with 49 classrooms participating in Year 2. Based on preliminary results, the district chose one of the interventions to be implemented in all K-2 autism support classrooms. Local staff and district personnel shadowed the program developers/trainers to develop local expertise in coaching.

Unanticipated challenges included poor communication with principals, which made direct assessments difficult; classroom staff changing classrooms based on seniority; difficulty in obtaining professional development days for training, and changes in district staffing, which inhibited the transfer of capacity for teacher coaching from the research team to the district. Some of these challenges were addressed by creating a monthly newsletter for families and district staff, working with the district and union to keep teachers in their classrooms, and reclassifying assistants as autism specialists. Because the district adopted the program, staff training was moved from weekends to professional development days, which greatly facilitated training. The issue of capacity transfer is challenging and may necessitate ongoing relationships between the district and researchers.

Conclusions: This type of large-scale partnership to conduct rigorous, meaningful research is feasible, but will require rethinking some issues related to intervention and research design.

125.002 Fidelity of Implementation of Evidence-Based Practice in Community Classrooms. A. Stahmer*[1], S. Reed[1], S. Shin[2] and D. S. Mandell[3], (1)*Rady Children's Hospital*, (2)*University of Pennsylvania*, (3)*University of Pennsylvania School of Medicine*

Background: Several behavioral methods have been identified as evidence-based practices (EBP) for children with autism spectrum disorders (ASD). In research studies examining the efficacy of these interventions, interventionists are required to meet strict fidelity of implementation criteria. It is likely that an integral part of moving these EBP into community settings is the correct implementation of these interventions by community providers. However, these EBPs require extensive training and may lack the flexibility needed for application in schools with more limited resources. Teachers express pervasive skepticism about the clinical utility of evidence-based ASD practices due to difficulties with adaptation to clinical settings (Stahmer et al., 2005). To date, fidelity of implementation of these interventions in classroom settings has not been tested. In addition, factors related to teachers' ability to master the intervention strategies (e.g., attitudes toward EBP,

teaching experience) have not been examined. Understanding areas of strength and difficulty for teachers in using these interventions and factors related to appropriate implementation is essential for translating EBPs to school programs. The Strategies for Teaching based on Autism Research (STAR) program is a comprehensive curriculum that uses EBPs to teach academic and social skills. Strategies include the highly structured discrete trial teaching (DTT), and a more naturalistic behavioral strategy pivotal response training (PRT) both of which are typically conducted individually. STAR was developed specifically for classrooms and is starting to be widely disseminated; however treatment integrity in community settings has not been systematically examined.

Objectives: To examine fidelity of implementation of the STAR program components, including DTT, PRT, and classroom environmental and visual strategies in urban classrooms.

Methods: Teachers in 20 classrooms assigned to the STAR condition of a randomized controlled field trial were videotaped monthly using DTT and PRT during the school day. In addition, classroom environments were coded for specific STAR program elements. Videotapes were coded for fidelity of implementation and rated for overall quality of teaching by undergraduate research assistants blind to the study hypotheses. Reliability of data coding was greater than 80% on all measures.

Results: 100% of teachers were willing to implement the DTT method on classroom taping days. Only 50% of teachers were willing to implement PRT on taping days. Of those that were videotaped using each method, 40% met overall fidelity of implementation in DTT and 0% in PRT. Quality of teaching ratings and use of classroom environment strategies were higher for teachers who met fidelity of implementation in DTT.

Conclusions: Urban public school teachers can implement evidence based intervention strategies. Teachers more frequently used antecedent strategies correctly than consequences in both DTT and PRT. Relationships between teacher characteristics and fidelity, and implications for community-based training and implementation will be discussed.

125.003 Student, Teacher and Classroom-Level Mediators of Outcomes for Children with Autism Spectrum Disorders. S. Shin*[1], A. Stahmer[2], S. C. Marcus[3] and D. S. Mandell[4], (1)*University of Pennsylvania*, (2)*Rady Children's Hospital*, (3)*University of Pennsylvania School of Social Policy and Practice*, (4)*University of Pennsylvania School of Medicine*

Background: Current studies show that intensive behavioral interventions are effective in improving cognitive and behavioral functioning for young children diagnosed with autism spectrum disorders. Little research has been conducted, however, for elementary school-age children. Even less has examined the impact of these interventions in community-based educational settings. With more than 250,000 students diagnosed with autism in the US served through the public education system, and some states' projections showing a doubling of this number by 2011, examining the best strategies to move evidence-based intervention into the public educational system is critical. The current study examined the effectiveness of an evidence-based intervention for children with autism in a large public school setting.

Objectives:

This study compares the effectiveness of the Strategies for Teaching based on Autism Research program (STAR) with that of Structured Teaching in kindergarten-through-second-grade autism support classrooms. In addition, we examine the moderating effects of student, teacher and classroom-level variables on student outcomes.

Methods:

178 students enrolled in 39 Kindergarten-2nd grade autism support classrooms in the Philadelphia public school district comprised the study sample. Subjects were administered an assessment battery in September and again in June, which included the Autism Diagnosis Observation Schedule as a general measure of symptom severity

and the and theDifferential Abilities Scale-II—Early Childhood Core Battery (DAS) as an outcome measure. Secondary outcome measures included the Adaptive Behavior Assessment System-II (parent report), PDD Behavior Inventory (teacher report), Aberrant Behavior Checklist (parent report), and Social Responsiveness Scale (parent and teacher reports).

Staff in each participating classroom was randomly assigned to training and ongoing support in STAR or Structured Teaching. STAR is an ABA-based classroom program which includes daily 1:1 sessions with each child using discrete trial and pivotal response training while integrating functional routines into academic curricula. The Structured Teaching instructional strategy emphasizes whole-class routines and setting up a structured physical classroom environment.

Results:

Overall, 16% of the sample experienced a gain of >10 points on the DAS, while 10% experienced a loss of 10 points during the study period. Students in STAR group showed an average increase of 9 points, compared with 6 points for students in the Structured Teaching group (p=.16). There was a significant interaction between intervention arm and teacher experience. In classrooms in which the teacher had <3 years experience teaching children with autism, there was little change in DAS score between groups (STAR = 7.8, ST = 8.6, p>.05). In classrooms with more experienced teachers, students in STAR classrooms experienced a 12.6-point gain in DAS score, compared with 3.5 points for students in Structured Teaching classrooms (p = .02). Additional analyses are ongoing to examine the effect of classroom characteristics, program fidelity and student characteristics on outcome.

Conclusions: Results will be used to discuss the importance of context, program fidelity and teacher experience in examining the effectiveness of evidence-based interventions as they move from research to community settings.

125.004 The Relationship Between Classroom Climate and Intervention Fidelity. H. E. Dingfelder*[1], S. Shin[1] and D. S. Mandell[2], (1)*University of Pennsylvania*, (2)*University of Pennsylvania School of Medicine*

Background: Interventions for children with autism spectrum disorders that have proven efficacious in research settings generally have not been effectively implemented in community settings. Challenges to successful implementation of interventions are apparent in AIMS (Autism Instructional Methods Study), an ongoing, randomized trial designed to test the effectiveness of an efficacious, teacher-delivered, curriculum-based intervention for children enrolled in autism support classrooms in a large, urban school district. Early observations suggest that a key reason for this variability is the extent to which the teachers perceive that their use of the intervention is expected, supported, and rewarded by their supervisors and other classroom staff. This shared perception is referred to as the organization's implementation climate. While a rich literature examines the role of the implementation climate in business settings, there is little study of the unique implementation climate in health and human services in general, and special education settings for autism specifically.

Objectives: The primary aim of this study is to examine the relationship between the climate of autism support classrooms in a large urban school district and the initial implementation of an evidence-based intervention. It is predicted that a strong classroom climate for the implementation of the intervention will lead to teachers' consistent, committed, and skilled use of the intervention. This commitment (known in the organizational literature as implementation effectiveness) is reflected in teachers' program fidelity, or the extent to which they deliver the intervention as intended by the program developers. To study this, we examine the relationship between 1) administrative and education support staff's acceptance of the intervention and 2) the climate of autism support classrooms and the implementation of an evidence-based intervention.

Methods: School principals and classroom assistants reported their acceptance of and support for the intervention, and teachers reported on classroom implementation climate. Baseline program fidelity was measured by videoing teachers implementing the program components in their classrooms. Coding strategies developed and validated for assessing the integrity of behavioral interventions for children with ASD in classrooms settings were used to provide quantitative, validated measures of the integrity of teaching methods. Trained research assistants and undergraduate students blind to study condition coded the tapes based on different criteria for each teaching technique.

Results: Data are currently being collected and analyzed. Results will be available by the time of presentation.

Conclusions: Studying the relationship between classroom climate and intervention fidelity is a key step in advancing our understanding of the best ways to support the implementation of efficacious autism interventions in special education settings. This study provides a strong foundation for intervention research targeting organizational climate as a way to support the implementation of evidence-based autism interventions, with the goal of improving services and outcomes for children with autism.

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126.001 A Population-Based Twin Study of Autism in California. J. Hallmayer*[1], J. M. Phillips[1], S. Cleveland[1], A. Torres[1], L. Lotspeich[1], C. Lajonchere[2], A. Fedele[2], J. Miller[2], T. Torigoe[2], J. K. Grether[3], K. S. Smith[3], J. Collins[4], S. Ozonoff[5], L. A. Croen[6] and N. Risch[7], (1)*Stanford University*, (2)*Autism Speaks*, (3)*California Department of Public Health*, (4)*CA Department of Public Health*, (5)*M.I.N.D. Institute, University of California at Davis*, (6)*Kaiser Permanente*, (7)*University of California San Francisco*

Background:

Autism has been referred to as the most heritable of the neurodevelopmental disorders. To date only three "population based" twin studies have been conducted each with very small samples of twin pairs (36 MZ and 30 DZ total). These studies reported a DZ concordance estimate of 0. This is clearly implausible, since the estimated sib recurrence risk is much higher. Currently we have no reliable heritability estimates and need to better understand twin concordance.

Objectives:

To estimate the probandwise concordance rates for autism in MZ and DZ twin pairs.

Methods:

Twin pairs for whom at least one child in the pair was receiving services for autism from the Department of Developmental Services (DDS) were identified. DDS operates a system of 21 Regional Centers (RC) that coordinate services for persons with autism, mental retardation, and other developmental disabilities. The electronic DDS client files were linked by California Autism and Developmental Disabilities Research and Epidemiology (CADDRE) staff to California live birth records, which provided information on twin status. In this study we recruited twin pairs born in California from the birth years 1987 to 2004.

Assessments were carried out by two sites: AGRE and Stanford. Zygosity was determined by genotyping.

Probandwise concordance rates in the twin pairs were calculated for two different definitions of autism. In the narrow definition, only twin individuals meeting criteria for autism on the ADI-R and autism on the ADOS are considered affected. The broader definition is based on the criteria published by Risi et al. (2006), which requires that criteria for autism spectrum disorder are met on the ADOS and criteria for autism in the domain of social reciprocity, and either the communication or restricted, repetitive behavior domain are met on the ADI-R.

Results:

We have identified 1122 twin pairs receiving DDS/RC services for autism. Of these 1007 twin pairs fulfill our eligibility criteria. A total

of 533 families expressed interest in participating in the study and agreed to be contacted by Stanford team members. Ten families turned out to be ineligible based on our exclusion criteria and 130 families decided not to participate because of the time commitment involved. So far assessments have been completed on 210 pairs of twins.

Concordance rates in MZ twins for the narrow and broad definition are higher (0.57 and 0.81 respectively) than for DZ pairs (0.13 and 0.19). Concordance rates for sex-discordant DZ twin pairs (0.08 for both the narrow and broad definition) are lower than concordance rates for both male-male DZ (0.19 and 0.30) and female-female DZ pairs (0.27 and 0.38). The risk for a co-twin to be affected is much higher if one of the affected twin individuals is female.

Conclusions: Autism concordance rates for DZ twin pairs are higher than previously published concordance rates of 0 for the narrow, and 0.1 for the broad definition. Further, the difference between MZ and DZ pairs (4.3-fold) is lower than previously reported.

126.002 CNV Atlas for Autism: A Gene Discovery and Clinical Research Tool. D. H. Ledbetter*[1], E. B. Kaminsky[1], D. Pickering[2], D. Golden[2], E. Aston[3], T. J. Gliem[4], T. Ackley[5], S. Huang[6], J. C. Barber[6], J. A. Crolla[6], R. K. Iyer[5], E. C. Thorland[7], A. R. Brothman[3], W. G. Sanger[2], S. Aradhya[4] and C. L. Martin[1], (1)*Emory University*, (2)*University of Nebraska Medical Center*, (3)*ARUP Laboratories*, (4)*GeneDx*, (5)*Michigan Medical Genetics Laboratories*, (6)*Wessex Regional Genetics Laboratory*, (7)*Mayo Clinic*

Background: Genome-wide oligonucleotide microarray analysis is now being used in the routine clinical evaluation of children with unexplained birth defects, developmental delay/mental retardation and autism/ASDs. These cytogenetic arrays have a 10-100 fold increased resolution to detect copy number variations (CNVs) compared to traditional G-banding analysis.

Objectives: We are utilizing copy number data from cytogenetic arrays to build a CNV Atlas for Autism to be used as a gene discovery and clinical research tool.

Methods: We have analyzed data from >15,500 whole-genome cytogenetic arrays from seven clinical diagnostic laboratories that are members of the International Standard Cytogenomic Array (ISCA) consortium. Approximately 15% of patients referred for clinical cytogenetic array testing have a primary indication of autism or ASD.

Results: Key results of our preliminary analysis relevant to autism include: 1) Microdeletion 16p11.2 is the second most common imbalance observed in all children referred for clinical array testing, observed in ~1/250 cases. Many of these children were referred in the first few years of life due to developmental delay and provide an opportunity for studies of early natural history and intervention. 2) Microdeletion 17q12, previously described in association with renal anomalies and diabetes, was identified in 10 cases and led to the delineation of a new syndromic phenotype including macrocephaly, characteristic facial appearance, and autism in males (6/6) but not females (0/3). Previous linkage and association studies, replicated by multiple groups, suggested a "male-only" peak in this same region of 17q, indicating a sex-specific locus for autism. 3) Review of small, de novo deletions in children with an indication of autism/ASD revealed a number of cases (n=22) in which only 1 or two genes were contained within the deleted segment, providing a highly efficient deletion mapping strategy for identification of autism candidate genes. A recently funded NIH Grand Opportunity (GO) grant will allow development and expansion of a CNV database from clinical cytogenetic testing with an estimated 200,000 cases within the next two years.

Conclusions: This free, public database will be a significant resource for the identification of candidate genes for autism and other developmental disorders, and allow detailed genotype-phenotype correlation studies for human CNVs.

126.003 Decreased Serum Hepatocyte Growth Factor (HGF) in Autistic Children with Severe Gastrointestinal Disease. A. J. Russo*, *Health Research Institute/Pfeiffer Treatment Center*

Background: Because a MET variant exists in the genome of a significant number of autistic individuals, we hypothesized that this might result in abnormal levels of serum HGF, particularly those with severe GI disease. Objectives: To assess serum Hepatocyte Growth Factor (HGF) levels in autistic children with severe gastrointestinal (GI) disease and to test the hypothesis that there is a relationship between GI pathology and HGF concentration. Methods: Serum from 29 autistic children with chronic digestive disease (symptoms for a minimum of 6–12 months), most with ileo-colonic lymphoid nodular hyperplasia (LNH—markedly enlarged lymphoid nodules) and inflammation of the colorectum, small bowel and/or stomach), and 31 controls (11 age matched autistic children with no GI disease, 11 age matched non autistic children without GI disease and 9 age matched non autistic children with GI disease) were tested for HGF using ELISAs. HGF concentration of autistic children with GI disease was compared to GI disease severity. Results: Autistic children with GI disease had significantly lower serum levels of HGF compared to controls (autistic without GI disease; $p = 0.0005$, non autistic with no GI disease; $p = 0.0001$, and non autistic with GI disease; $p = 0.001$). Collectively, all autistic children had significantly lower HGF levels when compared to non autistic children ($p < 0.0001$). We did not find any relationship between severity of GI disease and HGF concentration in autistic children with GI disease. Conclusions: These results suggest an association between HGF serum levels and the presence of GI disease in autistic children and explain a potential functional connection between the Met gene and autism. The concentration of serum HGF may be a useful biomarker for autistic children, especially those with severe GI disease.

126.004 Embryologically-Derived Measures of Dysmorphology Among AGRE Multiplex Autism Probands. C. Deutsch*[1], R. E. Butler[2], S. S. Nazarian-Mobin[3], B. S. Chambers[2], A. R. Shell[4], J. R. Cuomo[5], R. W. Francis[4], J. M. Stoler[6], M. M. Urata[3] and C. Lajonchere[2], (1)*Shriver Center and McLean Hospital, Harvard Medical School*, (2)*Autism Speaks*, (3)*Children's Hospital Los Angeles*, (4)*Eunice Kennedy Shriver Center*, (5)*Harvard University*, (6)*Children's Hospital Boston*

Background: A number of laboratories, including ours, have reported a statistical overrepresentation of craniofacial anomalies among individuals with autism spectrum disorders (ASDs). This excessive dysmorphology in a brain-based condition is plausible given the fact that the brain and face derive from common embryologic primordia and are shaped by shared forces during development. In fact, there are numerous examples of specific genetic and teratogenic disorders that have distinctive facial appearance. Common examples include Williams syndrome and fetal alcohol embryopathy. In the past, there have been difficulties rendering the diagnosis of these anomalies objective and reliable. Also, earlier methods focused on summary symptom counts which yielded robust group differences, but which provided little by way of biological interpretation.

Objectives: In the context of an endophenotyping initiative within the Autism Genetic Resource Exchange (AGRE), we have performed quantitative assessment of craniofacial dysmorphology on a collection of multiplex families. Our approach is to apply objective and reliable methodology to the diagnosis of craniofacial dysmorphology. We employ embryologic principles to provide potential insight into the developmental neurobiology of individuals with ASDs. Rather than studying single anomalies, we focus on embryologically-derived combinations of anomalies that are based on specific developmental factors.

Methods: We recruited 40 multiplex families with ASD from the AGRE program and acquired images using a noninvasive stereophotogrammetric device (3dMD, Atlanta). Surface images were then analyzed using 3D morphometry, and standardized scores were computed for craniofacial anomalies. These scores were computed on a continuously-distributed scale, conditioning on age, gender, and ethnicity.

Results: There was a marked excess of craniofacial anomalies among the probands with autism relative to the general population ($p < .0001$). We also analyzed dysmorphology as a function of facial embryonic primordia (Anlagen), discrete regions that are formed early in development

and which can be readily identified in the course of differentiation. The probands with ASD displayed an overrepresentation of anomalies within the frontonasal ($p < .005$), maxillary ($p < .002$), and auricular ($p < .0001$) Anlagen derivatives. In contrast, mandibular and orbital anomalies were not excessive.

Conclusions: Craniofacial dysmorphology, quantified using a combination of 3D imaging and statistical morphometry, was pronounced. These anomalies corresponded to specific embryologic regions: derivatives of the frontonasal, maxillary, and auricular primordia. There is an intimate developmental relationship between brain and face. Embryological "fate-mapping" studies have described how embryonic regions correspond to specific derivatives in both craniofacial and brain regions. Because there is a topographic correspondence between face and brain morphogenesis, craniofacial dysmorphology may delineate brain pathology. For instance, the frontonasal neural crest arises primarily from the neural fold area corresponding to the anterior telencephalon and the posterior diencephalon. Thus, brain anatomic regions are embryologically linked to specific craniofacial Anlagen, and the derivatives identified in this study may circumscribe areas of potential importance in ASD.

126.005 Genome-Wide Analysis Identifies Global Rare Variation in Autism. .. Autism Genome Project Consortium*, *AGP Institutions in*

Background: Autism spectrum disorders (ASDs) are highly heritable (≈90%), yet the underlying genetic determinants are largely unknown. Objectives: To understand the genetic and phenotypic heterogeneity in ASDs, the Autism Genome Project (AGP) Consortium conducted high-resolution genotyping and applied multiple analytical strategies to examine over 1,500 families for single nucleotide polymorphisms (SNPs) and copy number variation (CNV) affecting risk for ASDs. Methods: We analyzed 1,558 strictly defined ASD families with 1,000,000 SNPs. We conducted genome-wide association (GWA) analyses of SNPs and targeted analysis of SNP-tagged common CNVs to evaluate involvement of common alleles. We also analyzed array data to identify and characterize rare CNVs in autism families in comparison to large control datasets. Results: From four primary association analyses, the P-value for rs4141463 within *MACROD2* crossed the GWA significance threshold of $5x10^{-8}$. Two SNP-tagged common copy number variations (CNVs), rs12142922 (tagging exonic CNVR244.1 located at *GBP3*) and rs7576647 (tagging CNVR742_full), also showed strong association. Compared to controls, ASD cases carried a higher global burden of rare genic CNVs (1.19 fold, $P=0.012$), especially for loci previously implicated in ASD or intellectual disability (1.69 fold, $P=3.4x10^{-4}$). In addition, we identified a plethora of novel, rare, *de novo* and inherited CNVs implicating novel ASD genes including X-linked *PTCHD1* ($P=3.1x10^{-3}$), and the autosomal genes *SYNGAP1*, *DLGAP2*, and *SHANK2*. Hallmarks of these CNVs included combinations of *de novo* and inherited events in a given family, incomplete penetrance, and non-segregation in families. Conclusions: Our results reveal profound etiological heterogeneity in ASDs. These studies further underscore the need for larger datasets to detect common alleles that confer low to modest risk and highlight the important role that rare variation plays in ASD etiology. Since rare CNVs clearly contribute to ASD risk, we anticipate that rare, deleterious sequence variants will be equally important. Large-scale sequencing projects that target large candidate gene sets or whole exome or genome for analysis will test this hypothesis. Ultimately, larger well-characterized ASD cohorts will be required to elucidate the full range of both common alleles of low effect size and rare variants conferring substantial risk, such as those identified in this study. Despite the heterogeneity of ASD etiology, understanding the underlying genetic architecture will reveal gene networks that will ultimately serve as targets for therapeutic intervention.

126.006 Sex-Specific Genetic Effects of Autism Spectrum Disorders in a Genome-Wide Association Analysis. S. C. Chang*[1], C. Lange[2], J. Lasky-Su[3], M. J. Daly[4] and S. L. Santangelo[4], (1)*Department of Epidemiology, Harvard School of Public Health*, (2)*Department of Biostatistics, Harvard School of Public Health*, (3)*Channing Laboratories, Brigham and*

Women's Hospital and Harvard Medical School, (4)*Massachusetts General Hospital*

Background: For reasons not yet understood, there is a significant sex bias in the prevalence of autism, with a male-to-female ratio of 4:1. Some linkage and candidate gene association studies of ASD have employed a sex-spliting strategy and found genetic effects specific to families with only affected males (Male-only; MO) versus families containing at least one affected female (Female-containing; FC), supporting the possibility of sex-specific genetic heterogeneity.

Objectives: The goal of this study was to identify sex-specific genomic variants that underlie susceptibility to ASD using a family-based genome-wide association study (GWAS) approach.

Methods: We performed a GWAS analysis on 783 ASD families from the Autism Genetic Resource Exchange (AGRE), genotyped with the Affymetrix SNP Array v. 5.0. A series of stringent quality control (QC) procedures was performed on SNPs and individuals; Mendelian errors were reset to missing in the analyses. We used the multi-dimensional scaling (MDS) procedure for inferring population structure and restricted our final analysis to 2,423 individuals of European ancestry from 667 ASD families. Sixty percent of the multiplex European families were classified as male only (MO) while 40% contained at least one affected female (FC). A total of 337,319 autosomal SNPs, including 110 in the pseudoautosomal region (PAR) were analyzed. Association analysis was performed with the Pedigree-Based Association Test (PBAT) program, assuming an additive model. Applying a conservative Bonferroni correction for multiple testing resulted in a genomewide significance level of 1.48E-07.

Results: In the MO family set analysis we identified two novel loci for autism that reached statistical significance at the genomewide level (rs2535443, p = 3.8E-08, and rs311150, p = 1.2E-07); a third SNP, rs311149, in the same region showed evidence for suggestive association (p = 3.6E-07). These three markers, located in the introns of the XG gene in the PAR boundary of the short arm (PAR1) of Xp22.3, are in high linkage disequilibrium (LD) with each other (pairwise r^2 = 0.96-1.0). In addition, markers rs1328250, rs9521354, rs9521355, rs9521356, and rs1328244, located in a 600 kb intergenic region on chromosome 13q33.3 between the MYO16 and IRS2 genes, showed suggestive association to ASD (p = 5.3E-07, 9.2E-07, 1.5E-06, 9.2E-07, 2.6E-06, respectively) in MO families. MYO16 encodes an unconventional myosin protein predominantly expressed during brain development, and has shown protein-protein interactions with neurexin 1-_, a presynaptic membrane cell adhesion molecule that is associated with autism. These SNPs had moderate to complete LD with each other (r^2 = 0.63-1.0) and may serve as a proxy that captures the association of functional variants which regulate the expression or action of MYO16. These markers were not associated with ASD in the FC families despite the fact that the power analysis indicated there was adequate power to detect a risk effect in the FC family set, similar to that in the MO family set. Therefore the markers associated in the MO families may be sex-influenced loci.

Conclusions: Our results suggest that the pseudoautosomal boundary of PAR1 and the intergenic region on 13q33.3 may harbor novel male-specific genetic variants for ASDs.

126.007 Systematic Resequencing of X-Linked Synaptic Genes: Identification of Damaging Mutations in Autistic Spectrum Individuals. A. Piton*[1], J. Gauthier[1], F. F. Hamdan[1], S. 2. D. Team[1], L. Mottron[2], R. Joober[3], E. Fombonne[4], P. Drapeau[5] and G. A. Rouleau[1], (1)*CENUM*, (2)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (3)*Institut Douglas*, (4)*McGill University*, (5)*Groupe de recherche sur le systeme nerveux central*

Background: Autism spectrum disorder (ASD) is a common neurodevelopmental disorder that typically appears during childhood. Twin and epidemiological studies strongly support the role of genetic and environmental factors in this disease. Several linkage and association studies have been performed over the past decades, with limited success.

Objectives: We explored the hypothesis implicating genetic heterogeneity, in which rare highly penetrant mutations (some of which may be *de novo*) in different genes specific to single families would predispose to these diseases. This is supported by the recent findings that rare and *de novo* mutations in the *NLGN4X*, *NLGN3*, *SHANK3* and other synaptic genes are associated with ASD in a small number of families.

Methods: To identify rare damaging variants, we resequenced one hundred X-linked synaptic genes directly in a cohort of 142 ASD individuals.

Results: We found two truncating mutations: a polymorphism in *P2RY4* (p.W348X) and a *de novo* frameshift deletion in the calcium-related gene *IL1RAPL1* (I367SfsX6). Moreover, we identified around one hundred rare variants, with more nonsynonymous damaging variants than expected, which suggests the presence of disease-causing mutations. Promising rare variants, predicted to affect protein function or mRNA splicing, were identified in genes encoding proteins involved in various synaptic functions. Some of these genes (e.g., *TSPAN7*, *OPHN1*) were already associated with mental retardation (MR).

Conclusions: Our results indicate that large-scale direct resequencing of synaptic candidate genes constitutes a promising approach to dissect the genetic heterogeneity of ASD and to explore the hypothesis that a number of distinct, individually-rare penetrant variants are involved in the genesis of this condition.

127 Preschool Autism Communication Trial (PACT)

Organizer: J. Green *The University of Manchester*

PACT is the first large scale RCT to be completed to date on psychosocial intervention for autism. This panel provides a timely overview for the field of the rich clinical dataset and scientific material generated by this large trial. In addition to answering primary questions of treatment effectiveness, PACT was also designed as a developmental experiment, testing key aspects of early psychopathology of autism through innovative analysis of mediation. The presentations focus on primary ITT analysis of the trial and implications for current autism intervention practice and research; investigations of causal relationships between parent-child dyadic communication and autism development; and the value of patient-nominated outcome measures. We present a new quality of life family measure developed and validated during the PACT trial.

127.001 Parent-Mediated Communication-Focused Treatment for Preschool Children with Autism (MRC PACT); A Randomised Controlled Trial. J. Green*[1], T. Charman[2], H. McConachie[3], C. R. Aldred[4], V. Slonims[5], P. Howlin[6], A. Le Couteur[7], K. Leadbitter[4], K. Hudry[8], S. Byford[9], B. Barrett[9], K. Temple[10], W. MacDonald[1], A. Pickles[4] and T. PACT Consortium[4], (1)*The University of Manchester*, (2)*Institute of Education, University of London*, (3)*The University of Newcastle*, (4)*University of Manchester*, (5)*Guy's and St. Thomas' NHS Trust*, (6)*Institute of Psychiatry, King's College London*, (7)*Newcastle University*, (8)*Department of Psychology and Human Development, Institute of Education*, (9)*Institute of Psychiatry*, (10)*University of Newcastle*

Background: Accumulating evidence from recent randomized trials and systematic reviews[1,2,3,4] has suggested the potential effectiveness of early social communication interventions for autism. Positive reports have also come from studies of behaviourally focused approaches although evidence from the few randomised controlled trials in that area is more equivocal.[5] Firm inferences from all these studies to date have been somewhat limited however by size and heterogeneity of samples and sometimes aspects of methodology. The PACT trial aimed to provide a stringent test of parent-child communication-focused intervention in preschoolers with core autism, using the largest sample to date and a rigorous RCT design.

Objectives: To provide a stringent test of a parent-mediated communication-focused intervention for preschoolers with core autism, using a large sample and a rigorous RCT design (www.medicine.manchester.ac.uk/pact).

Methods: 152 children with core autism aged 2 - 4.11 were studied in a 3 site 2 arm single (assessor) blinded randomised controlled trial of a parent-mediated communication-focused intervention added to treatment as usual (TAU) against TAU alone. The primary outcome was severity of autism symptoms (total social communication algorithm items from the Autism Diagnostic Observation Schedule, ADOS). Complementary secondary outcomes were: 1) a standardised measure

of parent-child interaction (PCI)[2]; 2) blinded research rating of child language on the Preschool Language Scales; 3) parent reported (non-blind) ratings on the McArthur Communicative Developmental Inventory (MCDI; infant form raw scores), the Communication and Symbolic Behaviour Scales – Developmental Profile (CSBS-DP), and the Vineland Adaptive Behavior Scales (Parent Form); 4) Vineland Adaptive Behavior Scales, 2nd edition, Teacher Rating Form rated by teachers in nurseries, reception class or other appropriate out-of-family carers. Attention was paid in the study to the details of randomization and blinded ascertainment. All the analysis undertaken was pre-specified.

Results: Data analysis is complete but the results currently embargoed while undergoing review by the Lancet. Full data from the study will be available to be presented at IMFAR.

Conclusions: The implications of our results for autism intervention practice and research will be outlined.

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127.002 Analysing the Impact of Parent Communication Training On the Child with Autism: Learning From Trials.

A. Pickles*[1], J. Green[2], H. McConachie[3], T. Charman[4], C. R. Aldred[1] and T. PACT Consortium[1], (1)*University of Manchester*, (2)*The University of Manchester*, (3)*The University of Newcastle*, (4)*Institute of Education, University of London*

Background: Properly conducted therapeutic trials should be a rich source of information on how change in interaction, behaviour and functioning can be brought about. The careful design that is required for rigorous evaluation can also provide a unique opportunity for a detailed decomposition of how change diffuses through the interactional environment and to do this in a way that may be causally meaningful. Such analyses will be key to learning not just what interactions are sensitive therapeutic targets but also where transmission of effect is blocked or dissipates. Such knowledge acquisition is essential to the process of revision, refinement and enhancement of therapies that should be the aim of our therapeutic research. However, for us to be able to use trials in this way requires that we elaborate in parallel both our designs and our analysis of findings.

Objectives: We describe recent methodological concerns and advances that properly exploit randomisation even while examining relationships among post-randomisation measures and then consider some of the implications these have for measurement protocols and design.

Methods: Using the Pre-School Autism Communication Trial (PACT) as an illustrative vehicle we describe the combination of trajectory models that characterise the joint development of parent and child interaction during progress of the trial and counterfactual thinking that helps characterise the impact of treatment in a way that continues to exploit randomisation. We consider how these models can be extended to consider the transmission or disattenuation of effects to final outcome, and the appropriate ways in which we should assess the extent to which effects are transmitted along/mediated in the hypothesized manner. In so doing we

highlight some of the implicit but implausible assumptions commonly made in the analysis of mediation.

Results: Trial data is complete but due to a pre-publication embargo on the study findings we are unable to summarise the empirical findings in this abstract. However all data and analysis will be available for presentation at the IMFAR meeting.

Conclusions: Treatment trials can and should be viewed and designed both as tests of proposed treatments and as research tools with which to explore and refine the therapeutic pathway.

127.003 The Family Life Questionnaire: The Development of An Autism-Specific Measure of Family Life Functioning. D. Kapadia*[1], K. Leadbitter[2], W. MacDonald[1], R. Emsley[1], H. McConachie[3], J. Green[1] and T. PACT Consortium[2], (1)*The University of Manchester*, (2)*University of Manchester*, (3)*The University of Newcastle*

Background: The involvement of service users in the development of the design and outcome measures in treatment trials is a current priority in the field[1]. There is currently no specific measure of family quality of life for use in autism treatment trials or studies. We undertook to develop such a user nominated measure in the context of the MRC Preschool Autism Communication Trial (PACT), a large preschool treatment trial in autism funded by the UK Medical Research Council. The Trial, with its RCT methodology and large well defined sample, provided an optimal context for the development and initial evaluation of such a measure.
Objectives: To explore the internal and external validity of the Family Life Questionnaire. To ascertain this measure's sensitivity to change in a treatment trial.

Methods: Development of measure.
Initial focus groups were undertaken with families of young children with autism (none of whom was involved in the PACT trial). Groups were asked to nominate areas of child and family functioning that would be considered key markers of whether a pre-school autism treatment had been effective. From the focus group analysis 78 change markers were submitted to a national web-based consultation in collaboration with the UK National Autistic Society. The web consultation weighted each item for importance and clarity. The resulting refined questionnaire consisted of the 56 most highly nominated items in three domains a) experience of parenting their child; b) quality of family life; c) child development, social functioning and behaviour.
Data collection.
The Family Life Questionnaire (FLQ) was administered at baseline and 13 month endpoint to the 152 families involved in the PACT RCT.
Analysis plan.
A) Confirmatory factor analysis to explore the construct validity and assess whether the latent variable structure tapped by the measure fits the three domains previously specified; exploratory factor analysis added as necessary to explore further the latent factor structure. B) External validity investigated through relationships with the other trial measures, particularly the Vineland Adaptive Behaviour Scales (Parent Survey Form) and other baseline measures including demographic characteristics and child autism severity. C) The FLQ data is analysed for sensitivity to change between baseline and endpoint against the primary and secondary outcomes of the RCT.

Results: The data are complete. Results will be presented in the panel on each area of the pre-specified analysis plan as above.
Conclusions: We comment on the method used to generate this measure and its empirical validity. We discuss its potential usefulness within future autism treatment trials.

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128 The Role of the Corpus Callosum in Autism

Moderator: E. Marco *UC San Francisco*

Organizer: E. Sherr *UCSF*

The corpus callosum is the brain's major cortical white matter tract with nearly 200 million axons connecting the right and left cerebral hemispheres. Emerging evidence suggests that individuals with ASD have small or anatomically atypical corpus callosa. Furthermore, individuals with congenital

absence of the corpus callosum (AgCC) can have communication, executive function and social disabilities that are within the autism spectrum. Both groups experience sensory sensitivities that may play a role in learning and behavioral difficulties. In this session, we show that AgCC individuals have profound social deficits associated with decreased sensory processing. Moreover, AgCC participants have deficits in recognition of facial emotion that appears related to not looking at the eyes and the mouth, as found in ASD generally. We also provide important insights from MEG-based functional connectivity: resting state connectivity is decreased in frontal lobe regions and correlates with both executive function and overall social cognition performance. These findings underscore the role that disrupted long-range connectivity plays in autism.

128.001 Agenesis of the Corpus Callosum and the Autism Spectrum. Y. Lau*[1], E. Marco[2], L. B. N. Hinkley[1], Z. Strominger[1], R. Jeremy[1], P. Mukherjee[1], S. Nagarajan[1] and E. Sherr[3], (1)*University of California, San Francisco*, (2)*UC San Francisco*, (3)*UCSF*

Background: Agenesis of the corpus callosum (ACC), the congenital absence of the major interhemispheric commissure, occurs in 1:3,000 life births and can result in severe developmental impairment. Mildly affected patients can have social and communication deficits in the autism spectrum, although this has not been systematically addressed. Moreover, in many ACC cases other structures besides the corpus callosum are affected; how they influence clinical outcome is unclear. Objectives: We hypothesize that many ACC individuals have autistic traits. We secondarily hypothesize that the severity of these autistic traits correlate with MEG (magnetoencephalographic) measures of functional connectivity in non-callosal brain regions. Methods: Individuals from our ACC cohort were sent age grouped Autism Quotient (AQ) tests: Child (4-11 years), Adolescent (12-15 years), and Adult (16+ years). Child and Adolescent AQ tests were completed only by parents; Adult AQ tests were also completed by the ACC individual. The AQ is a standardized questionnaire developed and validated by Dr. Simon Baron-Cohen to assess autism traits in high functioning individuals. 409 AQ tests were mailed out and 101 tests were used in the final analysis: 44 children, 19 adolescents, and 38 adults. We also collected MEG resting state brain activity using a 275-channel biomagnetometer on Adult ACC individuals who visited our lab (n=10, IQ = 99.56 +/- 16.4). Neural sources were estimated using novel adaptive spatial filtering techniques and connectivity was estimated using imaginary coherence. Results: In children, AQ scores averaged 70.9 ± 20.2 compared to 41.7 ± 18.6 of the control children ($p < 0.0001$). The clinical cutoff score is 76 out of 141, and 40.9% ACC children exceeded the cutoff compared to 4.3% of the control child group ($p < 0.0001$). In adolescents, 26.3% exceeded the cutoff score compared to 0% in the control adolescent group ($p = 0.001$). In self-reporting Adults, 20% passed the cutoff compared to 2.3% in the control adult group ($p = 0.0004$). In contrast, when parents complete the assessment, 40% of ACC adults cross the threshold when using a comparative score. We tested the correlation between total Adult AQ scores and MEG resting state brain connectivity. We computed at each voxel the correlation (Pearson's r) between AQ scores and functional connectivity in a hypothesis independent way, and corrected for multiple comparisons using the false discovery rate (FDR) statistic. We found that the degree of connectivity in the right ventrolateral prefrontal cortex inversely correlated with the parent reported AQ score ($r = -0.86$; $p<0.1$; FDR corrected). When self-reporting scores were considered, however, no significant correlation was identified. Conclusions: Many ACC individuals, up to 10 fold more than control groups, exhibit social characteristics that exceed the AQ threshold screen for autism. Within the adult cohort, we find a correlation between the degree of autistic symptoms and underconnectivity within the right ventrolateral prefrontal cortex, a region implicated in social cognition. As deficits in frontal lobe connectivity and decreases in corpus callosum volume have been associated with autism, our findings strengthen these associations and provide a means to study this complex disorder.

128.002 Facial Emotion Recognition in Primary Agenesis of the Corpus Callosum. L. K. Paul*[1], M. W. Bridgman[1], W. S. Brown[2], M. L. Spezio[1] and R. Adolphs[1], (1)*Caltech*, (2)*Fuller Graduate School of Psychology*

Background: The corpus callosum is one of several structures thought to be abnormal in autism, in line with theories that autism arises from abnormal brain connectivity. Agenesis of the corpus callosum (AgCC) is a congenital condition in which the ~190 million fibers that normally connect the cerebral hemispheres fail to cross the midline. Primary AgCC is characterized by minimal additional neuropathology and intact general intelligence. However, individuals with Primary AgCC exhibit deficits in non-literal language comprehension, humor, theory of mind, and social reasoning (Paul et al., 2007), a profile strikingly similar to high-functioning autism, especially with regard to social interaction and communication (Badaruddin et al., 2007).

Objectives: In autism research, psychosocial deficits have been related to atypical eyetracking to faces and impaired emotion recognition (Pelphrey et al., 2002). We examined these measures in Primary AgCC, to see if they would show similarity to what has been found in autism, specifically impaired emotion recognition and reduced visual attention to the eyes in faces.

Methods: Nine adults with Primary AgCC and 9 neurotypical controls completed 4 tasks with the Ekman emotional faces: emotion recognition of upright faces and inverted faces, gender naming, and passive viewing. Participants were assessed for accuracy on the three recognition tasks. High-resolution eye-movement data collected throughout were analyzed according to examiner-designated facial regions of interest for absolute number of fixations and proportion of trial time fixating each ROI.

Results: The AgCC group was less accurate than controls in naming all emotions except happiness in upright faces. Naming of fear and anger was significantly impaired relative to controls. For upright faces, the AgCC group had smaller fractional dwell times and fewer fixations in the eye regions, and larger fractional dwell times and more fixations in the nose and mouth regions, compared to controls. Distribution of fixations across trial time indicates that control subjects generally fixated the eyes earlier in the trial than did AgCC subjects.

The AgCC group exhibited an inversion effect for emotion recognition, with a greater decline in performance than controls on happy, neutral and fearful inversions. Group difference was only significant for fearful faces. For inverted faces, fractional dwell times and number of fixations did not differ between groups.
AgCC subjects did not differ from controls in accuracy of gender identification, nor did they have significant differences in eye-tracking patterns during gender judgment. On the passive viewing task, the AgCC group exhibited a non-significant tendency toward lower fractional dwell time and fewer fixations in the eye regions.
Conclusions: Primary AgCC and autism share impairments in facial emotion recognition, which may be secondary to abnormal fixations to the features of faces. Specifically, participants with AgCC made fewer fixations to the eye region, with variable increases to mouth and nose regions of faces. These fixation abnormalities were relatively selective to emotion judgments of faces, and were associated with impaired recognition of emotion, especially fear and anger. These findings provide additional support for the connectivity hypothesis of social deficits in autism.

128.003 Individuals with Agenesis of the Corpus Callosum Show Atypical Sensory Processing. M. Arroyo*[1], Z. Strominger[1], W. Dunn[2], R. Jeremy[1], A. J. Barkovich[1], E. Sherr[3] and E. Marco[4], (1)*University of California, San Francisco*, (2)*University of Kansas*, (3)*UCSF*, (4)*UC San Francisco*

Background: Individuals with agenesis of the corpus callosum (AgCC) have social and communication deficits similar to those reported in autism spectrum disorders (ASD). Furthermore, there are a growing number of studies reporting atypical corpus callosum structure in cohorts with ASD. Consequently, AgCC cohorts serve as an excellent model for studying the role of the corpus callosum in cognition and behavior. Objectives: Based on anecdotal reports of diminished pain threshold in this population, we hypothesize that a greater percentage of individuals with AgCC will have "altered sensory registration" as measured by the Sensory Profile relative to healthy controls. Methods: AgCC subjects (n=14: partial AgCC n=5, complete AgCC

n=9) were recruited from the UCSF Brain Development Research Program and healthy controls (HC) (n=14) matched for age and gender were selected from the SP normative dataset. There were 6 adolescents (mean age 14 years, range 11-17) and 8 adults (mean age 33years, range 20-59) in each group. We selected individuals who were over the age of 11 and for whom we knew had IQ>70. We sent 20 adolescent and adult Sensory Profile (SP) questionnaires and received 14 (70% response rate.) The SP has 60 questions that are clustered to create 4 distinct quadrants: Low registration, sensory sensitivity, sensation seeking, and sensation avoiding. In order to combine the adolescent and adult score, all quadrants are broken into a 5-point classification system based on the normative dataset. A score of "5" or "1" indicates that the individual's behavior is greater than 2 standard deviations from the mean. Results: The AgCC group FSIQ fell in the normal range with a mean of 93.4 +/- 13.5. Using a Fisher's exact test, the AgCC group showed significantly different scores on the low registration quadrant relative to HC (p=0.03). The AgCC group tended to have lower sensory registration than the HC group (which translates to higher scores on the low registration quadrant). On analysis of discrete sensory domains (auditory, tactile and visual), we found that the AgCC group scored significantly different only on the auditory domain (p=0.02). Conclusions: Individuals with AgCC, like those with ASD, show atypical sensory processing. This difference is mainly found in the auditory domain and in the low registration quadrant. These findings will help understand the pathophysiology of sensory processing and guide interventions for all those with abnormalities of the corpus callosum.

128.004 Functional Connectivity and Executive Function in Agenesis of the Corpus Callosum. L. B. N. Hinkley*[1], E. Marco[2], A. M. Findlay[1], R. Jeremy[1], Z. Strominger[1], M. Wakahiro[1], P. Mukherjee[1], S. Nagarajan[1] and E. Sherr[3], (1)*University of California, San Francisco*, (2)*UC San Francisco*, (3)*UCSF*

Background: As callosal deficits have been consistently reported in autism, studying individuals with agenesis of the corpus callosum (AgCC) provides unique insight into how disruption of interhemispheric and other long-range connectivity affects behavior and cognition. Moreover, individuals with AgCC may have symptoms in the autism spectrum, suggesting an important mechanistic overlap. Objectives: Here, we examine resting-state functional connectivity of magnetoencephalography (MEG) data in people with anomalies of the corpus callosum (partial absence: pAgCC; complete absence: cAgCC) using novel source-space reconstruction techniques and imaginary coherence. We also compare functional connectivity to performance on tasks of processing speed and executive function, cognitive deficits shared by many AgCC and autistic individuals. Methods: Fourteen participants with AgCC (8 cAgCC, 6 pAgCC) and fourteen IQ and age-matched control subjects enrolled in this study. All individuals with AgCC were evaluated with the Weschler Adult Intelligence Scale III and Delis-Kaplan Executive Function Scale (D-KEFS). Four minutes of resting-state (alert; eyes closed) data was collected using a 275-channel biomagnetometer (VSM MedTech) using a sampling rate of 600Hz. A single, artifact-free epoch (60s) was selected from this period and neural activity during the resting session in the alpha band (8-12Hz) was computed using adaptive spatial filtering techniques (beamforming). Functional connectivity was estimated using imaginary coherence (IC), a metric that overcomes estimation biases in EEG/MEG source-space reconstructions. Connectivity maps between groups were compared (non-parametric unpaired t-test) and voxelwise correlations between IC and D-KEFS scores were computed across AgCC participants. Corrections for multiple comparisons were computed using a false discovery rate (FDR). Results: Our results show significant underconnectivity in the brains of AgCC individuals in two key cortical hubs: left dorsolateral pre-frontal cortex (DLPFC; $p<0.05$ FDR corrected) and right posterior parietal cortex (PPC; $p<0.1$, FDR corrected). For both DLPFC and PPC, there is a trend for the pAgCC group to have greater interhemispheric connectivity relative to the cAgCC group. We found that in the right PPC, the AgCC group trends toward greater intrahemispheric connectivity and this finding appears to be equally contributed to by both the cAgCC and pAgCC group. These data

suggest that not only is there decreased interhemispheric connectivity in AgCC, but that it is specifically related to critical integrative brain regions. Functional connectivity was related to performance on neuropsychological tests. The degree of connectivity of higher-order auditory regions in the left hemisphere (middle and superior temporal gyrus) positively correlated with verbal processing speed. The degree of connectivity of left DLPFC correlated with problem-solving abilities and second-order language comprehension, as measured by the Tower and Proverbs tests within DKEFS. Conclusions: Congenital disruption of callosal development can result in faulty functional coupling of higher order cortical fields. This can be measured during the brain's "resting state". That performance on cognitive tests correlates with connectivity in critical areas supports the concept that connectivity is a key component of performance generally. These insights may help us to target interventions to AgCC individuals and may help us to understand and treat related disorders of connectivity such as autism and schizophrenia.

129 Very Early Interventions for ASD: Research Challenges and Promising Results

Moderator: A. Wagner *National Institute of Mental Health*

Organizer: A. Wagner *National Institute of Mental Health*

It has been shown that many children with ASD can be reliably identified by two years of age. It is generally accepted that early intervention takes advantage of brain plasticity in early development, but there is a need for empirical evidence of the efficacy of such interventions. This panel presents three early intervention studies from the NIH-funded Studies to Advance Autism Research and Treatment (STAART) Centers that address this need. Results will be presented from a pilot pharmacology trial for children ages 30 – 58 months (Sikich et al), a nursery-school based intervention with children ages 23 – 33 months (Landa et al), and a home-based intervention for 18- to 30-month-olds (Dawson et al). In the context of describing their studies and results, the investigators will discuss the special design and measurement challenges encountered when conducting treatment studies in toddlers and very young children, and the ways in which they each addressed those challenges. Ann Wagner, Ph.D., Chair of the NIH Autism Coordinating Committee, will introduce each of the studies and discuss implications.

129.001 A Feasibility Study of Year-Long Placebo-Controlled Fluoxetine Treatment in Young Children with Autism. L. Sikich*[1], E. Hollander[2], E. Anagnostou[3], K. G. Lapp[4], T. C. Bethea[5], L. Soorya[6], L. Sullivan[7], D. Hirtz[8] and A. Wagner[9], (1)*University of North Carolina*, (2)*Albert Einstein College of Medicine*, (3)*Bloorview Research Institute, Bloorview Kids Rehab*, (4)*University of North Carolina, Chapel Hill*, (5)*University of North Carolina, Chapel HIll*, (6)*Mount Sinai School of Medicine*, (7)*Boston University*, (8)*National Institutes of Health*, (9)*National Institute of Mental Health*

Background: Serotonergic differences have been demonstrated in many individuals with autism, with low levels of synthesis during early childhood when critical neuronal connections are forming. Fluoxetine increases serotonin levels and was hypothesized to facilitate more typical brain development in children with autism during the highly plastic period between ages two and six years. However, it was unclear whether a long-term double-blind placebo-controlled developmentally-focused trial was feasible and which outcome measures might be most appropriate.

Objectives: The objectives of the study were to 1) determine enrollment rate; 2) determine the extent of premature withdrawal; 3) evaluate differences in side effects and 4) evaluate the potential sensitivity to change of various outcome measures.

Methods: Children 30-58 months with autistic disorder confirmed by ADI-R and ADOS were randomly assigned to 12 months of flexible dose treatment with placebo or fluoxetine (1-20mg/day). Dosing was initiated at 2mg and could be increased by 2mg every 3 weeks. Dose could be reduced at any time. Major outcomes were assessed via parent report or by an independent clinician at months 0, 3, 7 and 12. Outcomes included the Clinical Global Impressions Improvement Score (CGI-IS), PDD Behavior Index (PDD-BI), Preschool Language Scale-4, MacArthur Communication Inventory (MCI), Stanford Binet (IQ), Vineland, Bracken School Readiness, BRIEF-P, RBS-R, Social Reciprocity Scale (SRS), Aberrant Behavior Checklist (ABC), and Caregiver Strain Questionnaire.

Results:

Twenty-nine children were enrolled with nineteen (mean age 42.8 ± 7.3 months) randomized to either fluoxetine (8) or placebo (11) over 18 months across two sites. The mean duration of treatment was 33 months with 44% completing the entire year of treatment. Two children in the fluoxetine group and 4 in the placebo group experienced behavioral activation. More children in the fluoxetine group than in the placebo group experienced increased crying (3 vs 0), abdominal discomfort (3 vs 0), rash (5 vs 2), incidental injury (4 vs 0) and other eye disorder (3 vs 0). One person withdrew early due to adverse effects in the fluoxetine group compared to four people in the placebo group. The CGI-IS, IQ, Bracken, ABC stereotypy and RBS-R did not show any consistent differences between groups. Several other measures showed consistent numeric differences favoring fluoxetine treatment over time including PDD-BI subscales for autism, specific fears, aggressiveness, social approach, and sematic pragmatic competence, Vineland standard scores, ABC-irritability, lethargy, and hyperactivity subscales and some SRS subscales. The Caregiver Strain Questionnaire showed consistent, statistically significant benefits of fluoxetine treatment for internalizing and objective stress.

Conclusions: It is feasible to conduct a multisite randomized controlled trial of fluoxetine in young children with autism though recruitment is likely to take about twice as long as other pharmacologic studies in autism. The Caregiver Strain Questionnaire appears to be sensitive to change with fluoxetine in this heterogeneous population.

129.002 Short and Longer Term Outcomes for Toddlers with ASD Enrolled in Early Intervention. R. Landa*[1], A. Faherty[1] and E. Stuart[2], (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins Univ. School of Public Health*

Background: Very early intervention for autism has the potential to optimize outcomes and perhaps even prevent a cascade of increasing separation from peers with typical development with regard to the development of social and communication functioning. Data from studies of preschoolers are beginning to show promise that even core deficits of autism may be ameliorated by targeting deficits such as joint attention in intervention. The study described herein is one of the largest intervention studies to date involving 2-year-olds with autism spectrum disorders (ASD); the data reveal insights into the important effects of early intervention.
Objectives: To determine whether core deficits of ASD could be ameliorated through targeting such deficits in early in life.
To examine the longer-term outcomes of 2-year-olds enrolled in intervention that targeted social communication and language development.
Methods: Forty-nine toddlers with ASD (23-33 months of age at enrollment) participated in a 6-month nursery school-based comprehensive early intervention for 10 hours per week. Children were matched on verbal and non-verbal mental age, as well as severity of autism symptoms, then randomly assigned to one of two intervention conditions that were identical except that one condition was saturated with instruction targeting joint attention, social imitation, and affect sharing (Interpersonal Synchrony condition). Dependent variables included Receptive and Expressive Language T scores (Mullen Scales of Early Learning), nonverbal developmental quotient (mean of Mullen Fine Motor and Visual Reception T scores), frequency of initiation of joint attention and shared positive affect (Communication and Symbolic Behavior Scales Developmental Profile), and imitation score on a structured imitation elicitation task.
26 of these children were assessed 2 to 6 years after entering the study. Dependent variables: Stanford Binet VIQ and NVIQ; ADOS algorithm scores.
Results: Ninety percent of the children entered the study NV developmental quotients in the significantly impaired range. Children in both groups made significant improvement in receptive and expressive language and in imitation (measured within a structured elicitation task) from pre- to post-intervention ($p=0.008$ to 0.001), but only the Interpersonal Synchrony group made significant gains in joint attention and shared affect ($p's=0.01$). Gains were sustained through the follow-up period, but significant

improvement (p=0.001) during this period was limited to language.
Of the 26 children assessed in the longer-term followup study, 42% and 50% fell with the average range for VIQ and NVIQ, respectively. 73% showed significant improvement in autism symptoms per the ADOS algorithm scores.

Conclusions: These findings suggest that intensive early intervention emphasizing interpersonal synchrony can improve core deficits of autism involving joint attention, imitation, and shared affect in the short term. Furthermore, enrollment in very early comprehensive intervention that heavily targets communication functioning may facilitate an alteration in the course of development with the potential of achieving typical levels of verbal and nonverbal cognitive functioning, as well as decreased severity of autism symptoms.

129.003 The Early Start Denver Model: Moderators of Response to An Early Intervention for Toddlers with Autism Spectrum Disorder. G. Dawson*[1], S. J. Rogers[2], J. Munson[3], M. Smith[3], J. Winter[3], J. Greenson[3], A. Donaldson[4] and J. Varley[3], (1)*UNC Chapel Hill*, (2)*M.I.N.D. Institute, University of California at Davis*, (3)*University of Washington*, (4)*Portland State University*

Background: Studies of the efficacy of early behavioral intervention for improving outcomes for preschool-aged children with autism spectrum disorder (ASD) have yielded positive results. Less is known about the outcomes of children receiving early intervention below age 2 _ years. As more children are diagnosed with ASD during the infant-toddler period, the availability of efficacious interventions that can be delivered at a young age is a significant priority.

Objectives: A randomized clinical trial of an early intervention designed for toddlers with ASD was recently published (Dawson et al., 2010, *Pediatrics*). This study evaluated the efficacy of the Early Start Denver Model (ESDM), a comprehensive developmental behavioral intervention. Compared with children who received community-based intervention, children who received ESDM showed significant improvements in IQ, adaptive behavior, and autism diagnosis. Similar to previous studies of early intervention for autism, there was significant inter-subject variability in response to the intervention. This presentation will describe the results of new analyses examining several potential moderators of response to intervention, including IQ and severity of autism symptoms, among others.

Methods: Forty-eight children diagnosed with ASD at between 18 and 30 months of age were randomly assigned to: (1) ESDM intervention, based on developmental and applied behavioral analysis principles and delivered by trained therapists and parents for 2 years; or (2) referral to community providers for intervention commonly available in the community.

Results: Compared with children who received community-based intervention, children who received ESDM showed significant improvements in IQ, adaptive behavior, and autism diagnosis. Two years after entering intervention, the ESDM group showed significantly improved cognitive abilities, as measured by the Mullen Scale for Early Learning. On average, the ESDM group's early-learning composite score improved 17.6 standard score points (1 SD: 15 points) compared with 7.0 points in the comparison group relative to baseline scores. The ESDM group maintained its rate of growth in adaptive behavior compared with a normative sample of typically developing children. In contrast, over the 2-year span, the comparison group showed greater delays in adaptive behavior. Children who received ESDM also were more likely to experience a change in diagnosis from autism to pervasive developmental disorder, not otherwise specified, than the comparison group.

Conclusions: This randomized, controlled trial demonstrated the efficacy of a developmental behavioral intervention for toddlers with ASD for improving cognitive and adaptive behavior and severity of diagnosis. Results of this study underscore the importance of early detection of and intervention in autism. Results of analyses examining several factors that contribute to intervention response will be presented.

Model Systems Program

130 Animal Models

130.121 142 Effect of Maternal Omega-6 Rich Diets and Prenatal Stress On Autistic-Like Sociability Deficits in Mice. K. L. Jones*, M. J. Will, P. M. Hecht, C. L. Parker, K. M. Morman and D. Q. Beversdorf, *University of Missouri*

Background: Multiple studies have reported prenatal stress as a potential risk factor for the development of autism spectrum disorder (ASD). In rodents, a significant reduction in sociability is seen in prenatally stressed offspring of genetically stress-susceptible dams. Certain dietary factors that contribute to stress reactivity may, therefore, exacerbate prenatal stress-mediated behavioral changes in adult offspring. Adults with a diet rich in omega-6 polyunsaturated fatty acids (PUFAs) display increased stress reactivity.

Objectives: In our study, we wished to examine the effects of prenatal diet and prenatal stress on social behavior in the adult offspring in mice.

Methods: Pregnant C57BL/6J dams were placed into a chronic variable stress group or a control group, and were also placed into a control diet or a diet rich in omega-6 PUFAs, in a 2 x 2 design. Mice placed in the chronic variable stress group were given one stressor per day beginning on gestational day 6 until the birth of the offspring. We subsequently tested the adult offspring (N = 86) beginning on postnatal day 60 for sociability, anxiety, and locomotor functioning using a 3-chambered social approach task, an elevated-plus maze, an open field task and a rotarod task.

Results: We found no differences between groups in the open field and the rotarod tasks ($p > 0.05$). We did find a main effect of diet in the elevated-plus maze, with offspring whose mothers were exposed to a high-omega-6 PUFA diet during gestation showing increased anxiety levels ($p = 0.038$). Additionally, these offspring displayed decreased levels of sociability in the 3-chamber social approach task, as they did not spend significantly more time with a stranger mouse than a novel object ($p = 0.65$), whereas mice exposed to the control diet during gestation did spend significantly more time with a stranger mouse than a novel object ($p < 0.001$). No main effects of prenatal stress were observed, and no interaction between diet and stress was observed.

Conclusions: Our findings indicate that a maternal diet rich in omega-6 PUFAs during produce changes in sociability consistent with those observed in ASD. This provides evidence for a possible environmental risk factor that contributes to the production of autistic-like behavior in mice. Exploration of the relationship between prenatal diet and ASD in humans will be necessary to determine the role of this finding in clinical ASD, and further investigation into the mechanism of action of this effect is warranted.

130.122 143 Functional Dissection of the Autism Susceptibility Gene Slc25a12 in Model Systems. T. Sakurai*[1], N. Ramoz[2], M. Gazdoiu[1], N. Takahashi[1], N. P. Dorr[1], M. A. Gama Sosa[1], R. De Gasperi[1], G. A. Elder[3] and J. D. Buxbaum[1], (1)*Mount Sinai School of Medicine*, (2)*INSERM*, (3)*Mount Sinai School of Medicine, James J. Peters VA Medical Center*

Background: SLC25A12 encodes a mitochondrial aspartate/glutamate carrier (AGC1), which is an important component of the malate/aspartate shuttle, a crucial system supporting oxidative phosphorylation and ATP production. The gene has been identified as a susceptibility gene for autism spectrum disorders (ASDs) (e.g., Ramoz et al, Am J Psychiatry, 2004) and is responsible for a neurodevelopmental syndrome when both alleles are mutated (Wibom et al, NEJM, 2009). Objectives: To understand the role of AGC1 in brain development as a means of relating alterations in this gene to neurodevelopmental disorders. Methods: We have developed mice with a targeted disruption of the Slc25a12 gene and we have developed BAC transgenic mice overexpressing this gene. Mice are characterized in biochemical, neuropathological and behavioral studies, followed by confirmatory in vitro studies. Results: Slc25a12-knockout mice, which showed no AGC1 by immunoblotting, were born normally but displayed delayed development and died around 3 weeks after

birth. In P13-14 knockout brains, the brains were smaller with no obvious alteration in gross structure. However, we found a reduction in myelin basic protein (MBP)-positive fibers, consistent with a previous report. Furthermore, the neocortex of knockout mice contained abnormal neurofilamentous accumulations in neurons, suggesting defective axonal transport and/or neurodegeneration. Slice cultures prepared from knockout mice also showed a myelination defect, and reduction of Slc25a12 in rat primary oligodendrocytes led to a cell-autonomous reduction in MBP expression. Myelin deficits in slice cultures from knockout mice could be reversed by administration of pyruvate, indicating that reduction in AGC1 activity leads to reduced production of aspartate/N-acetyl aspartate (NAA) and/or alterations in the NADH/NAD+ ratio, resulting in myelin defects. AGC1 heterozygotes showed reduction of Mag expression in brains, and showed mild spatial learning impairment in Morris water maze testing, and alterations in social behavior. We have also developed mice overexpressing AGC1 using BAC transgenic technology that ensures transgene expression in a pattern similar to the endogenous AGC1. We confirmed 2-3 fold over expression of AGC1 both at RNA and protein levels. We did not observe overexpression of oligodendrcyte/myelin genes in these mice. Currently, we plan to analyze these mice morphologically and behaviorally. Conclusions: Our data implicate AGC1 activity in myelination and in neuronal structure, and indicate that while complete loss of AGC1 leads to hypomyelination and neuronal changes, subtle alterations in AGC1 expression could affect brain development contributing to increased autism susceptibility. Studies relating genotype at the SLC25A12 locus with head circumference and cognitive measures in human subjects are underway. Supported by the Seaver Foundation.

130.123 144 Influence of Partner Cues On Social Behaviors in the BTBR Mouse Model of Autism. M. Yang*, A. M. Katz, M. Weber and J. N. Crawley, *National Institute of Mental Health, National Institutes of Health*

Background: BTBR T+ tf/J (BTBR) is an inbred strain that exhibits low sociability in our three-chambered social approach task and low reciprocal social interactions in a neutral arena (Bolivar et al., 2007; McFarlane et al., 2008). Previous findings demonstrated that the social deficits in BTBR are not attributable to postnatal maternal care or to circadian phase, and their absence of corpus callosum is unlikely to be the primary cause (Yang et al., 2009).

Objectives: The present study tests specific features of a novel social animal that may deter BTBR from approaching other mice. Experiment 1 compares social approach behaviors elicited by a salient social olfactory cue vs. a live behaving mouse. Experiment 2 compares the subject's social scores when the partner is a highly social C57BL/6J (B6) which frequently initiate social interactions, versus when the partner is a low sociability BTBR.
Methods: **Experiment 1:** To test for social approach behaviors towards a live animal, a novel mouse was placed under an inverted wire cup located in one side chambers, and an control empty cup was placed in the other side chamber. To test for approach behaviors elicited by social olfactory cues, soiled bedding obtained from unfamiliar cages of group-housed mice was placed under the cup in one side chamber, and clean bedding was placed under the control cup in the other side chamber.
Experiment 2: Social interactions in three types of social pairs were tested: a) pairs of two B6, b) pairs of two BTBR, and c) pairs of one B6 and one BTBR. A juvenile cohort was tested on postnatal day 21 and an adult cohort was tested between 8-16 weeks of age. The same testing procedure was used for the juvenile and the adult test. After a 1 hour isolation period, two age- and sex-matched non-littermates were simultaneously placed in a neutral arena and their interactions were videotaped for 10 min.

Results: Experiment 1 revealed that BTBR displayed strong approach behaviors towards olfactory social cues, but low approach to a live, awake novel mouse. A previous report showed that B6 mice exhibit high social approach towards soiled nesting material from novel mice (Ryan et al., 2008). In our study, BTBR spent as much time with the novel home cage odors as did B6 in the Ryan study. Experiment 2 found that BTBR

exhibited low reciprocal social interactions when paired with either highly social B6 partners or low sociability BTBR partners, generally do not reciprocate when approached or solicited. In contrast, B6 exhibited high sociability to both B6 and BTBR partners, maintaining high levels of social interests even when the BTBR did not reciprocate. Similar results were obtained from juvenile and adult pairs, and from male pairs and female pairs.

Conclusions: Our results support the interpretation that BTBR are interested in social olfactory cues, but avoid contact with novel mice, independent of any strain-specific behavioral or olfactory cues emitted by the novel mice. These findings might have face validity to the description that some autistic individuals recognize components of social cues, but avoid or respond inappropriately to direct social contact.

130.124 145 Modeling An Autism Risk Factor in Mice Leads to Permanent Changes in the Immune System. E. Hsiao*, *California Institute of Technology*

Background: Maternal infection can lead to the development of autistic endophenotypes in the offspring. Modeling this maternal infection risk factor in mice yields offspring with behavioral abnormalities and neuropathology resembling those characteristic of autistic individuals. A similar phenotype in the offspring can be obtained by activating the mother's immune system by injection of the double-stranded, synthetic RNA, poly(I:C). The cytokine IL-6 is a key mediator of the effects of maternal immune activation (MIA) on the fetus. Moreover, MIA activates downstream IL-6 signaling pathways in the placenta and in subpopulations of neurons in the fetal brain. In addition, IL-6 mRNA is induced in both of these tissues, which raises the possibility of a feed-forward mechanism that could lead to the permanent changes in immune status seen in the autistic brain and peripheral immune system. Studies have reported amplified immune responses in both peripheral tissues and the gastrointestinal tract of autistic subjects.

Objectives: We aim to study whether MIA during early fetal development alters later immune function in adult offspring.

Methods: Spleens and mesenteric lymph nodes were isolated from adult offspring of poly(I:C)- or saline-injected mothers. Tissues were mechanically and enzymatically disrupted to generate single cell suspensions. CD4+ T cells were isolated by magnetic bead separation (Miltenyi) and stimulated with PMA/ionomycin. IL-6 and IL-17 levels were measured from supernatants and normalized against number of cells.

Results: CD4+ T cells from spleen and mesenteric lymph nodes of adult poly(I:C) offspring display elevated levels of the pro-inflammatory cytokines IL-6 and IL-17 in response to stimulation *in vitro*.

Conclusions: MIA leads to significant changes in lymphocytes from the spleen and mesenteric lymph node of adult offspring. This observation indicates that MIA can cause permanent changes in immune status of the offspring.

130.125 146 Neonatal Administration of Propionic Acid Alters Startle Response Magnitude in Adolescent Rats. K. A. Foley*, L. J. Tichenoff, K. -. P. Ossenkopp and D. F. MacFabe, *University of Western Ontario*

Background: : Dietary and gastrointestinal system influences may contribute to the manifestation of behaviors seen in autism spectrum disorders (ASDs). Propionic acid (PPA) is a short chain fatty acid and a by-product of enteric bacteria that enters systemic circulation and the CNS by passive and active transport. We have found that PPA in adult rats produces behavioral and neuroinflammatory brain changes similar to that seen in ASD patients. Both hyper- and hypo-responsiveness to sensory stimuli have been described for human ASD.

Objectives: Examine startle response magnitude and prepulse inhibition (PPI) in adolescent male and female Long-Evans rats exposed to PPA as neonates.

Methods: Male and female Long-Evans rat pups were injected subcutaneously twice a day, 6 hours apart, on post-natal days (PND)

0, 2, 4, 6, 8 with either PPA (500 mg/kg) or phosphate buffered saline (PBS). On PND 44-46, animals were placed in a startle apparatus for one 20 min session. Sixty trials were presented: 10 pulse-alone trials followed by 50 startle and prepulse trials - 10 each of pulse alone, no pulse, 73 dB, 76 dB, and 82 dB prepulse-pulse. In Experiment 1, animals were placed in the startle apparatus in the absence of any drug. In Experiment 2, animals were given a challenge injection of PPA (500 mg/kg, IP) and then placed in the startle apparatus.

Results: In Experiment 1, animals that received PPA as pups displayed significantly greater startle responses than animals that received PBS. There were no significant differences between treatment groups in habituation to the acoustic startle. Upon PPA challenge as adolescent, effects of neonatal drug treatment disappeared and a significant sex difference was found, with males displaying greater startle responses than females. In Experiment 2, female rats that received PPA as pups displayed significantly greater % PPI than male rats that received PPA as pups, while there was no difference in rats that received PBS as pups.

Conclusions: PPA administration in developing rat pups produces a hypersensitivity to acoustic stimuli in both male and female adolescent rats. Upon PPA challenge, however, male adolescent rats were hypersensitive compared to females, regardless of neonatal treatment. Increased inhibition is observed only in female rats that received PPA as pups and were challenged. Recurrent PPA administration may mimic recurrent infections of PPA producing gut bacteria in sensitive paediatric populations, offering further support for the PPA rodent model of ASDs.

130.126 147 Neuroligin-Deficient Mutants of *C. Elegans* Have Sensory Deficits and Are Hypersensitive to Oxidative Stress.

J. B. Rand*[1], J. W. Hunter[2], G. P. Mullen[1] and J. M. Heatherly[2], (1)*Oklahoma Medical Research Foundation*, (2)*Oklahoma Medical Research Foundation/University of Oklahoma Health Sciences Center*

Background: Neuroligins are postsynaptic cell adhesion proteins originally identified by their binding to presynaptic proteins called neurexins. Although the interaction between neuroligin and neurexin is capable of inducing synaptogenesis under certain conditions, recent studies suggest that neuroligins function primarily in the maturation and/or maintenance of synapses. There are four neuroligin genes in humans, and studies have shown that mutations in the genes encoding neuroligin 3 and neuroligin 4 are associated with autism spectrum disorders (ASDs).
Objectives: We examined the expression, localization and biological functions of neuroligin in a simple model organism, the nematode *Caenorhabditis elegans*. We are using *C. elegans* for these studies because it has a simple nervous system, and is well suited for genetic, molecular and behavioral analyses.
Methods: We determined the cellular expression and sub-cellular localization of *C. elegans* neuroligin using fluorescent reporters and neuroligin::YFP fusion proteins. We also compared wild-type animals to *nlg-1* null mutants using a set of behavioral tests, lifespan measurements, toxicity tests, and quantitation of oxidatively damaged proteins.
Results: *C. elegans* has a single neuroligin gene (*nlg-1*), and approximately one-sixth of *C. elegans* neurons express a neuroligin transcriptional reporter. Neuroligin-expressing cells include some sensory neurons, interneurons, and a subset of cholinergic motor neurons, as well as body-wall muscles. *nlg-1* null mutants are viable, and they do not appear deficient in any major motor functions. However, they are defective in a subset of sensory behaviors and sensory processing; these deficits are strikingly similar to traits frequently associated with ASDs. *nlg-1* mutants are also hypersensitive to oxidative stress (*i.e.*, exposure to paraquat); this is an unexpected phenotype for a synaptic mutant. Like many other stress-sensitive mutants, *nlg-1* mutants have a reduced lifespan and an increased level of oxidative damage to proteins. *nlg-1* mutants are also hypersensitive to the toxicity of inorganic ($HgCl_2$) and organic (thimerosal) mercury compounds and copper compounds, but not to cadmium ($CdCl_2$).

Conclusions: The grossly normal structure and function of the nervous system in *nlg-1* null mutants are consistent with current models emphasizing the importance of neuroligin in synaptic maintenance, rather than synaptogenesis. Our data on the sensitivity of *nlg-1* mutants to oxidative stress (*e.g.*, paraquat) and mercury compounds support an important model for how both genetic and environmental contributions to a neurological disorder can have a single underlying basis.

Furthermore, although several studies have demonstrated a correlation between elevated markers of oxidative stress and ASDs, the precise relationship between autism and oxidative stress is not clear. Our *C. elegans* studies demonstrate that loss of the synaptic protein neuroligin is not merely correlated with oxidative stress, but actually causes the oxidative stress. If oxidative stress is a consequence of aberrant synaptic structure and/or transmission in *C. elegans*, then perhaps similar defects in humans have similar consequences. This raises the intriguing possibility that in humans, specific types of neuronal disruption (including mutations affecting synaptic adhesion proteins) may be the cause, and not the result, of oxidative stress.

130.127 148 Scent Marking as a Measure of Olfactory Communication in Shank1 Null Mutant Mice. F. I. Roullet*[1], R. Saxena[1], M. Wöhr[1], A. Y. Hung[2], M. Sheng[2] and J. N. Crawley[3], (1)*National Institute of Mental Health*, (2)*Massachusetts Institute of Technology*, (3)*National Institute of Mental Health, National Institutes of Health*

Background: Mouse models of autism provide translational strategies to test hypotheses about causes and to develop treatments. While assays are available for social interaction and repetitive behaviors in mice, there is a need for relevant methods to assess communication impairments. We are currently developing behavioral tools to assay olfactory communication in mice. SHANK genes, which code for synaptic scaffolding proteins, have been implicated in autism spectrum disorders.

Objectives: The present study examines Shank1 null mutant mice for interest in social olfactory cues and potential olfactory communication impairments.

Methods: Scent marks deposited by a male mouse in response to a spot of female urine in an open field were quantitated in Shank1 null mutants, heterozygotes, and wildtype littermates, using methods previously described (Arakawa et al., 2007; Roullet et al., 2009). Ultrasonic vocalizations emitted by the subjects and locomotor activity were simultaneously recorded as previously described (Roullet et al., 2009; Wöhr et al., 2009). Scent marking, locomotor activty and time spent were measured for both the entire open field and in a proximal zone within 10 cm of the female urine spot.

Results: Shank1 -/- mice deposited a lower number of scent marks within 10 cm around the female urine and spent less time within this proximal area. Scores for the entire open field showed no genotype differences in the total number of scent marks deposited in the presence of the female urine, nor in the total locomotor activity. In the absence of a female urine spot, Shank1 -/- had lower locomotor activity, consistent with the previous report (Hung et al., 2008) and our companion poster (Silverman et al., 2009). When comparing the total number of ultrasonic vocalizations, genotype differences were not significant. All genotypes started to emit calls about 1 minute after exposure to female urine.

Conclusions: Our results suggest that Shank1 null mutant mice have reduced interest in female urinary pheronomones, which could indicate deficits in olfactory communication.

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130.128 149 The Dog as a Genetic Model to Investigate Overlap in Social, Attention, and Activity Behaviors. L. Lit*, D. Bannasch and J. Schweitzer, *University of California at Davis*

Background:

Currently, there are limited animal models to provide insight into genetic underpinnings of social behaviors and the often comorbid inattention/hyperactivity behaviors observed in autism spectrum disorders (ASDs). Social interactive behaviors between domestic dogs (Canis familiaris) and humans have been well documented experimentally. Additionally, owner reports of social and attention/activity behaviors have been used to characterize variability in naturally occurring dog behaviors that are homologous to those relevant to ASDs. It has been hypothesized that a limited subset of wild canids originally displayed the social characteristics necessary to interact with humans, ultimately resulting in domestication.

Objectives:

Determine whether there would be an overlapping set of genes associated with social behaviors and attention/activity behaviors in domestic dogs.

Methods:

We asked owners of 14 dogs (1 Basset Hound, 1 Black Russian Terrier, 2 Dalmatians, 1 Petit Basset Griffon Vendeen, 7 Nova Scotia Duck Tolling Retrievers, and 2 mixed breed dogs) to complete surveys comprising owner report of social and attention/activity behaviors observed in their dogs. Social behaviors subscales 1) initiation of reciprocal social behaviors (INIT), 2) response to social interactions with humans (RSPNS), and 3) communication with humans (COMM); as well as attention (ATT) and activity (ACT) subscales were derived from responses using factor analysis. Genome-wide SNP data for these dogs was generated using 127K Affymetrix canine single nucleotide polymorphism (SNP) arrays. Using subscales as input, we performed genome-wide quantitative trait association to determine SNPs associated with each subscale.

Results:

Overlapping SNPs associated with both a social subscale and either an attention or activity subscale were identified. Most SNPs corresponded to genes or regions homologous to those in humans associated with autism, ADHD, and schizophrenia.

Conclusions:

These findings contribute to the validity of the domestic dog as an animal model to investigate overlap in genetic backgrounds of social and attention/activity behaviors.

130.129 150 A Role for HGF/SF-Met Signaling in the Developing Cortex. J. M. Smith*, G. J. Martins, C. Plachez and E. M. Powell, *University of Maryland School of Medicine*

Background:

Recent research has suggested that organization of neural circuitry may be altered in autism spectrum disorders (ASD). Hepatocyte growth factor/scatter factor (HGF/SF) and its receptor, Met, are involved in the development of the forebrain, and MET has been identified as a susceptibility loci for autism. In neural tissue, HGF/SF binding to Met induces a signaling cascade that can influence cell migration, proliferation, and formation of neurite processes.

Objectives:

HGF/SF and Met are known to be expressed in the developing telencephalon, and changes in HGF/SF or Met expression appear to alter proliferation and formation of processes in neurons. This study employed mutant mice with a targeted mutation of Met in the cerebral cortex to examine how

changes in HGF/SF-Met signaling could lead to alterations in neural circuitry.

Methods: This study employed transgenic mice with a targeted signaling mutant of Met in the cerebral cortex, along with immunohistochemical, biochemical and anatomical techniques to examine the effects of HGF-Met signaling on neural development.

Results: Mice lacking normal Met expression in the cerebral cortex show alterations in several aspects of cortical structure. Reduced HGF/SF-Met signaling in these mice leads to alterations in the laminar structure of the cortex. We also found alterations in cell proliferation in the developing cortex, as well as changes in pyramidal cell dendritic structure, which may contribute to the alterations in laminar structure.

Conclusions: Our data suggest that Met signaling is required in the mouse forebrain for proper cortical lamination, neuronal proliferation, and formation of processes. These alterations could disrupt the formation of neuronal circuitry. Such disruptions can lead to profound neurological and behavioral consequences such as those portrayed in ASD.

130.130 151 Comprehensive Behavioral Phenotyping of Neuroligin 2 Mutant Mice. S. Turner*, D. D. Diagne, M. J. Harris, R. Saxena, J. L. Silverman and J. N. Crawley, *National Institute of Mental Health, National Institutes of Health*

Background: Neuroligin (NLGN) genes code for a family of cell adhesion molecules at postsynaptic sites on neurons. Neuroligin-2 deletion reduces inhibitory neurotransmission. Point mutations in several neuroligins have been reported in autistic individuals.
Objectives: To understand the consequences of *Nlgn2* mutations relevant to the diagnostic and associated symptoms of autism, comprehensive behavioral phenotyping on a line of Neuroligin-2 (*Nlgn2*) mutant mice was conducted on multiple measures of social interactions, olfactory communication, repetitive behaviors, anxiety-related behaviors, neurodevelopmental milestones, and a series of control measures for physical abilities.

Methods: *Nlgn2* knockout (KO) mice were the generous gift of Nils Brose from the Max-Planck-Institute for Experimental Medicine, Göttingen, Germany. *Nlgn2* male and female littermates from heterozygous breeding pairs were used for behavioral studies.
Developmental milestones, elevated plus-maze and light/dark anxiety related behaviors, a general health battery, neurological reflexes, sensory measures including olfactory habituation/dishabituation, acoustic startle threshold and prepulse inhibition, motor functions including open field locomotion and rotarod, juvenile reciprocal social interactions and adult social approach were assayed in *Nlgn2* knockout, wildtype, and heterozygous mice, using methods previously described (Crawley, 2008; McFarlane et al., 2008; Chadman et al., 2008).

Results: Adult *Nlgn2* null mutants did not differ from their wildtype and heterozygote littermates on standardized measures of general health, neurological reflexes, hot plate and tail flick pain sensitivity tasks, or open field activity. Adult social approach did not differ across genotypes. No motor stereotypies or repetitive behaviors were detected in any genotype. A trend toward higher anxiety-like scores was detected in the light/dark task, but not in the elevated plus-maze. Results are in progress for developmental milestones and juvenile reciprocal social interactions.
Conclusions: At present, our data indicate normal scores in *Nlgn2* mutant mice on behavioral measures relevant to the diagnostic symptoms of autism. These findings extend and generally confirm previous reports using other cohorts of *Nlgn2* mutant mice (Hines et al., 2008; Blundell et al., 2009).

Keywords: neuroligin, animal model, social behavior

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130.131 152 Development and Temporal Dynamics of Repetitive Behavior. M. Lewis*, Y. Tanimura and M. Yang, *University of Florida*

Background: Although restricted, repetitive behaviors are diagnostic for autism relatively little is known about the development of such behaviors. Developmental patterns derived from longitudinal studies have not been reported and little is known about the trajectories of repetitive behaviors in atypical versus normative development. Moreover, the temporal structure of repetitive behavior has received scant attention although the temporal dynamics of repetitive behavior and developmental changes in such dynamics may prove critical to understanding neuroadaptations that mediate repetitive behavior. Appropriate animal models could provide a wealth of information about how repetitive behaviors develop including age-dependent changes in temporal organization. Our lab has employed a deer mouse (*Peromyscus maniculatus*) model that involves spontaneous expression of high rates of repetitive motor behavior.

Objectives: To characterize developmental trajectories of repetitive behavior in deer mice and model its temporal organization. We also sought to determine if temporal structure changed systematically with development.

Methods: We assessed repetitive behavior in deer mice at weekly intervals following weaning and subjected these data to a group-based trajectory modeling procedure (PROC Traj). This allowed us to calculate the number of discrete developmental trajectories that best accounted for individual animal data. We also used a Poisson process to model the distribution of discrete sequential repetitive behaviors at three points in development. This allowed us to determine differences in the temporal organization of repetitive behavior, independent of frequency, across developmental time periods within a trajectory group as well as at the same developmental time point across trajectory groups.

Results: Three discrete developmental trajectories best accounted for individual animal differences. Trajectory 1 represented a small percentage of mice (11%) that exhibited a low, flat trajectory. Trajectory 2 (41%) showed a gradual progression from low levels of stereotypy at week 1 post-weaning to high levels by week 6 post-weaning. Trajectory 3 (48%) exhibited high levels of repetitive behavior by week 1 post-weaning and a relatively flat trajectory. Significant differences both within and across developmental trajectory groups were also found. Trajectory 1 mice showed poorly organized (more random) behavior that did not vary across development. Trajectory 2 mice showed a marked change in temporal organization across development going from least organized at week 1 to most organized (more regular or periodic) at week 6. Trajectory 3 mice showed the highest level of organization (least random) at week 1 with a modest increase in organization across development.

Conclusions: Individual developmental curves of repetitive behavior in deer mice resolved into three discrete trajectory groups. These groups were associated with significantly different temporal dynamics at each developmental time point. In addition, each developmental trajectory group showed a different pattern of change in temporal organization across development. This latter finding suggests the importance of temporal dynamics in driving development and neuroadaptations. These findings also point to the potential importance of developmental trajectory and temporal dynamics in

determining variable response to treatment and timing of interventions in individuals with ASD.

130.132 153 Effects of Acute Serotonin Reuptake Inhibitor Treatment and Serotonin Depletion On Sociability in Juvenile BALB/Cj and C57BL/6J Mice. A. H. Fairless*[1], E. Gordon[1], R. Y. Shah[1], H. C. Dow[1], S. C. Allen[1] and E. S. Brodkin[2], (1)*University of Pennsylvania School of Medicine*, (2)*University of Pennsylvania*

Background: Autism spectrum disorders (ASDs) are a group of neurodevelopmental disorders characterized, in part, by deficits in social behaviors. Many studies have associated ASDs with hyperserotonemia and abnormal regulation of brain serotonin, and serotonergic neurotransmission has been implicated in a variety of social behaviors in humans and animals. The serotonergic system also mediates various forms of anxiety, and several of these are heightened in patients with ASDs. The role of serotonin in the development of sociability (tendency to seek social interaction) and anxiety during prepubescence is not well understood. Previous work has demonstrated that prepubescent BALB/cJ mice show reduced sociability relative to prepubescent C57BL/6J mice. Objectives: We systemically manipulated the serotonergic system with the selective serotonin reuptake inhibitor (SSRI) citalopram and the serotonin depletor p-chlorophenylalanine (PCPA) in prepubescent C57BL/6J and BALB/cJ mice. We assessed the acute effects of these pharmacological agents in a social choice test and the elevated zero maze test (EZM). We hypothesized that acute citalopram would decrease sociability in the social choice test and increase non-social anxiety-related behaviors (anxiogenesis) in the EZM. We further hypothesized that PCPA would increase sociability and decrease anxiety-related behaviors (anxiolysis). Methods: In the first experiment, 31-day-old male and female BALB/cJ and C57BL/6J mice received a single i.p. injection of citalopram (10 mg/kg) or saline, and a half-hour later were tested for sociability towards an unfamiliar, gonadectomized A/J 'stimulus' mouse. In a second experiment, 29-to-33-day-old male BALB/cJ mice received a single i.p. injection of citalopram (1 or 10 mg/kg) or saline, and were then tested for sociability a half-hour later. The following day, they received another injection of citalopram at the same dose or of saline, and were then tested on the EZM a half-hour later. In a third experiment, male BALB/cJ and C57BL/6J mice received 3 days of twice-daily injections of PCPA (100 or 300 mg/kg/day) or saline. On the fourth day, the 29-to-33-day-old mice were tested for sociability, then received a final injection of PCPA at the same dose or of saline. On the fifth day, mice were tested on the EZM. Results: In the first experiment, the experimental groups did not differ in their locomotor activity or their exploratory behaviors prior to exposure to the stimulus mouse. Citalopram-treated mice showed lower sociability than saline-treated mice, and this effect was more pronounced in the BALB/cJ mice than the C57BL/6J mice (social investigation time, Wilcoxon-Mann-Whitney tests: C57BL/6J saline vs. citalopram, $U = 59$, $p < 0.001$; BALB/cJ saline vs. citalopram, $U = 49$, $p < 0.01$). No differences due to sex were detected. The results of the second and third experiments will be presented. Conclusions: The results of these experiments will clarify the relationship between sociability and non-social anxiety during the little-studied developmental period of prepubescence in mice. These experiments will also elucidate the role that serotonin plays in these processes during prepubescence, and this may provide insights into the neural mechanisms of reduced sociability and heightened anxiety-related behaviors, two behavioral endophenotypes highly relevant to ASDs.

130.133 154 Longitudinal Assessment of Fgf17-/- Mouse Social Behavior On the C57Bl/6 Background. E. C. Ihle*[1], K. Scearce-Levie[2], N. Devidze[3], R. Hoch[1] and J. L. Rubenstein[1], (1)*UCSF*, (2)*Genentech*, (3)*Gladstone Institute*

Background: *Fgf17* mutant mice on a mixed background (129X1/SvJ, C57Bl/6NCrl) have a reduction both in the size of the dorsomedial frontal cortex and in the extent of frontal cortex subcortical projections, as well as cerebellar defects. In addition, *Fgf17*$^{-/-}$ pups at post-natal day (PND) 8 emit fewer isolation-induced ultrasonic vocalizations (USVs) than their wild-type littermates. Furthermore, *Fgf17* $^{-/-}$ adults show reduced affiliative interactions and interaction time

with a novel conspecific. Because behaviors are strain-dependent it was uncertain whether the phenotype characterized in the original description of *Fgf17* $^{-/-}$ mouse behavior resulted from the loss of *Fgf17* function, or was related to the decreased social interaction typical of the 129X1/SvJ strain.

Objectives: We re-examined the behavioral repertoire of *Fgf17* $^{-/-}$ mice at the N5 generation of crossing onto the C57Bl/6 background, both during early post-natal development and late in life, to confirm and extend the results of the original behavioral analyses.

Methods: Pups were generated from *Fgf17*$^{-/-}$ males mated with *Fgf17*$^{-/-}$ females of the N5 backcross generation. On PND 8, pups from 2 litters of each genotype were tested for their USVs in response to maternal isolation, according to the protocol used in the original behavior analysis. After these pups reached late adulthood (11-12 months of age) their social behaviors were assessed according to previously published protocols. Data were analyzed using linear regression and repeated measures ANOVAs.

Results: There was a statistically significant difference in vocalization patterns between N5 *Fgf17*$^{-/-}$ pups and *Fgf17*$^{+/+}$ pups. *Fgf17*$^{-/-}$ mutants showed a trend toward a statistically significant negative effect on total vocalizations as well as a statistically significant negative effect on potentiation (i.e., *Fgf17*$^{-/-}$ pups vocalize less overall, and have less potentiation after maternal contact). When these pups were tested as aged adults (11-12 months old), there were genotype-based differences in their social behaviors. In a test of social exploration, *Fgf17*$^{-/-}$ adult mice had significantly more brief interactions, and showed trends toward fewer extended interactions, as well as more aggressive and mounting behaviors (similar to the results from the original behavior analysis). In a test of social approach, *Fgf17*$^{-/-}$ adults were also significantly slower to approach the side of the chamber occupied by a novel stimulus mouse. In another test of social interaction, transmission of food preference, there was a sex difference in the effect of genotype: *Fgf17*$^{-/-}$ females ate more cued social food, while *Fgf17*$^{-/-}$ males ate less cued social food, than their wild-type counterparts.

Conclusions: In a more homogeneously C57Bl/6 background, *Fgf17*$^{-/-}$ mice continue to exhibit social deficiencies that were generally comparable to the original phenotype. These results suggest that the *Fgf17*$^{-/-}$ mutants' decreased USVs as pups and abnormal social interactions as adults are likely to result directly from the absence of Fgf17. In these behavioral analyses, mice lacking *Fgf17* manifested impairments in two of the three symptom domains (reciprocal social interaction and communication) characterizing autistic spectrum disorders. Repetitive behavior, the third symptom domain, has yet to be tested.

130.134 155 Pharmacological Treatment of Repetitive Behavior in Deer Mice: Targeting Striatal Heteromeric Receptor Complexes. A. M. Van Matre* and M. Lewis, *University of Florida*

Background: Restricted repetitive behaviors are extremely common in many neurodevelopmental disorders and are one of the three diagnostic criteria for autism. The deer mouse (*Peromyscus maniculatus*) model of repetitive behavior is a particularly useful model because the repetitive motor behavior develops early, persists through much of the lifetime of the animal, and occurs spontaneously (i.e. without a specific pharmacological or environmental challenge). Preliminary evidence from our laboratory indicates that the repetitive motor behavior exhibited by these mice is a result of a neurobiological imbalance of activation between the direct and indirect pathways of the basal ganglia. The direct and indirect basal ganglia pathways are thought to work in an antagonistic fashion; activation of the direct pathway enhances basal ganglia output and promotes motor behavior whereas activation of the indirect pathway reduces basal ganglia output and inhibits movement. The imbalance between the direct and indirect pathways in the deer mice seems to be caused by decreased activation of the indirect pathway that allows direct pathway activation to over-excite the cortex. On neurons of the direct and indirect pathways

there are heteromeric complexes of receptors that exhibit further antagonistic relationships. These receptor complexes include dopamine D1 and adenosine A1 receptors on direct pathway neurons and dopamine D2, adenosine A2A, and glutamate mGluR5 receptors on indirect pathway neurons.

Objectives: 1) to assess whether drugs affecting these individual dopamine, adenosine, or glutamate receptor subtypes are effective at reducing repetitive behavior in deer mice; 2) to determine whether combinations of these drugs are more effective at reducing repetitive behavior (and hence increasing indirect pathway activation) than any of the drugs are alone; 3) to improve our understanding of the individual roles of dopamine D2, adenosine A2A, and glutamate mGluR5 receptors in the functioning of the indirect basal ganglia pathway.

Methods: We examined the effects of an adenosine A2A agonist (CGS21680), a dopamine D2 antagonist (L-741,626), and a glutamate mGluR5 positive allosteric modulator (CDPPB) individually and in combination on repetitive behavior in deer mice.

Results: When administered individually, the adenosine A2A agonist, the dopamine D2 antagonist, and the mGluR5 positive allosteric modulator do not significantly reduce repetitive behavior in deer mice. When co-administered, however, the A2A agonist and D2 antagonist significantly decrease the rate of stereotypy in deer mice. We are presently continuing this series of experiments by adding the mGluR5 positive allosteric modulator to the drug cocktail to assess whether there is a further reduction in repetitive behavior.

Conclusions: These data further suggest that decreased indirect pathway activation may mediate the expression of repetitive behavior and that targeting the heteromeric receptor complexes on the indirect pathway neurons may offer pharmacotherapeutic benefit for individuals with neurodevelopmental disorders who exhibit restrictive repetitive behavior.

130.135 156 The Impact of Gabrb3 Expression Variation On Autism Spectrum Disorder Related Phenotypes in Mouse. L. Herzing*, S. Zeng, N. Chiu, M. Yasvoina and K. Kugle, *Northwestern University Feinberg School of Medicine*

Background: Several lines of evidence support a link between GABRB3, a GABA receptor subunit, and autism spectrum disorders. Total or conditional loss of this gene results in frequent post-natal lethality in mouse, with survivors exhibiting seizures and behavioral disorders. In contrast, haploinsufficiency results in variable gene expression and mild phenotypes that are gender, age and deletion parent-of-origin dependent.

Objectives: To determine the phenotypic consequences of intermediate levels of Gabrb3 expression.

Methods: ShRNA-mediated Gabrb3-knockdown animals were generated on a C57Bl/6 background. Behavioral phenotypes were assessed in these, heterozygous gene knockout and wild-type control animals using standard protocols, including activity (wheel-running), anxiety (open field), exploratory (place preference & T-maze), socialization (interest, preference & memory: tethered & free interactions) and perseveration (radial maze).

Results: As expected, both Gabrb3-knockdown (KD) and heterozygous knockout (+/-) animals show behavioral differences from wild-type C57Bl/6 animals, with Gabrb3-KD animals exhibiting a phenotypic spectrum intermediate between $Gabrb3^{+/-}$ and total-knockout (KO) animals. Post-natal lethality or gender imbalance in KD animals is not evident, but cannot be ruled out in the founder generation due to small numbers. Unlike $Gabrb3^{+/-}$ animals, Gabrb3-KD animals exhibit hyperactivity reminiscent of surviving KO animals, but they do not exhibit the severe seizures seen in KO animals.

Conclusions: Phenotypic analyses of sh-mediated Gabrb3 knockdown animals complement studies using knockout and haploinsufficiency models, while avoiding early lethality and parent-of-origin dependent complications.

130.136 157 Behavioral Phenotypes of Shank1 Mutant Mice. J. L. Silverman*[1], C. L. Barkan[1], S. S. Tolu[1], S. Turner[1], R. Saxena[1], D. D. Diagne[1], A. Y. Hung[2], M. Sheng[2] and J. N. Crawley[1], (1)*National Institute of Mental Health, National Institutes of Health*, (2)*Massachusetts Institute of Technology*

Background: The etiology and biological markers of autism are not currently known, but strong evidence exists for a genetic component and several synaptic genes have been implicated. *SHANK* genes encode a family of scaffolding proteins located on the postsynaptic side of excitatory synapses. Mutations in some *SHANK* genes have been detected in several autistic individuals.
Objectives: To understand the consequences of SHANK mutations relevant to the diagnostic and associated symptoms of autism, comprehensive behavioral phenotyping on a line of *shank1* mutant mice was conducted on multiple measures of social interactions, social olfaction, repetitive behaviors, anxiety-related behaviors, and a series of control measures for physical abilities.
Methods: *Shank1* mutant mice, generated by Hung et al., 2008 as previously described, were imported to NIMH in Bethesda, MD, and bred as heterozygotes. All experiments were conducted and analyzed by investigators who were uniformed of the genotype during the behavioral tasks. Assays included two anxiety-related tasks (elevated plus-maze and light/dark exploration), open field locomotor activity, a battery of general health parameters, a sequence of neurological reflexes, sensory measures including olfactory habituation/dishabituation, acoustic startle threshold and prepulse inhibition, rotarod coordination and balance, juvenile reciprocal social interactions, and adult social approach (Chadman et al., 2008; Crawley et al., 2008; MacFarlane et al., 2008).
Results: Adult *shank1* null, heterozygote, and wildtype littermates displayed no significant differences on adult social approach. Juvenile reciprocal social interactions appeared to show similar scores across genotypes. *Shank1* mutants were similar to their wildtype and heterozygous littermates on standardized measures of general health, neurological reflexes and sensory skills including acoustic startle threshold, prepulse inhibition, and pain sensitivity. Locomotor activity in the open field and time spent in the center of the arena were lower in the null mutants, as previously reported (Hung et al., 2008). A partial anxiety-like phenotype was detected in the null mutants in some components of the light/dark task, as previously reported (Hung et al., 2008).
Conclusions: At present, our data indicate normal scores in *shank1* mutant mice on behavioral measures relevant to the diagnostic symptoms of autism. Our findings replicate and extend a previous study using other cohorts of *shank1* mutant mice (Hung et al., 2008), indicating a moderate anxiety-like phenotype and hypoactivity. Null mutation of the *shank1* gene in mice did not produce social deficits on the tasks conducted.

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130.137 158 Constructing a Transgenic Mouse Model Based On SLC25A12, MARK1 and PRKCB1 Gene Dosage Imbalance Mimicking Gene Expression Changes Found in Brain of ASD Patients. A. M. Lepagnol-Bestel[1], J. M. Moalic[1], J. Hager[2] and M. J. Simonneau*[1], (1)*INSERM U894*, (2)*IntegraGen*

Background: Although autism is one of the most heritable neuropsychiatric disorders, its underlying genetic architecture is poorly understood with a contribution of both multiple rare structural variations and common genetic variants. To comprehensively examine the hypothesis that common variation is important in autism, we are studying the effects of dosage imbalance of genes associated to autism spectrum disorders (ASDs) in mouse models. We recently reported that SLC25A12 and MARK1 were associated to ASDs and were overexpressed in post-mortem frontal cortex

(BA 42) of patients with ASDs (Lepagnol-Bestel et al., Mol. Psychiatry, 2008; Maussion et al., Human Molecular Genetics, 2008). Lintas et al. (Mol. Psychiatry, 2009) reported that PRKCB1 gene haplotypes were significantly associated to ASDs and PRKCB1 gene expression was reduced in post-mortem temporocortical regions of patients with ASDs. Currently, we are studying the effect of dosage imbalance of SLC25A12, MARK1 and PRKCB1 in mouse models. Objectives: The goal of our study is to use these animal models to first understand the pathogenesis of ASD associated with specific gene dosage imbalance of SLC25A12, MARK1 and PRKCB1 and then to pharmacologically manipulate these model systems. Methods: Mouse transgenic mice were developed using standard techniques. For Slc25a12 and Mark1, we used a ~3.2 kb mouse Camk2a promoter and a short hairpin (sh) Prkcb1 construct with a CMV promoter. Results: Using in vitro cultures of mouse cortical neurons, we found that overexpression of Slc25A12 and Mark1 induced changes in dendrite length and dendritic spine morphology. The individual mouse models with dosage imbalance of Slc25a12, Mark1 and Prkcb1 are analyzed using biochemical,and neuropathological approaches. Characterization of dendritic spine morphology in these mice will be presented. Conclusions: Such mouse models with modified dosage of key genes associated to ASDs are expected to be instrumental in the characterization of intermediate phenotypes such as abnormal dendritic spine morphology and in the development of novel therapeutic strategies.

130.138 159 Intraventricular Infusions of Enteric Short Chain Fatty Acids Induce Behavioural, Neuropathological and Epigenetic Changes in Rats- Further Development of a Novel Rodent Model of Autism. D. F. MacFabe*[1], R. Agarwal[2], L. J. Tichenoff[1], A. R. Taylor[1], E. LaGamma[2] and B. B. Nankova[2], (1)*University of Western Ontario*, (2)*New York Medical College/Westchester Medical Centre, Valhalla NY, USA*

Background: Diverse cell-cell interaction, neuroinflammatory and metabolic processes are implicated in the pathophysiology of autism spectrum disorders (ASDs). Environmental agents may modulate these factors through epigenetic mechanisms. Propionic (PPA) or butyric acids (BA) are short chain fatty acids (SCFA) present in diet, and are also a product of enteric bacteria fermentation. SCFA have widespread effects on many of the above systems and may thus be possible environmental triggers in ASD. We have shown that PPA can elicit consistent ASD related brain and behavioural changes in rodents, while BA can induce genes implicated in catecholamine, enkephalin and CREB related processes *in vitro*.

Objectives: To examine the effects of chronic intracerebroventricular infusions of SCFA on behaviour, neuropathology and gene expression in rats.

Methods: Adult rats received infusions of pH 7.5 buffered PPA or BA (.26M) or PBS vehicle (0.1M) twice daily for 7 treatment days. Immediately following microinfusion, the animals were placed into an automated open field (Versamax,Ethovision) and a variety of locomotor/social activity variables were assessed for 30 minutes. After sacrifice brains were examined either neuropathologically for innate neuroinflammation, or via microarray analysis (Affymetrix Rat Genome GeneChip 230 2.0 microarrays/MetaCoreTM platform) for ASD related markers/genes.

Results: SCFA infusions increased locomotor activity and induced social impairment. Only PPA produced increased innate neuroinflammation (GFAP,CD68) but both PPA and BA increased vimentin immunoreactivity. Comparison analyses of the microarray data was performed from three brain regions: hippocampus, neocortex and the caudate nucleus. While similar number of gene IDs were found differential regulated in both, hippocampus (BA- 1052; PA 1060, common gene IDs 769) and neocortex (BA- 1185, PA-862; common gene IDs 574), the expression of significantly less genes was affected in the caudate nucleus (BA-87, PA -61 common genes 22), suggesting region-specific responses to SCFA. The expression of autism candidate genes such as BDNF was down regulated in all three regions consistent with human data (Adegbola A. et al., 2008), TLR2 and TLR7 and ceruloplasmin (Fatemi et al., 2005),

GCH1 (serotonin biosynthesis, Hranilovic D. et al., 2008) genes were up-regulated. Enrichment analysis (MetaCore) based on common genes identified functional ontologies like immune response TLR signaling, classic complement pathway, cell adhesion – ECM remodeling, inflammatory response as major processes affected by SCFA infusion.

Conclusions: SCFA produce behavioural, neuropathological and gene expression effects reminiscent of ASD when intraventricularly infused in rats, providing further evidence of a plausible dietary/gut/CNS link to this disorder

130.139 160 The Human AVPR1A BAC Transgenic Mouse: Generation and Validation of a Preclinical Model for Elucidating the Role of AVPR1A in Autism Spectrum Disorders. R. A. Charles*[1], T. Sakurai[2], M. A. Gama Sosa[2], G. A. Elder[3], L. J. Young[4] and J. D. Buxbaum[2], (1)*Mount Sinai School of Medicine, Seaver Autism Center*, (2)*Mount Sinai School of Medicine*, (3)*Mount Sinai School of Medicine, James J. Peters VA Medical Center*, (4)*Emory University*

Background: Multiple genetic studies have demonstrated a significant association between arginine vasopressin receptor 1A (AVPR1A) and autism spectrum disorders (ASDs). Furthermore, animal models have demonstrated the importance of the AVPR1A receptor in mediating behaviors associated with ASDs. Specifically, studies have shown that *Avpr1a* knockout mice demonstrate profound impairment in social behaviors and reduction in anxiety-like behavior and that these behaviors are rescued by reexpression of the receptor. Due to the interspecies differences in receptor pharmacology and receptor expression between mice and humans, studies of this receptor in rodents have limited translation to human studies. We propose that generating a mouse expressing the human form of AVPR1A will provide a more relevant *in vivo* system in which we can better understand the human AVPR1A receptor and its role in modulating behaviors associated with ASDs, while ultimately providing a model for preclinical evaluation of treatments targeting the receptor.

Objectives: The purpose of this study is to generate BAC transgenic mice expressing human AVPR1A and to validate these animals, followed by further biochemical and behavioral analyses.

Methods: We have generated two lines with human *AVPR1A* by injecting BAC DNA into oocytes harvested from C57BL/6xC3H F1 hybrid mice and subsequent backcrossing of the BAC founders to wildtype C57BL6. Integration of the BAC was tested by PCR genotyping using primers directed at the non-conserved 5'UTR of gene. mRNA expression of human and murine AVPR1A was measured by quantitative RT-PCR on whole brain samples and mRNA distribution of human AVPR1A was mapped by *in situ* hybridization on fresh frozen slide-mounted sections using DIG-labeled RNA probes. Protein expression of human and mouse AVPR1A were mapped in transgenic and wildtype animals by performing autoradiographic ligand binding using AVPR1A selective ^{125}I ligands.

Results: Quantitative PCR showed that whole brain levels of mouse and human AVPR1A mRNA are similar in BAC transgenic mice. In control animals, as expected, ligand binding was observed in previously documented areas including the lateral septum, bed nucleus of stria terminalis and medial amygdala. In the human BAC transgenic mice, ligand binding was more intense and widely distributed to areas in which primate AVPR1A is highly expressed such as the intralaminar nucleus of the thalamus, striatum and regions of the brain stem and spinal cord. In situ hybridization studies for localization of mRNA appear to correlate to the findings of ligand binding studies.

Conclusions: Using BAC transgenesis we generated a mouse model that robustly expresses human AVPR1A and is being used in further matings to create a fully humanized AVPR1A mouse model. Most importantly, transgenic mice show a similar expression pattern as found in humans and primates, including expression in many regions distinct from the endogenous murine receptor, indicating that human receptors are regulated by cis acting elements. Given that that differential expression patterns of AVPR1A have been suggested as important

determinants of behavioral differences between species, mice expressing the human receptor may be informative of human AVPR1A signaling and circuitry with possible therapeutic relevance to ASDs.

130.140 161 Transient Expression of Serotonin 5-HT4 Receptors in the Developing Thalamocortical Projections. S. Janusonis*, E. Slaten, M. Hernandez, A. Chen, R. Albay and R. Lavian, *University of California, Santa Barbara*

Background: The 5-HT_4 receptor is an unusually complex serotonin receptor that may underlie the co-morbidity of central and peripheral abnormalities in autism spectrum disorders (ASDs). 5-HT_4 receptors are expressed in the developing brain, the gastrointestinal (GI) system, and blood platelets. Mice lacking the 5-HT_{1A} receptor, another serotonin receptor expressed in the brain and the GI system, show both elevated levels of anxiety (Gross et al., 2002) and elevated serotonin levels in blood platelets (Janu_onis et al., 2006). Likewise, abnormal function of 5-HT_4 receptors may potentially alter brain development and lead to GI and blood serotonin pathologies.

Objectives: As part of our system-level approach (Janu_onis, 2008; Albay et al., 2009), in the present study we investigated the expression of 5-HT_4 receptors in the developing embryonic forebrain in mice.

Methods: We studied the expression of 5-HT_4 receptors in the mouse forebrain at embryonic days 13, 15, 17, and at postnatal days 3 and 14 by using immunohistochemistry, immunoelectron microscopy, tract tracing, and quantitative RT-PCR.

Results: The embryonic thalamocortical projections transiently expressed 5-HT_4 receptors, suggesting that 5-HT_4 receptors may be important for the normal development of these major sensory and limbic projections. Also, the 5-HT_4 receptor expression in the forebrain changed from axonal to somatic around birth. From embryonic day 13 to 17, the telencephalic mRNA levels of the 5-$HT_{4(a)}$ and 5-$HT_{4(b)}$ splice variants increased nine- and five-fold, respectively, whereas the levels of the 5-$HT_{4(e)}$ and 5-$HT_{4(f)}$ variants remained low and statistically unchanged throughout the studied period of embryonic development.

Conclusions: These results show that during development the 5-HT_4 receptor expression in the forebrain undergoes a dynamic regulation. Since the serotonin system is highly conserved in mammalian species, our findings also suggest that perturbation of this regulation may be a contributing factor in ASDs. We are currently investigating whether 5-HT_4 receptors exhibit the same expression dynamics in the developing human brain.

130.141 162 Changing GABAergic Tone Influences Prefrontal Mediated Cognition. G. B. Bissonette*[1], M. Bae[1], T. Suresh[1], G. Schoenbaum[1] and E. M. Powell[2], (1)*University of Maryland, Baltimore*, (2)*University of Maryland School of Medicine*

Background: In a constantly changing environment, the ability to shift from one learned behavioral strategy to another more adaptive strategy is imperative. Recent research has suggested that alterations in behavioral flexibility may be an underlying factor in the cognitive deficits seen in autism/autism spectrum disorder (ASD). Mutations to MET, the receptor of the hepatocyte growth factor/scatter factor (HGF/SF), have been genetically linked to ASD.

Objectives: Alterations in HGF/SF sensitivity in neurons leads to anatomical deficits in the frontal cortex of adult animals. These deficits affect a particular type of interneuron, the fast spiking parvalbumin interneurons. This study used multiple lines of mice, those with increase or reduction of HGF/SF through development. These mice were behaviorally tested on reversal learning tasks to understand the cognitive implications of altered prefrontal GABAergic tone.

Methods: These studies used transgenic mutant mouse lines with behavioral and electrophysiological techniques to understand the role of GABA in both simple elicited behaviors and more complex cognitive tasks, mirroring human tasks.

Results: Reduction in the number of GABAergic interneuron in the adult prefrontal cortex leads to increased anxiety, deficits in

tasks of behavioral flexibility, increased seizure susceptibility and deficits in learning and memory. The postnatal addition of supplemental HGF/SF can rescue the anatomical deficits as well as several of the behavioral deficits; however the rescue merely altered the learning and memory deficit.

Conclusions: These data suggest that GABAergic tone may have important implications for understanding complex disorders such as autism spectrum disorder. Changes in the GABAergic tone of the prefrontal cortex may lead to different abilities to handle tasks requiring different cognitive load. This in turn, may manifest itself in more broad and widespread cognitive deficits, such as observed across autism spectrum disorder.

130.142 163 Preferential Differentiation of TH17 Cells in Offspring of Immune-Activated Dams in a Prenatal Mouse Model of Autism. M. Mandal*[1], A. Marzouk[2], R. Donnelly[3] and N. M. Ponzio[2], (1)*UMDNJ - Graduate School of Biomedical Sciences*, (2)*UMDNJ - New Jersey Medical School*, (3)*UMDNJ - New Jersey Medical School and Graduate School of Biomedical Sciences*

Background: Results of clinical studies show that infection of women with certain pathogens during pregnancy leads to a higher frequency of neurological disorders, such as schizophrenia and autism in their children. These results are supported by studies in rodents in which infectious pathogens (or agents that mimic viral or bacterial infections) given to pregnant dams during pregnancy, lead to immunological, neurological, and behavioral abnormalities in their offspring. Maternal cytokines (particularly IL-6) appear to mediate at least some of the observed abnormalities. However, the experimental design of these rodent models of autism that do not totally replicate the human scenario.

Objectives: A major objective of our study is to optimize existing mouse models of autism (that currently use immunologically naïve pregnant dams) to more closely resemble the human situation, in which the immune systems of women have been previously stimulated either by natural infection or immunization prior to pregnancy. Thus, a more robust mouse model of autism could be developed, and reveal factors that are significant in the etiology and/or pathogenesis of this disorder that current models don't consider.

Methods: Female C57BL/6 (B6) mice were immunized i.p. with irradiated Balb/c spleen cells. One month later, these "immune" female B6 mice were mated with syngeneic B6 males. On gestational day12.5, pregnant females were injected i.p. with polyinosinic-polycytidylic acid (pI:C; 20 mg/kg) or PBS (control). Sera from pregnant dams were analyzed for the presence of multiple cytokines by Luminex assay. Phenotype (FACS analysis) and functional studies (proliferation, cytotoxicity, cytokine production) were performed on spleen cells from the offspring of pI:C-injected (vs. PBS-injected) dams.

Results: Significantly higher levels of IL-6 were present in maternal sera of pI:C-injected immune dams than in pI:C-injected immunologically naive dams. FACS analysis of activated spleen cells from offspring of pI:C-injected immune dams showed >5-fold increase in the percentages of CD4+ T Helper (TH) cells with intracellular IL-17A (TH17 cells) than spleen cells from offspring of PBS-injected immune dams. However, spleen cells from offspring of pI:C-injected naïve dams failed to show any increase in TH17 cells after similar activation. In addition, affinity-purified CD4+ T cells from offspring of pI:C-injected (vs. PBS-injected) immune dams also showed significantly greater ability to differentiate towards TH17 cells after activation and culture under TH17 polarizing conditions.

Conclusions: Immunization prior to immune activation during pregnancy caused higher production of IL-6 in maternal peripheral circulation, and promoted the development of pro-inflammatory TH17 cells in their offspring. Th17 cells have been implicated in mediating the incidence and/or progression of various inflammatory and autoimmune phenomena. Thus, the increase in TH17 cells in offspring of pI:C-injected immune dams indicate a pro-inflammatory phenotype, which may contribute to neuroinflammatory processes that have been observed in the

brain and gastrointestinal tract of autistic individuals, and in experimental animal models of autism.

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130.001 22 fMRI of Citalopram Treatment in Autism. S. Greeter[1], L. Sikich[2], C. Alderman[2], A. Rittenberg[2], L. Turner-Brown[3], T. Holtzclaw*[4], J. W. Bodfish[5], J. Richey[4] and G. Dichter[2], (1)*University of North Carolina School of Medicine*, (2)*University of North Carolina*, (3)*UNC-Chapel Hill*, (4)*Carolina Institute for Developmental Disabilities*, (5)*University of North Carolina - Chapel Hill*

Background:

Multiple functional magnetic resonance imaging (fMRI) studies have implicated frontostriatal brain regions, including the anterior cingulate and prefrontal cortex, as a neurobiological mediator of restricted and repetitive behaviors in autism spectrum disorders (ASDs). Despite the emergence of pharmacotherapeutic agents that reduce autism symptoms, no studies to date have assessed changes in regional brain activation assessed with fMRI in response to autism treatments.

Objectives:

In the present study, we used fMRI to investigate changes in regional brain functioning in individuals with an ASD due to citalopram treatment administered in a randomized placebo controlled double-blind context. Citalopram is a selective serotonin reuptake inhibitor (SSRI) that has shown promise in reducing repetitive behaviors for some, but not all individuals with autism. We sought to determine the effects of citalopram treatment, relative to placebo treatment, on frontostriatal functioning in participants with high functioning autism. We also sought to assess for potential relations between changes in restricted repetitive behaviors and changes in regional brain function due to citalopram treatment. Finally, in an exploratory manner we investigated whether pre-treatment fMRI scans predicted response to treatment.

Methods:

We assessed twelve individuals with an ASD (IQ > 70) who demonstrated high levels of repetitive behaviors as defined by baseline Children's Yale-Brown Obsessive Compulsive Scales (CYBOCS-PDD) scores of eight or greater. Brain activation in response to a visual oddball target detection task was assessed both before and after double-blind treatment with citalopram or placebo administered for 12 weeks. The Clinical Global Impressions (CGI), CYBOCS-PDD, and The Repetitive Behavior Subscale Revised (RBS-R) were administered at both scan sessions.

Results:

Consistent with recent larger-scale clinical trial data, both treatment groups showed significant symptom reductions on measures of global functioning and of repetitive behaviors. Additionally, there were no significant differences in response to citalopram or placebo treatment. Brain imaging data revealed increased activation to target events in the inferior frontal gyrus (IFG) and the anterior cingulate cortex (ACC) and decreased activation in the superior frontal gyrus (SFG) after treatment with either citalopram or placebo. Further, less activation to target events in the IFG and the ACC at baseline predicted greater improvement in RBS-R total scores after treatment. RBS-R total scores were correlated with pretreatment activation in the IFG and the ACC and post-treatment activation in the IFG and ACC.

Conclusions:

These pilot data provide preliminary evidence that autism treatments that reduce symptoms produce measurable changes in brain activation. Future studies with larger samples and different compounds should continue to investigate the utility of fMRI to predict response to treatment and to elucidate the potential mechanisms of action of effective autism interventions.

130.002 23 Meta-Analysis of Functional Neuroimaging Studies Reveals Enhanced Engagement of Visual System in Autism. F. Samson*[1], T. A. Zeffiro[2], I. Soulières[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: The repeated observation that many autistics possess unique perceptual capabilities in figure/ground segmentation, visual search and block design has motivated the suggestion that they may utilize an overall greater engagement of the visual system across a wider variety of task conditions. Moreover, this enhanced perceptual activity may be associated with reduced activity in frontal cortex during social, reasoning, and visuospatial tasks. Meta-analysis of functional imaging studies allows quantitative assessment of the evidence supporting these assertions.

Objectives: To determine whether existing functional neuroimaging studies have shown: (1) an overall differential engagement of the visual system in autism; and (2) whether any differential visual system activity in autism is general across tasks or specific to particular visual domains.

Methods: We performed a PubMed search to identify PET and fMRI studies utilizing visual tasks with autistic and non-autistic groups. Of a total of 95 studies, 22 were rejected because of low power ($n<10$), 21 because of partial brain coverage, 11 because results were not reported in a standard anatomical space, and 9 because only between-group contrasts were presented. The remaining 32 articles reporting 1251 within-group foci in a standard anatomical space were included. First, Activation Likelihood Estimation (ALE) maps reflecting the regions of convergence for all tasks were computed within and between groups (FWHM = 8mm, $p_{FDR}=0.05$). Second, the contrasts were classified according to their domain specificity (face, object, and written language tasks) and the within- and between-groups activation maps recomputed.

Results: First, the ALE results for the meta-analysis of all coordinates for both groups revealed activity in occipito-temporal (BA 17, 18, 19, 37), frontal (BA 6, 8, 9, 46, 47), parietal (BA 7, 40) and insular cortex. Between group comparisons revealed higher activity in the visual system (BA 17, 18, 19, 37) and lower activity in frontal areas (BA 6, 9, 44) in autistics. Second, comparison maps for each domain revealed specific between-group differences. In the face processing domain, greater primary visual and antero-medial fusiform activity, combined with reduced inferior frontal gyrus ALE values were seen in autistics. In the object processing domain, a pattern of higher ALE values in extrastriate cortex, superior parietal lobule and precuneus combined with lower values in inferior and medial frontal gyri were seen in the autistics. For tasks involving written language, higher activity was seen in the reading network (BA 17, 37, 22 and 45) in autistics.

Conclusions: This literature meta-analysis demonstrates greater activity in the autistic visual system for a range of tasks. Moreover, domain-specific activity increases in visual areas specialized for face, object, and language tasks were observed in autism. An overall stronger engagement of the visual system is therefore a task-independent and robust finding in autism and is possibly related to their well-documented enhanced visual abilities.

130.003 24 Microstructural Changes in Face Processing Pathways in Autism: Diffusion Tensor Tracking (DTT) with Behavioral Comparison. T. E. Conturo*[1], D. L. Williams[2], E. L. Williams[3], C. D. Smith[4], E. Gultepe[1], E. Akbudak[1], M. S. Strauss[5] and N. J. Minshew[6], (1)*Washington University School of Medicine*, (2)*Duquesne University*, (3)*University of Louisville*, (4)*University of Kentucky*, (5)*University of Pittsburgh*, (6)*University of Pittsburgh School of Medicine*

Background: Recognition of faces/face emotions is commonly impaired in adults/children with autism. Given the importance of face processing in autism, the ability to measure face-processing pathways with DTT (Smith et.al., 2009, JMRI), and the potential of pathway abnormalities to produce strong behavioral effects, we tested for abnormalities in face-processing pathways in autism. In an initial study (Conturo et.al., 2008, JINS), the right hippocampo-fusiform (HF) pathway involved in face recognition had reduced minimum-diffusivity (D-min, intrinsic across-fiber diffusivity; Smith et.al., 2009). Objectives: Characterize/interpret DTT abnormalities in face-processing pathways by

comparison to sensitive neuropsychological tests (NPTs).
Methods: Custom diffusion-tensor MRI data were acquired in 17 participants with high-functioning autism meeting ADOS/ADI criteria (age 16-53) and 17 individually-matched controls from 2002-2006. For comparison, we acquired sensitive custom NPTs of: face-memory (Best et.al., IMFAR2009); face-gender identification (Wilkinson et.al., IMFAR2009); and face-emotion recognition (Rump et.al., 2009) in the autism participants. We also examined the relationship to symptom severity during development as measured by the ADI.
Results: Autism participants were separated into lower/higher face-recognition subgroups using face-memory and Benton NPTs. The lower-performance subgroup had significantly slower D-min in both right HF ($p = 0.019$) and right amygdalo-fusiform (AF) pathway ($p = 0.011$). Gender/emotion NPTs showed a strong relation to DTT for both right HF/AFpathways. The DTT-NPT correlation was very high (e.g., $r = 0.995/0.463$ without/with one outlier; AF vs. face-gender NPT). All NPTs showed the same relation of slower D-min with lower performance for both pathways, indicating that the D-min reduction in autism-vs-controls described in (Conturo, et al., 2008) is functionally significant. The unusual reversal of the expected DTT-NPT relation supports a mechanism of small-diameter axons in right AF/HF. This interpretation parsimoniously accounts for the reversed DTT-NPT relation because small-diameter axons have slower transmission speed. This biologic mechanism is also consistent with: small cell bodies in hippocampus (Bauman et.al., 2005) and minicolumns (Casanova et.al., 2002); reduced fMRI correlations (Just et.al., 2004; Kleinhans et.al., 2008); lengthened reaction times (Townsend et.al., 1996); slowed electrophysiology (McPartland et.al., 2004); and symptom abatement with fever (Curran et.al., 2007). A correlation between ADI, Section A (reciprocal social interactions) and right HF D-min ($r = -0.413$; $p = 0.047$; slower D-min associated with childhood social impairment) suggests an early-developmental process, consistent with known impairments in face processing in young children. The D-min reduction is unlikely to be due to intervening variables (e.g., behavioral therapy) since participants do not report any consistent therapy. Any therapy effects would thus average out (and would oppose the reversed DTT-NPT relation). Finally, the high DTT-NPT correlation suggests that axonal diameter is a strong determinant of function, despite intervening variables. [More subtle secondary changes can occur in left AF/HF (Conturo et.al, 2008), consistent with relative sparing of object processing in autism (Humphreys et.al., 2008).]
Conclusions: A strong association between decreased D-min and decreased function (as measured by behavioral NPTs) occurred in right AF/HF in autism, supporting a mechanism of small-diameter axons. A similar DTT-ADI relation was found, suggesting that this mechanism occurs in childhood, and persists into adulthood.

130.004 25 Neural Correlates of Response Inhibition and Response Monitoring in Autism. S. Spinelli*, M. C. Goldberg, S. E. Joel, J. J. Pekar and S. H. Mostofsky, *Kennedy Krieger Institute, Johns Hopkins University School of Medicine*

Background: Several studies provide evidence for deficits in executive functions in autism, including on measures of response inhibition and response monitoring. These deficits may be particularly important in autism because they may lead to decreased ability to flexibly allocate resources to guide attention, thoughts and actions, and consequently may contribute to increased perseveration and repetitive behavior. Recently published functional magnetic resonance imaging (fMRI) findings reveal that, during correct response monitoring, adults with autism showed increased activation in rostral anterior cingulate cortex (rACC) compared to healthy controls, and that rACC activity was correlated with ratings of restricted and repetitive behavior (Thakkar et al 2008). A similar correlation between ACC function and repetitive behaviors was found with an executive function measure of shifting abilities using fMRI in adults with autism (Shafritz et al 2008).

Objectives: To examine the neural correlates of response monitoring and response selection/inhibition in children with high-functioning autism (HFA), and its correlation with measures of restricted/repetitive

behavior extracted from the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview (ADI).

Methods: 13 children with HFA and 16 typically developing (TD) children completed a functional MRI scan while performing a Go/No-Go task. The neural correlates of correct response inhibition and commission errors (failure to inhibit responding to No-go stimuli) were examined using event related analysis to assess response inhibition and response monitoring, respectively. Groups were matched for commission errors, gender, age (8 to 12 years old) and non-verbal IQ (WISC IV Perceptual Reasoning Index).

Results: Contrast of commission (incorrect No-go) vs correct inhibition on No-go trials revealed that children with HFA showed increased activation in the medial prefrontal cortex (mPFC, BA10/9/32) and the left temporal gyrus (LTempG, BA20/21/22) compared to TD children. Subsequent analysis for each separate trial condition (commission error and correct inhibition trials) revealed abnormal activation in HFA in both regions and for both trial conditions. During correct inhibition, children with HFA showed significant deactivation in the mPFC and LTempG in contrast to TD children who showed no changes. During commission error, children with HFA showed significant activation in the mPFC and LTempG while TD children showed deactivation in these regions. Moreover, in children with HFA deactivation in the LTempG during correct inhibition was significantly correlated with measures of restricted/repetitive behavior (ADOS, $p<0.009$, ADI, $p<0.06$).

Conclusions:

Compared to the TD group, children with HFA show abnormal neural activity in the mPFC/rACC and LTempG during correct and incorrect response inhibition. In the present study, activation in the mPFC was not correlated with restricted and repetitive behavior scores. However, we found a significant correlation with deactivation in the LTempG. Currently, there is only limited data examining relationships between neural circuitry involved in response inhibition and response monitoring and repetitive behaviors in HFA. Further studies are warranted, however, our data and previous findings suggest that repetitive behaviors associated with autism might reflect dysfunction across a wider network of executive circuitry.

Shafritz KM, et al. (2008), *Biol Psychiatry* 63:974-980.

Thakkar KN, et al. (2008), *Brain* 131:2464-2478.

130.005 26 Quantitative Analysis of the Shape of the Corpus Callosum in Autism. M. F. Casanova*[1], A. S. El-Baz[1], A. E. Switala[1], E. L. Williams[1], D. L. Williams[2], N. J. Minshew[3] and T. E. Conturo[4], (1)*University of Louisville*, (2)*Duquesne University*, (3)*University of Pittsburgh School of Medicine*, (4)*Washington University School of Medicine*

Background: Multiple neuroimaging studies of the corpus callosum have suggested the presence of morphometric abnormalities in autistic patients. There is at present a convergence of findings from structural studies indicating that any significant abnormality is always manifested as a smaller corpus callosum. This applies to both areal (i.e., single midsaggital measures) and volumetric assessments. The fact that the corpus callosum is smaller in autism is all the more striking when considering that total brain size appears, on average, to be increased.

Objectives: The study aimed to elucidate the nature of the corpus callosum abnormality in autism. It complemented previous morphometric studies by quantitating the shape of the corpus callosum boundary.

Methods: Seventeen high-functioning, autistic individuals were recruited (fourteen male, three female, all between 16 and 51 years of age). An equal number of non-autistic control subjects were enrolled, matched pairwise by age and sex with the autistic participants. T1-weighted images were acquired with Siemens MAGNETOM Vision 1.5 T scanners using an MPRAGE acquisition sequence. The corpus callosum was segmented from each image using a probabilistic model for corpus callosum shape. Boundary surfaces of the segmented corpora callosa were mapped into a standardized pseudocylindrical coordinate

system (z, _, _) to facilitate their comparison with each other. For each point z along a curvilinear axis from the genu to the splenium, and for each angle _ measured clockwise about this axis from anatomical right, _(z, _) is the perpendicular distance from the axis to the boundary surface. The transformed surfaces were aggregated pointwise into a statistical parametric map of pairwise t statistics with 16 degrees of freedom. Regions of statistically significance were derived from the associated P-values using the method of Benjamini and Hochberg with a false discovery rate $q^* = 0.05$.

Results: White matter in autism was reduced bilaterally along the body of the corpus callosum, apart from an increase in the region proximal to the right cingulate gyrus. There was also a reduction at the extreme posterior end of the structure. There was otherwise no significant difference around the mid-sagittal plane.

Conclusions: Results from our study indicate a generalized reduction of the corpus callosum in autism. The findings acquire relevance from previous neuroimaging studies that varied among themselves in regards to a preferred anatomical subdivision (e.g., genu, body, splenium). Generalized findings, involving the rostro-caudal extent of the corpus callosum, is expected from a mechanism involving corticalization, i.e. a mitotic event affecting periventricular germinal cells and the total number of cortical minicolumns.

130.006 27 Reduced Differentiation of Functional Networks Subserved by Posterior Superior Temporal Sulcus in Autism Spectrum Disorder. P. Shih[1], B. Keehn[2], J. Oram[1], K. M. Leyden[1] and R. A. Müller*[1], (1)*San Diego State University*, (2)*San Diego State University / University of California, San Diego*

Background: Socio-communicative impairments are among the most salient features of autism spectrum disorder (ASD). The posterior superior temporal sulcus (pSTS) is anatomically situated in a multimodal integrative location and has been implicated in the processing of language, biological motion, and social information. Thus, abnormalities in the development of functional networks supported by pSTS may underlie some of the deficits in ASD.

Objectives: To employ functional connectivity MRI (fcMRI) to investigate the organization of intrinsic functional networks subserved by pSTS in individuals with ASD and typically developing (TD) individuals.

Methods: Forty 9-18 year-old participants, 20 diagnosed with ASD and 20 age-, handedness-, and IQ-matched TD individuals, performed four runs of a visual search task in an event-related fMRI design (totaling 496 time points). Connectivity of networks existing independent of task effects can be detected in low-frequency fluctuations. Therefore, to isolate signals of interest, the timeseries were bandpass filtered (.008<f<.08 Hz), and the task paradigm, six motion parameters, and linear trends were included as regressors in a general linear model. To separate distinct signals within our regions of interest at the individual subject level, singular value decomposition of the fMRI timeseries from every voxel in pSTS was performed to obtain the singular timeseries that account for the greatest variance and thus are most representative of the functional network signals occurring within pSTS. Each of these timeseries was correlated with the whole brain and Fisher's r-to-z' transformations were applied to the resultant maps. To separate the networks subserved by pSTS at the group level, principle component analysis was performed on z' connectivity maps. The functional connectivity of each network was further assessed within and between groups using t-tests.

Results: We found three networks subserved by pSTS in each hemisphere. The main network contained bilateral connections from pSTS with inferior frontal gyrus (IFG) and subcortical regions. The second pSTS network included connections with posterior cingulate cortex (PCC), precuneus, medial prefrontal cortex (mPFC), and IFG, possibly containing connectivity supporting processes related to theory-of-mind. The third network indicating connections between pSTS and area MT+, a region known for motion processing, was present in the TD group, but not in the ASD group. Direct-group comparisons of

connectivity maps showed that in the ASD group several of the networks contained abnormally increased connectivity with superior frontal, middle frontal, and temporo-occipital regions and decreased connectivity in mPFC and superior parietal regions. Interestingly, in the ASD group, all three bilateral networks had largely overlapping connections, whereas much less overlap between networks was seen in the TD group.

Conclusions: We examined the functional connectivity of pSTS in each hemisphere and found that it participates in three distinct functional networks. The ASD group showed both abnormally increased and decreased connectivity. Generally, greater connectivity was reflected in correlations with regions outside of typical networks. Specifically, all three networks were less distinct in the ASD group and overlapped largely with one another, possibly due to reduced functional differentiation into separate, well-defined networks.

130.007 28 Reduced Inter-Hemispheric Functional Connectivity in Toddlers with Autism. I. Dinstein*[1], L. T. Eyler[2], R. Malach[1], M. Behrmann[3], E. Courchesne[4] and K. Pierce[4], (1)*Weizmann Institute of Science*, (2)*University of California San Diego*, (3)*Carnegie Mellon University*, (4)*University of California, San Diego*

Background: An intriguing characteristic of the human brain is that neural activity in functionally related cortical areas fluctuates spontaneously in a correlated/synchronized manner during rest and sleep. Such synchronized activity, in the complete absence of stimulus or task, is thought to be a feature of neural networks that share a common sensory, motor, or cognitive function and may be a product of strong anatomical connections linking functionally related brain areas. A prominent feature of this synchronization is its anatomical selectivity. In particular, the strongest synchronization occurs between corresponding inter-hemispheric cortical sites (e.g. right and left auditory cortex).
It has been hypothesized that some of the atypical behavioral symptoms in autism may arise from a reduction in long-range cortical connections needed for normally synchronized cortical activity. Several recent studies have reported reduced functional connectivity in adults with autism, but this issue has not been addressed in babies with autism.
Objectives: To characterize and compare inter-hemispheric functional connectivity patterns between toddlers with autism ages 12-42 months and age matched typical controls.
Methods: Using a prospective population based screening method (Pierce et al., in review), 20 toddlers at-risk for autism and 20 typical controls 12-42 months old were recruited and participated in functional and structural MRI scans during natural sleep. Toddlers at-risk for autism were tracked until their 3rd birthday and only those with confirmed diagnoses were included in this experiment. fMRI pre-processing included standard motion correction, spatial smoothing, removal of the global mean, and removal of linear trends. During the fMRI scan, children were exposed to a soft auditory soundtrack. However, we extracted evoked auditory responses by "projecting out" all brain responses correlated with the experiment design. Several bilateral anatomical regions of interest were defined including inferior frontal gyrus (Broca's area), superior temporal gyrus (Wernicke's area), lateral occipital cortex, anterior intraparietal sulcus, and primary motor cortex. We computed the correlation between right and left ROIs in each subject separately and averaged across individuals of each group. Functional connectivity maps were created between each of the ROIs and the rest of the cortex in each group separately so as to compare the spatial selectivity of inter-hemispheric correlations.
Results: Both toddlers with autism and typically developing controls showed strong and selective inter-hemispheric correlations in several brain areas including occipital, parietal, and motor regions. These correlations were similar in strength and spatial selectivity to those reported in adult subjects. However, toddlers with autism exhibited reduced inter-hemispheric correlations in a subset of cortical areas, which included insular cortex and putative language-related Broca's and Wernicke's areas.
Conclusions: Children as young as 12-42

months old already exhibit adult-like inter-hemispheric correlations indicative of a somewhat mature functional organization. However, children with autism, already at this young age, exhibited a difference in the functional organization of the cortex characterized by reduced inter-hemispheric synchronization in language areas during sleep. This neural characteristic may serve as an early biomarker of autism and may be useful for predicting developmental outcome.

130.008 29 Statistical 3D Shape Analysis of Lateral Ventricles in Autism. Q. He, Y. Duan* and J. H. Miles, *University of Missouri*

Background:

Autism is a heterogeneous neurodevelopmental disorder of unknown etiology marked by social, emotional and communication impairments. The ventricular system is a structure in the center of the brain filled with fluid. Enlargement of the ventricles in autism has been reported in previous works. However, the magnitude of the differences revealed by volume analysis is limited, because it does not consider how shapes overlap each other. Shape analysis can precisely locate morphological changes in brain structures which cannot be reflected in volume measurements, thus it becomes more and more popular in neuroimaging community. Very few studies have been done with regard to the shape morphology of the ventricles in autism.

Objectives:

The aim of this paper is to study the shape differences of the lateral ventricles between autistic children and normal controls. 3D models of ventricle shapes are compared to reveal the shape difference at every surface location.

Methods:

Children with autism were recruited from the Thompson Center for Autism and Neurodevelopmental Disorders. Control subjects with matching gender, age and ancestry were recruited from the community. Student t-test was used to compare the ages and χ^2 test was used to compare the gender ratios. There was no significant difference between the two groups in terms of age, gender and race. This study was approved by the Health Sciences Institutional Review Board. The parents or legal guardians of all subjects provided written consent for participation in this study.

The 3D ventricle models were obtained using the semiautomatic segmentation software that has been developed in our previous work. Six anatomical landmarks were identified. Pseudo-landmarks on the surface were then interpolated using the method in our previous work. Generalized Procrustes Analysis is performed on all the 3D shapes in order to eliminate the shape differences caused by translation, rotation and scaling. Difference between groups at every surface location was tested using Hotelling T^2 two-sample metric. Since comparisons are made at thousands of surface points, we adopted False Discovery Rate estimation (FDR) for p-value correction.

Results:

From the overlaid average structures of the two groups, we find that the posterior horn of both ventricles in autistic children are bent more inward, the anterior horn of the left ventricle is bent more downward and the anterior horn of the right ventricle is bent more outward in the autistic children. A two-tailed alpha level of 0.05 is chosen as the significance threshold for the raw p-values. The raw significance maps of both ventricles show significant shape difference in part of the anterior and posterior horns between autistic children and controls, but the corrected significance maps show no shape difference between the two groups.

Conclusions:

This paper studies the shape differences of the lateral ventricles between autistic children and controls. The overlaid mean structures show shape difference in the anterior and posterior horns, but statistical testings do not show any significance in those differences. This may be due to small sample size and further experiment needs to be done when more data are available.

130.009 30 Structural Brain Changes and Attention-Deficit Hyperactivity Symptom Severity in Young Persons with Autism Spectrum Disorder. C. Ravichandran*[1], J. E. Lainhart[2], A. Froelich[2], M. B. DuBray[2], T. Abildskov[3], E. D. Bigler[3], A. L. Alexander[4] and N. Lange[5], (1)*McLean Hospital/Harvard Medical School*, (2)*University of Utah*, (3)*Brigham Young University*, (4)*University of Wisconsin*, (5)*Harvard University*

Background: The high degree of inter-individual heterogeneity found in autism spectrum disorder (ASD) is a well-recognized major impediment to effective study and treatment. Variation in the severity of features of other psychiatric disorders often but not always associated with autism, including attention-deficit hyperactivity (ADHD), is a relevant but understudied contributor to this heterogeneity. Research associating structural brain changes, including changes in caudate volume and asymmetry, with ADHD and, separately, with ASD suggest in combination that variation in ADHD severity may contribute to the heterogeneity in structural brain changes present in ASD.
Objectives: The goal of this study was to investigate changes in regional brain volume and asymmetry in young persons with ASD and ADHD. Our primary hypotheses were that caudate volume is increased in ASD and that this volumetric increase is negatively correlated with ADHD severity. We studied other regional and global volumes to determine whether any findings supporting our hypotheses were specific to the caudate nucleus and to support hypothesis generation for future research.
Methods: Structural MRI scans and the Conners' ADHD/DSM-IV Scales (CADS) were completed for N = 36 high-functioning males with ASD 6-15 years of age and N = 20 typically developing aged-matched males. Regional brain volumes by hemisphere were extracted using FreeSurfer software, including total cortex, gray matter, white matter, the head of the caudate nucleus, putamen, globus pallidus, thalamus, hippocampus, and amygdala; total brain volume, intracranial brain volume, and volumes of the posterior, mid-posterior, central, mid-anterior and anterior corpus callosum were also extracted. These volumes and their asymmetries were compared between the groups and associated with CADS total score among those individuals with ASD.
Results: We observed a highly significant increase in CADS total score in our ASD sample ($p<0.001$). We also found a significant association between ASD and reduced rightward caudate asymmetry ($p=0.006$). No association was found, however, between hemispheric asymmetries and CADS total score in our ASD sample. Neither the volumes nor asymmetries of any of the other brain structures we examined were associated with ASD or ADHD severity.
Conclusions: Our preliminary findings suggest that the development of typical rightward asymmetry of caudate volume is disrupted in autism independently of ADHD severity. Our findings also suggest that the volumetric correlates of ADHD in autism are different from correlates reported in non-autistic individuals with ADHD. Similar clinical ADHD phenotypes may have different underlying neurobiological mechanisms in individuals with and without autism. Longitudinal volumetric, diffusion tensor imaging, and fMRI studies are needed to identify unique signatures of brain development in autism with and without ADHD, and in ADHD with and without autism.
Disclaimer: The project described was supported by grant numbers RO1 MH080826 and RO1 MH084795 from the National Institute of Mental Health and the Corneel Fellowship at McLean Hospital. 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.

130.010 31 The Development of Amygdala-Fusiform Structural Connectivity and Face Processing in High Functioning Autism. N. Tottenham* and K. Gillespie, *UCLA*

Background: Individuals with autism spectrum disorders (ASD) show impairments in face emotion processing, which may be related to differences in visual attention (less eye-contact than typically developing (TD) individuals (Klin et al. 2002)). Individual differences in gaze behavior have been associated with alterations in amygdala and fusiform gyrus (FG) in adults with ASD (Dalton et al., 2004), and decreased attention to the eyes predicts less ability to recognize fear and increased social anxiety (Corden et al., 2007). Given the strong bidirectional

connections between these two neural regions, we assessed the integrity of these structural connections as they related to face expression processing. Moreover, we administered a laboratory-based intervention that encouraged eye-contact and evaluated its effect on face expression processing. Objectives: To examine the development of amygdala-fusiform structural connectivity as it relates to face emotion processing in ASD and to examine the effect of a laboratory-based intervention on face emotion processing. Methods: Reaction times (RT) to facial expressions (angry, fear, happy, neutral) were collected from children, adolescents, and adults with and without ASD. Two separate blocks were presented that either directed visual attention to the eye region (EYE) or allowed for natural viewing (NATURAL). In order to direct attention to the eye region, participants were instructed to identify the location of a cue placed in the eyes of the face stimulus. Additionally, the integrity of white matter tracks between the amygdala and fusiform gyrus was assessed using diffusion tensor imaging (DTI) with fractional anisotropy (FA) as the index. Results: Under natural viewing conditions [NATURAL], TD adults were slower when responding to fear faces relative to other expressions, consistent with our previous work (Hare, Tottenham et al., 2005). In contrast, the ASD group showed no evidence of this slowing to fear. There were no group differences in adolescents and children. Slower RTs to fear faces were associated with stronger connectivity between amygdala and FG. The eye-contact intervention [EYE] was effective in that, when making eye-contact, the ASD adults performed like the TD adults under natural viewing conditions (i.e., showed evidence of slowing to fear faces). FA values showed group differences in developmental change, where FA values were higher in TD than in ASD individuals during adolescence, while there were no group differences in adulthood. Conclusions: These findings suggest, as others have (Dalton, et al., 2004; Klin et al., 2002), that face processing impairments in ASD may be the result of decreased eye-contact. The current study extends these findings and shows that a laboratory-based eye-contact intervention may equate performance across TD and ASD adults. Moreover, individual differences in face expression processing may be the result of decreased connectivity between the amygdala and FG. The development in connectivity seemed delayed in the ASD group, where the group differences disappear by adulthood.

130.011 32 Viewing Images of Restricted Interests Elicits BOLD Response in Neural Reward System. C. Cascio*[1], J. H. Foss-Feig[2], A. A. Cosby[3], C. P. Burnette[3], M. Blanco[1] and S. M. Bolton[3], (1)*Vanderbilt University School of Medicine*, (2)*Vanderbilt University*, (3)*Vanderbilt School of Medicine/Kennedy Center for Research on Human Development*

Background: The experimental neurobiological study of repetitive behaviors in individuals with autism spectrum disorders (ASD) has historically focused on global deficits in behavioral flexibility that emerge from frontostriatal dysfunction. These reliably measurable neurobehavioral constructs have come to serve as a proxy for repetitive behaviors as a whole, resulting in a neglect of both the heterogeneity of repetitive behaviors and the potential role of emotion and motivation in repetitive behaviors. While many repetitive behaviors are not conducive to experimental study using neuroimaging, restricted interests can be assessed in this way.

Objectives: To determine whether neural reward systems (e.g. orbitofrontal cortex (OFC), amygdala, insular cortex, ventral striatum) are active when individuals with ASD view images related to their restricted interests, relative to a visual baseline, and whether the BOLD response in these areas was greater in a group of children with ASD than a control group whose members have a regular hobby.

Methods: Nine children with ASD and seven children with TD, ages 8-17, completed the study. Children and parents were given a questionnaire to assess hobbies and activities engaged during spare time. Parents were given the Yale Special Interests Interview (Volkmar and Klin, 1996) to assess the presence and severity of restricted interest. Information from the interview and questionnaires was used to create an "Own Interest" image stimulus set. Several of

each child's "Own Interest" images were pooled to create an "Others' Interest" stimulus set for use as a visual baseline. This provided consistency between conditions in image complexity and size. A block design was implemented in 5 runs, each containing 15 presentations of each condition. Image processing and analysis was performed in SPM5; contrast maps were created for each subject and entered into a group level model. Regions of interest were chosen to include bilateral amygdala, OFC, insula, and nucleus accumbens. Percent signal change in these regions were correlated with variables obtained from the ADI-R and ADOS, the Yale Special Interest Interview, and an operant behavioral "button press" task, in which subjects used key presses to control the display time of images in both categories, yielding a quantitative measure of the reward value of the images. After the scan, recognition memory was tested for each subject to ensure that they attended to the images in each condition.

Results: Both individuals with ASD and controls showed activation in OFC, amygdala, and insular regions in the "Own Interest – Others' Interest" contrast. This difference was significantly greater in the ASD group for the insula and OFC. Percent signal change extracted from this region correlated with differential display time in the operant button press task.

Conclusions: Although behavioral sciences have long since established that restricted interests are rewarding for individuals with ASD, this study provides the first neurobiological evidence that neural reward pathways are involved in restricted interests.

130.012 33 WHITE MATTER Parcellation IN LOW-IQ CHILDREN with and without Autistic Disorder. M. R. Herbert*[1], L. O'Brien[2], N. Shetty[1] and D. Ziegler[3], (1)*Massachusetts General Hospital*, (2)*Colby College*, (3)*MIT*

Background: The contribution of white matter to volumetric differences between brains of individuals with autism and with typical development has largely been based on data from high functioning individuals. We previously reported a disproportionate contribution of white matter, and in particular of superficial (radiate) white matter, to volume increase in high functioning autistic school-aged boys, and also in age-matched children with developmental language disorder. Here we report complementary results using the same analyses in autistic and non-autistic children with low IQ.

Objectives: To compare volumes of clustered white matter parcellation units in low-IQ children with autistic disorder (LAD) and non-autistic low IQ children (NALIQ) with those from typically developing (TD) and high-functioning autistic disorder (HAD) groups.

Methods: Participants (aged 4.5-11 years) were assessed during preschool years using the Wing Autistic Disorder Interview Checklist and by expert clinicians. HAD children (9M,) had non-verbal IQ ≥ 80 while LAD (13M, 2F) and NALIQ (4M, 6F) had non-verbal IQ < 80; there were 29 TD children (14M/15F). MRI scans were collected during school-age years beginning in 1989 on either a GE 1.5 Signa or Siemens 1.5T scanner. Grey-white segmentation, cortical parcellation, and white matter parcellation of T1-weighted images were performed according to extensively validated methods developed by the Center for Morphometric Analysis, MGH (Meyer, 1999; Makris, 1999). Superficial (radiate) white matter parcellation units were determined by contiguity to gyral-based cortical parcellation units; deep white matter was divided using an algorithm keyed to topographical landmarks pertinent to tract architecture. To perform group comparisons, effect sizes were calculated (mean volume for diagnostic group minus mean volume of control group divided by pooled standard deviation of both groups). Because the volumes were found to be normally distributed, we used univariate regression models to compare each group to controls; sex, age, and diagnostic status were included as covariates. Proportionalized volumes (volume of interest divided by total brain volume) were also analyzed.

Results: We found significant differences in volumes of the superficial (radiate) white matter underlying the frontal ($p=.001$), temporal ($p=.018$), and occipital ($p=.018$) lobes (HAD > LAD > TD). When LAD were

compared to TD using proportionalized volumes, only frontal lobe white matter was significantly larger in the mixed gender analysis (p=.011) but less so for boys only (p=.041). In contrast, we found no significant differences between NALIQ and TD for any white matter regions.

Conclusions: These results suggest that LAD shows a lesser degree of superficial white matter enlargement than HAD. This finding is distinct what is seen in the IQ-matched NALIQ group, which showed no significant differences from TD, suggesting that the effects of autism are distinct from the effects of low IQ. While the number of females in the current study was relatively small, our preliminary results suggest that girls may exhibit disproportionate volumetric changes. This finding underscores the importance of studying females with autistic disorder.

130.013 34 MRI Measurement of Intracranial MPAs (minor physical anomalies) in Autism. G. Fung*[1], Y. Y. Fung[2], C. Cheung[1], Y. You[1], G. M. McAlonan[1] and S. E. Chua[1], (1)*University of Hong Kong*, (2)*Harvard University*

Background:
Autism is a neurodevelopmental disorder in which MPAs (minor physical anomalies, particularly of the face) are thought to occur more frequently. MPAs form during the same time window as brain developmental abnormalities are thought to begin ie in the first trimester of fetal life. MPAs may therefore represent a convenient biomarker for neurodevelopmental anomaly. Traditionally, measurement of MPAs has depended on direct observation of the subject which is bias-laden. Using MRI brain scan, observer bias can be avoided, multi-centre data collection facilitated, and early diagnosis is a realistic goal.

Objectives:
In this study we aimed to establish an MRI measurement protocol of intracranial MPAs in autism and determine the extent to which there are significant differences in intracranial landmarks in autism. Specific preliminary objectives were to measure optical and aural MPAs in children with autism who are age- and gender-matched to healthy children, 'blinded' to subject identity. Longer-term, the objective is to identify a reliable endophenotypic marker is to assist early diagnosis, facilitate early treatment, and enhance future outcome in autism.

Methods:
We conducted a pilot study of MPAs in a sample of children aged 7- 14 with autism (n=25), compared with their age and gender matched controls (n=46). MPA measurements were performed using MRI and blind to group membership. Intra-class coefficient ICC was 0.95.

Results:
We noted the following preliminary results in this sample :
(1) Eye-ear distance : Significant effect of group between autism and control in Left Ear Height (Autism mean: 108; Control mean: 103)(p<.0005) and a near-to-significant difference in Interorbital (Autism mean: 23.36; Control mean: 22.14)(p<.053).
(2) Inter-lens/interorbital distance : Significant positive correlations between Interlens/Interorbital distance and age in controls but not in patient group.
(3) Inter-optic distance : Larger inter-orbital nerve angle in controls (mean: 66 degrees) than autism (mean: 62 degrees)(p<.18) but only the autism group showed significant negative correlation between the inter-optic angle and age (r=-.617,p<.001).

Conclusions:
Measurement of intracranial MPAs using MRI scan is feasible and straightforward. Significant differences between children with autism and typically developing controls can be identified. Smaller inter-optic angle in the autism group is compatible with early developmental changes in brain because the inter-optic angle reduces from wide angle during embryological life to become fixed at around 68 degrees by age 3.

130.014 35 Music, More Than Language, Engages Typical Language Pathways in Autism Spectrum Disorder (ASD). G. Lai*[1], A. Newhouse[1], H. Hancock[1], E. Huang[1], J. Briones[1], E. Mandel[1], H. D. Schneider[1], J. Schwarzenberger[2], W. S. Millar[1] and J. Hirsch[1], (1)*Columbia University*, (2)*University of California Los Angeles*

Background: While music and language are known to recruit overlapping neural systems

in healthy subjects, music processing is often preserved and may even be enhanced in ASD despite impairments in language. This divergence raises the question of how these two systems are organized in ASD.
Objectives: We combined functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) to investigate the functional and structural organization of language and music in ASD and to determine whether music in ASD recruits areas that overlap with typical language pathways.
Methods: Speech and music stimuli (with and without vocals) were presented passively during fMRI to investigate functional neural responses to language and music. fMRI scans were acquired from 12 ASD children (mean age=12.40, SD=4.69) and 12 age-matched controls (mean age=12.06, SD=4.03). DTI scans were acquired from 16 ASD children (mean=11.02, SD=3.72) and 16 age-matched controls (mean age=11.17, SD=4.39). DTI tractography was used to identify white-matter pathways originating from the auditory cortex. To determine if pathways typically associated with language are "miswired" or attenuated in ASD, we compared the termination points and integrity (mean fractional anisotropy (FA)) of isolated tracts between control and ASD groups. To investigate the involvement of specific tracts with language or music function, we used covariation analyses to determine relationships between functional activity and structural integrity.
Results: During speech presentation, ASD children showed decreased activation in Broca's area relative to control children. In contrast, music stimuli (with and without vocals) engaged Broca's area in ASD children corresponding to regions activated for speech in controls. Tractography analyses isolated dorsal and ventral projections originating from the auditory cortex for both ASD and controls. Dorsal pathways correspond to the arcuate fasciculus and ventral pathways to the inferior occipitofrontal fasciculus, both of which are implicated in normal language functioning. These pathways terminated within the same areas in the inferior frontal gyrus for both groups, indicating that these connections were not "miswired" in ASD. However, comparisons of the integrity (mean FA) of the tracts showed an attenuated left dorsal pathway in ASD relative to controls ($p<0.05$). In ASD, Broca's activity during music conditions overlapped with terminations of dorsal pathways and also correlated with the integrity of the attenuated dorsal path. However, during speech stimulation the integrity of the dorsal path did not correlate with activation in Broca's area.
Conclusions: We demonstrate that music engages Broca's area to a greater extent than language in low-functioning ASD children via impaired left dorsal projections typically associated with language processing. Findings of music-specific access to impaired language pathways suggests neurobiological validity for music therapies in children with ASD and may guide the development of future treatments for language disabilities in general.

130.015 36 Neural Activation to Emotional Faces in Adolescents with Autism Spectrum Disorders. S. J. Weng*, M. Carrasco, J. R. Swartz, J. L. Wiggins, N. Kurapati, I. Liberzon, S. Risi, C. Lord and C. S. Monk, *University of Michigan*

Background:

Autism spectrum disorders (ASD) involve a core deficit in social functioning and impairments in the ability to recognize face emotions. Adolescence is a period where the social environment of peers can increase in complexity and others have reported that younger adolescents might have poorer social functioning than adolescents at older ages. Despite these reports, no known study has examined the association of age and amygdala function in ASD during adolescence. Moreover, there have been inconsistencies among studies surrounding the patterns of activation in neural structures involved in face processing. These conflicting reports can be partly explained by group differences in attention allocation to face stimuli. It is therefore crucial that neuroimaging studies on face processing, limit differences in attention between groups. Consequently, we adopted an emotional faces task designed to constrain group differences in attention in a sample of adolescents with ASD and typical controls. We used functional MRI to characterize activation in the amygdala, ventral prefrontal cortex (vPFC), and striatum, three structures

involved in socio-emotional processing, in adolescents with ASD.

Objectives:

The present study had two objectives. The first objective was to examine amygdala, ventral prefrontal and striatal function in ASD and control adolescents during the viewing of socio-emotional stimuli (facial expressions). The second objective was to characterize how amygdala activation relates to age during adolescent development for individuals with ASD.

Methods:

Twenty-two adolescents with ASD and 20 healthy adolescents viewed emotional (happy, fearful, and sad) and neutral faces that were briefly presented (250ms) during functional MRI acquisition. To monitor attention, subjects were asked to identify the gender of each face.

Results:

Relative to healthy adolescents, those with ASD showed greater activation in the amygdala, $t(40)=2.29$, $p=.027$, vPFC, $t(40)=2.65$, $p=.011$ and striatum, $t(40)=3.30$, $p=.002$ to faces relative to baseline (corrected for multiple comparisons). Additionally, in the contrast of sad vs. baseline, adolescents with ASD relative to controls demonstrated greater bilateral activation in the amygdala, vPFC and striatum. To establish statistical significance, we used a small volume correction approach false discovery rate (FDR) $p<.05$ on these regions of interest (ROIs). Moreover, in the ASD group, there was a negative correlation between age and mean activation from the whole bilateral amygdala region of interest ($t(39)=1.94$, $p=.060$); younger adolescents showed greater activation than older adolescents. There were no group differences in accuracy or reaction time in the gender identification task.

Conclusions:

The present findings suggest that neural correlates of ASD may be characterized as heightened activation of socio-emotional structures when group differences in attention are minimized. The heightened activation of the amygdala is most pronounced when youth with ASD are transitioning into adolescence.

130.016 37 Neural Bases of Implicit Learning in Young Adults with Autism Spectrum Disorder. C. L. Klein*[1], L. G. Klinger[1], R. K. Kana[2], B. G. Travers[1], R. Montague[3] and M. R. Klinger[1], (1)*University of Alabama*, (2)*University of Alabama at Birmingham*, (3)*Baylor College of Medicine*

Background:

Klinger and Dawson (2005) and Klinger, Klinger, and Pohlig (2007) hypothesized that the social and language processing impairments in ASD may be caused by a dysfunction in implicit learning. Implicit learning is learning without the conscious effort to learn, and without the conscious knowledge of what was learned (Reber, 1993), and is thought to underlie the development of social intuition (Lieberman, 2000). Additionally, recent studies have pointed to ASD as a neurological disorder, with anatomical, functional, and connectivity differences associated with some of the behavioral differences in individuals with ASD (Courchesne et al., 2001; Just et al., 2004; Sears et al., 1999). It is theorized that the implicit learning impairments seen in persons with ASD may be due to a more general underlying neural dysfunction evidenced by diminished activation in the basal ganglia, specifically the caudate nucleus, and diminished communication between areas of the brain in persons with ASD, specifically the caudate and medial temporal cortex.

Objectives:

This study examined the relationship between implicit learning deficits in individuals with ASD and parents of persons with ASD and associated differences in brain activation.

Methods:

Twelve high-functioning children and adolescents with ASD and 17 age and verbal ability matched typically developing controls, 10 parents of participants with ASD, and 9 parents of typically developing participants

completd this study. The data were collected using a Siemens 3T Allegra fMRI scanner at the Baylor College of Medicine (Houston, TX). While in the scanner, participants viewed twenty-three grammatical letter strings constructed using a Markovian grammar chain (such as "VXVV"). After this initial exposure, participants were told that there were complex rules that defined how the letter strings were formed, and that all the previously seen letter strings followed those rules. During a following test phase, participants saw more letter strings, and were asked to indicate if the strings followed the same rules as those in the exposure phase.

Results:

The grammar effect was calculated as the difference between the proportion of correct responses to grammatical test items and nongrammatical test items. A greater percentage of correct responses to grammatical items during test indicates an automatic learning of the relationships between the letters (the rules), and is taken as evidence of implicit learning. Behaviorally, participants with ASD showed a significantly smaller grammar learning effect (M = +2%) than typically developing participants (M = +16%), $t(27) = 2.51$, $p = .02$. Additionally, parents of participants with ASD showed a smaller grammar effect (M = +4%) than parents of typically developing participants (M = +14%), $t(17) = 2.93$, $p < .01$. Initial functional analyses reveal less activation in the areas of the anterior cingulate and caudate for participants with ASD compared to typically developing participants in contrasts of grammatical versus nongrammatical stimuli, $t(27) = 2.77$, $p < .005$. Similar differences in these areas are also found in the parent groups.

Conclusions:

Diminished activation in the caudate nucleus and cingulate cortex may underlie differences in implicit learning, which are found to be associated with ASD symptomatology.

130.017 38 Reduced Right Frontoinsular Activity in Novelty Detection in Autism. M. A. Ferguson*[1], J. S. Anderson[1], T. J. Druzgal[1], A. L. Froehlich[1], M. B. DuBray[1], J. A. Nielsen[1], E. D. Bigler[2] and J. E. Lainhart[1], (1)*University of Utah*, (2)*Brigham Young University*

Background: A core phenotype of autistic spectrum disorders (ASD) is a detail-oriented cognitive strategy, wherein individuals with autism are attentive to details in their stimulus environment but may not appropriately perceive salient generalizations from available details. Moreover, individuals with autism often exhibit insistence on sameness, wherein they resist changes in their environment or routine.

Objectives: We examined differences in brain activation in the recently described salience detection network between ASD and typically developing (TD) subjects using fMRI and a visual oddball task to assess whether a core deficit exists in autism related to extracting salient information from sensory stimuli.

Methods: Subjects participated in a visual oddball task wherein uniformly colored circles (blue) flashed onto a screen at two second intervals, with 15% of the stimuli displaying a variant color (green). Subjects were instructed to depress a button for each variant stimulus. A total of 40 subjects were tested, 25 ASD, 15 TD. Subjects were all males, group-matched for age and IQ.

Results: TD and ASD populations showed significant activation of the salience detection network including bilateral fronto-insular cortex, anterior cingulate cortex, left posterior temporal, bilateral dorsolateral prefrontal, as well as primary motor cortex. ASD subject data demonstrated a significantly reduced activation of the right fronto-insular cortex when compared to TD activation ($p=0.001$ uncorrected).

Conclusions: The right fronto-insular cortex is hypoactive in ASD subjects relative to TD subjects during detection of novel visual stimuli. This area has been hypothesized to play a pivotal role in the allocation of attentional resources, more specifically, in switching between default-mode and attentional networks. This finding may contribute to a neurological basis for impaired extraction of salient information in individuals with autism.

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130.018 39 Social Mirroring: The Role of Mirror Neurons in Decoding Emotions and Intentions From Actions in Autism. R. K. Kana* and H. D. Deshpande, *University of Alabama at Birmingham*

Background: Although the role of mirror neurons in action understanding and action imitation has been well documented, its specific role in processing social and affective stimuli needs more clarity. Mirror neurons may play a vital role in action understanding, emotion recognition, and attribution of intentions. These functions may be impaired in autism due to deficits in anatomical and functional integrity of mirror neurons. The current study investigated the role of different components of mirror neurons in inferring emotion and intention.

Objectives: The primary goal of this fMRI study is to examine the role of mirror neurons in action recognition in general, and in decoding emotions and intentions from actions in high-functioning individuals with autism.

Methods: Data from two studies are reported here: in the first one, participants were presented with still images of stick figure characters depicting actions in a randomized blocked design format. In the physical task, participants identified the physical action depicted by the stick figure (e.g. *cartwheeling*), and in the *emotion* task, participants identified the emotion or mood depicted by the stick figure (e.g. *sad*). This study has four high-functioning individuals with autism and two control participants (data collection is progressing). In the second study, 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 from given alternatives. This study has 12 high-functioning adolescents with autism and fourteen matched controls. The data acquired from a Siemens 3T Allegra scanner were analyzed using Statistical Parametric Mapping (SPM8).

Results: In study 1, while the control participants showed greater activation in inferior frontal aspect of the mirror neuron system while detecting emotions, participants with autism activated inferior parietal area. In study 2, while intentional causal attribution was associated with greater activation in bilateral temporoparietal junction (TPJ) and inferior frontal gyrus (IFG), participants with autism did not show activation in the inferior frontal cortex. In addition the participants with autism showed reliably weaker functional connectivity between TPJ and IFG.

Conclusions: The findings of these studies indicate the specific role of mirror neurons (especially the anterior components of MNS) in emotional and intentional aspects of action understanding, which has direct implications for core social functions like empathy. In addition, participants with autism seem to show reduced activation and reduced connectivity in anterior areas of the MNS associated with processing intentions and emotions. 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.

130.019 40 Sub-Linear Response in the Autistic Brain to Paired Finger Stimulation. 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: The search for a neural phenotype for autism is ongoing. It is widely accepted that differences in the brains of persons with and without autism are expressed in neural circuitry and are pervasive through much of the brain. An attractive candidate proposed for a neural phenotype is reduced inhibition in the neural circuitry. To test this, an electrophysiological assay of synaptic inhibition is desirable. Objectives: Inhibition levels typically increase

sharply with increase in stimulation level. The tactile stimulation of two neighboring parts of the body as compared to one will elicit a higher level of inhibition, and will reduce the evoked response. More specifically, the reduced inhibition hypothesis predicts that the response to the simultaneous stimulation of two fingers relative to the sum of responses to the stimulation of each finger individually will be larger in autistic than typically developing brains. We tested this prediction with magnetoencephalography (MEG). Methods: We recorded the neural response to passive tactile stimulation of the thumb (D1), index finger (D2), and both fingers combined (D1,D2) of the dominant (right) hand of young adult participants (13 high-functioning persons with autism spectrum disorder or ASDs and 17 typically developing persons or TDs, matched for gender and age) while they remained awake in an eyes-closed supine posture in a 248-sensor MEG scanner. For each participant, the sensor in the contralateral cortex that had the largest evoked response (0-300 ms from stimulus onset) to D1,D2 relative to baseline was automatically selected. We then computed the somatosensory evoked potentials (SEPs) in the chosen sensor to the stimulation of D1 alone, D2 alone, and D1,D2. For each of the two early SEP components, M50 (S1) and M100 (S2), group (ASD, TD) response to D1,D2 was linearly regressed to the sum of the responses to the stimulation of D1 and D2 each, and optimal least-squares slopes (D1,D2 vs. D1+D2) computed. In a complementary analysis, the three sensors that respectively recorded the largest evoked response to D1, D2 and D1,D2 were selected for otherwise identical calculations as before. Results: M50: In comparison to the sum of the responses to individual D1 and D2 stimulation (D1+D2), the response to D1,D2 was significantly sub-linear in ASDs but comparable in TDs; the difference in slopes of the two groups was significant. The complementary analysis also yielded identical results, which contradict the reduced inhibition hypothesis. M100: In ASDs, the response to D1,D2 was comparable to D1+D2; in TDs, the D1,D2 response was significantly sub-linear as compared to D1+D2; the difference in slopes between the two groups was significant. However, the complementary analysis found no such significant difference. Conclusions: The simultaneous stimulation of a pair of neighboring fingers elicited significant decline in the early response and increase in the mid-latency response in autism compared with control young adults. The findings fail to support the idea of reduced inhibition but suggest instead a more complex, evolving dynamical kind of inhibition in the circuits of autistic brains.

130.020 41 The Cingulum Bundle in Developing Children and Adolescents with Autism Spectrum Disorders: A Diffusion Tensor Tractography Study. S. Ameis*[1], C. Rockel[1], L. Soorya[2], E. Hollander[3], J. Fan[2] and E. Anagnostou[4], (1)*The Hospital for Sick Children, University of Toronto*, (2)*Mount Sinai School of Medicine*, (3)*Albert Einstein College of Medicine*, (4)*Bloorview Research Institute, Bloorview Kids Rehab*

Background: In the autism spectrum disorders (ASD), brain overgrowth in early life may drive white matter dysconnectivity. Impaired white matter connectivity within limbic circuitry may contribute to the socio-emotional dysfunction that characterizes ASD. Structural examination of white matter connections can now be achieved using diffusion tensor imaging (DTI), a novel technique that can infer properties of white matter tissue in the living human brain. Preliminary DTI evidence has pointed to structural disturbance within the cingulum bundle, a key limbic white matter tract, in adults with ASD. Objectives: This study aims to examine structural connectivity of the cingulum bundle in developing children and adolescents with ASD, compared to controls, using diffusion tensor tractography. Methods: Diffusion tensor images were acquired for 18 children and adolescents with ASD (age range 7-18 years; mean 12.2 ± 3.1) and 17 age and sex matched healthy controls (age range 8-17; mean 12.6 ± 3.3) on a 3T Siemens Allegra head-dedicated MRI system. Deterministic tractography was performed using a single region of interest approach to reconstruct the cingulum bundle. Average fractional anisotropy, axial diffusivity, radial diffusivity, and mean diffusivity values, were quantified for the right and left cingulum bundle. Independent samples t-tests were performed to determine between-group differences in DTI indices: (1) in the overall

sample of participants, (2) in a sub-group of developing children within the overall sample, and (3) in a sub-group of developing adolescents within the overall sample. We define children as those participants that were under the age of 12 at the time of scanning, and adolescents as participants 12 years of age and older, at the time of DTI scanning. Results: The results of our study show that mean diffusivity is significantly increased in ASD in the left cingulum bundle ($p = .044$), when considering the overall sample of participants. No other differences in the overall sample were found. However, when developing children with ASD were compared to matched controls, mean diffusivity was significantly increased in the ASD group for the left ($p = .004$) and right ($p = .042$) cingulum bundle. Radial diffusivity was also significantly increased for the left ($p = .035$) and right ($p = .049$) cingulum bundles, in developing children with ASD. No other differences were found among the sub-group of developing children. Interestingly, when developing adolescents with ASD were compared to matched controls, no differences in DTI measures were found between groups. Conclusions: Our results suggest potential disruption of the cingulum bundle, in ASD. Exceptionally striking, were findings of altered mean diffusivity and radial diffusivity in the cingulum bundle in developing children with ASD but not in developing adolescents, possibly indicating immaturity of the cingulum bundle that is specific to children with ASD. In particular, significant increases in radial diffusivity in developing children with ASD, potentially indicates impaired myelination of the cingulum bundle during the childhood phase of brain development.

130.021 42 The Neural Basis of Pronoun Selection in Autism. A. Mizuno*[1], Y. Liu[1], D. L. Williams[2], T. A. Keller[1], N. J. Minshew[3] and M. A. Just[1], (1)*Carnegie Mellon University*, (2)*Duquesne University*, (3)*University of Pittsburgh School of Medicine*

Background: Personal pronouns, such as 'I' and 'you,' are unfixed labels which require a mapping to their referent that is contingent who is using them. Atypical production of pronominal expressions has been reported in children with autism (referring themselves with the pronoun "you"), but the underlying neural basis has not been understood, nor has the phenomenon been studied in adults with autism.

Objectives: The aim of the current study was to compare the brain activation pattern and functional connectivity of adults with high functioning autism and controls using fMRI in a perspective-taking task which requires reversing personal pronouns 'I' and 'you' depending on who is referring.

Methods: Participants were 15 adults with high-functioning autism and 15 matched neurotypical adults. In one condition of the perspective-taking task, participants were asked to designate generate a response from either a first- or second-person perspective. In the other condition, they were asked to designate the person who was facing to the object. Both conditions used proper names as an additional control for the use of pronouns. The main condition of interest required participants to reverse a pronoun, such as responding with "I" when asked about "you."

Results: Both groups exhibited similarly distributed brain activations across cortical regions. However, for the pronoun reversal conditions, the group comparison indicated greater activation for the autism group, particularly in the right posterior temporal and the frontal areas. The autism group also showed reliably lower functional connectivity than the control group for the frontal-temporal and frontal-parietal connections in the pronoun reversal condition, as well as significantly increased response time.

Conclusions:

Updating of a referential reference (a deictic expression) constituted a larger challenge for adults with high-functioning autism (whose verbal IQ is within the normal range) than for controls. The findings suggest that diminished frontal-posterior collaboration may be that source of lower performance in producing a perspective shift in autism. The loci of the network may implicate an interaction of three functional networks. In addition to the Theory of Mind network, involving in making an inference of an other's mental state, the Mirror Neuron System may contribute to cognitive mapping

for self-and-other relationships, and executive system may provide the ability to adaptively monitor the appropriate pronominal referent ('I' versus 'you' depending on who is referring). The coordinated activity of the cortical regions in these networks may constitute a "perspective-taking network," and the disruption of the network may explain atypical social communication and pragmatic usage of language in autism.

130.022 43 The Neural Mechanisms Underlying Global and Local Information Processing in High-Functioning Children with Autism. H. M. Wadsworth*[1], S. L. Kumar[2] and R. K. Kana[2], (1)*Department of Psychology, University of Alabama at Birmingham*, (2)*University of Alabama at Birmingham*

Background: A comprehensive account of the nature of information processing in autism should involve explaining both disordered processing as well as intact or superior abilities. Two theories which have sought to explain these patterns are the Weak Central Coherence hypothesis (Frith, 1989) and the Enhanced Perceptual Processing account (Mottron et al., 2006). Both models suggest that the default information processing in typical individuals is global, and that in individuals with autism it is local or detail-oriented. While the default local processing in autism may underlie their difficulties with higher cognitive functions, it may be an advantage in low level visuospatial tasks. The latter is especially the case in visual search tasks where ignoring the global patterns makes it easier to find embedded targets. While the advantage in local level processing is well documented in autism (Happé & Frith, 2006), less is known about the nature of the neural circuitry underpinning this phenomenon.

Objectives: The primary aim of this study was to investigate the neural mechanisms involved in processing global versus local aspects of visual information in high-functioning children with autism.

Methods: Four high-functioning children (age range: 10-15 years) with autism and two typical control participants took part in this fMRI study (data collection is in progress). The stimuli consist of larger geometric shapes made of smaller ones. In the *global* task, participants are asked to identify the bigger picture whereas in the *local* task, they are asked to identify the parts that make up the bigger picture. The stimuli were presented in an event-related format. The fMRI data collected from the Siemens 3.0T Allegra scanner at the UAB Civitan International Research Center was analyzed using SPM8.

Results: The results indicate that while the control participants activated more in local processing task, the participants with autism showed more activation in global processing. More The control participants showed greater activation in the posterior parietal regions in the local task relative to the global task. Participants with autism, on the other hand, showed greater levels of activation in posterior parietal, in middle occipital, and in the dorsolateral prefrontal cortex in the global task. The results reported here are preliminary at this point, and reveals just a trend.

Conclusions: Greater activation in autism in frontal and occipital regions in global processing might indicate their relative difficulty in seeing the global pattern. Whereas, the increase in activation in parietal regions in control participants while processing local detail may suggest their increased effort to spot the local details in the geometric figures. Overall, the relative difficulty faced by controls and autistics may be different for different conditions since the default information processing style in each of these groups is different.

130.023 44 Understanding Sarcasm in a Speaker's Remark: An fMRI Study in Children and Adolescents with ASD. N. Colich*[1], J. D. Rudie[1], A. T. Wang[2] and M. Dapretto[1], (1)*University of California, Los Angeles*, (2)*Mount Sinai School of Medicine*

Background: Social communication and language deficits are core to autism spectrum disorders (ASD). In particular, individuals with ASD show consistent impairment in processing pragmatic language when attention to multiple social cues (e.g. facial expression, tone of voice) is often needed to infer a speaker's communicative intent. Differing activation patterns have been

reported in individuals with ASD during pragmatic language tasks (Knaus et al., 2007; Tesink et al., 2009). In these studies, individuals with ASD showed stronger activity in primary language and secondary language association areas as well as more bilateral activation profiles in these regions than neurotypical controls. We also observed hyperactivity in right inferior frontal gyrus as well as in bilateral temporal regions when ASD children relied upon event knowledge or prosodic cues to ascertain whether a speaker's comment was sincere or sarcastic, likely reflecting more effortful processing (Wang et al., 2006).

Objectives: Here we sought to build upon our prior work examining how facial affect and prosodic cues aid in the ability to infer a speaker's communicative intent (Wang et al., 2007). specifically, we examined, both at behavioral and neural levels, whether children and adolescents with ASD differ from typically developing (TD) children and adolescents in their processing of sincere versus sarcastic remarks.

Methods: While undergoing fMRI, a sample of ASD children and adolescents and matched TD controls viewed cartoon drawings of characters in different everyday situations while listening to short scenarios. Each vignette ended with either a sincere or sarcastic comment made by one of the characters. Eighteen scenarios were presented, each lasting fifteen seconds (interspersed with eight blocks of rest). As in the prior study we conducted using the same stimuli (Wang et al., 2007), participants decided whether or not a speaker meant what they said. However, unlike our prior study where we manipulated task instructions to direct the subjects' attention to different social cues, all participants were given neutral instructions to simply pay attention. Here we sought to directly compare activity associated with processing sarcastic versus sincere remarks both within and between groups.

Results: Children and adolescents with ASD and their matched TD controls performed the task of determining whether a speaker's remark was sincere or sarcastic equally well, showing longer response times for scenarios ending with sarcastic remarks. Both groups also showed significant activity in canonical language areas, as well as visual cortices for both types of scenarios (sincere versus sarcastic endings). However, only the TD group showed significantly greater activity in Broca's Area for sarcastic compared to sincere remarks. Also, while the TD group showed strong left lateralized responses in both frontal and temporal language areas, the ASD group showed a more bilateral pattern of activity within language networks.

Conclusions: The present findings contribute to a growing body of evidence suggesting decreased left lateralization in individuals with ASD during language processing tasks. At least for high-functioning individuals with ASD, the increased activity in right hemisphere homologues of canonical language areas in the left hemisphere may reflect compensatory mechanisms supporting normative behavioral performance.

130.024 45 Volumetric Brain Differences in Adults with Autistic Spectrum Disorder - the Result of Two Distinct Neuropathological Mechanisms?. C. M. Murphy*[1], C. Ecker[2], P. Johnston[1], E. Daly[3], D. Robertson[4], D. Murphy[3] and M. R. C. AIMS Consortium[5], (1)*King's College London, Institute of Psychiatry*, (2)*Institute of Psychiatry, King's College London*, (3)*Institute of Psychiatry*, (4)*Institute of Psychiatry, King's College*, (5)*Institute of Psychiatry, London; University of Oxford; University of Cambridge, UK*

Background: Previous neuroimaging studies investigating brain anatomy in Autism Spectrum Disorder (ASD) have typically examined volumetric measures in either individual brain regions or in the whole brain (e.g. voxel-based approaches). However, cortical volume (CV) is the product of cortical thickness (CT) and surface area (SA). Therefore, it is unknown whether previous reports of differences in CV of individuals with ASD are driven by differences in CT, SA or both. This is potentially highly significant as recent evidence suggests that CT and SA may have distinct genetic determinants. CV may therefore represent at least two distinct sources of genetic effects. The region-specific influence of CT and SA on CV has, however, not yet been explored.

Objectives: This first aim of this study was to investigate volumetric brain differences in

adults with ASD by exploring CT, SA and CV in isolation. Secondly, we aimed to examine the relationship between these volumetric measures (i.e. degree of spatial overlap) in order to elucidate their potential multi-factorial aetiology.

Methods: Structural MRI data was collected on 84 well-characterized adult males with ASD (right-handed, mean age = 26 yrs, mean FSIQ = 110), and 84 age/IQ matched healthy right-handed male controls. Subjects were recruited with the support of the MRC AIMS (Autism Imaging Multi-centre Study) program. All individuals with ASD were diagnosed using ADI-R, ADOS, and ICD-10 research criteria. For each participant, a set of three morphological parameters (CV, CT, SA) was obtained at each spatial location on the cortical surface (i.e. vertex) using FreeSurfer software (http://surfer.nmr.mgh.harvard.edu). Initially, a vertex-based approach employing the general linear model (GLM) was used to examine differences in individual volumetric measures between groups. Subsequently, we examined the degree of spatial overlap between maps representing significant differences for each morphometric feature.

Results: Overall, individuals with ASD had significantly larger values in all three parameters (CV, CT and SA). Furthermore, there was little spatial overlap between maps for CT and SA, suggesting an independent and region specific effect of CT and SA, particularly in frontotemporal regions. Overall, the map of CV was a linear combination between CT and SA, with region-specific parameter weights.

Conclusions: The data suggests that volumetric brain differences in adults with ASD are the result of region-dependent variations in two distinct volumetric measures, CT and SA. These two morphological parameters most likely have distinct genetic and neuropathological mechanisms and should therefore be explored independently. We suggest that the spatial pattern presented here may reflect the multifactorial aetiology of ASD, and that future research should include examination of both CT and SA to explore the specific genetic and neuropathological underpinnings of ASD.

130.025 46 fMRI Correlates of Relational Memory Difficulties in Autism Spectrum Disorder. S. B. Gaigg*[1], D. M. Bowler[2], C. Ecker[3], B. Calvo-Merino[1] and D. G. Murphy[3], (1)*City University London*, (2)*City University, London*, (3)*Institute of Psychiatry, King's College London*

Background: It is now well established that individuals from across the Autism Spectrum exhibit a rather unique pattern of memory strengths and weaknesses. Their free recall performance is usually attenuated, they experience difficulties in remembering the personally experienced past (i.e. episodic memory) and they tend not to use organisational strategies efficiently to facilitate memory. By contrast, they tend to experience few problems on tests of recognition or cued recall and their memory for factual knowledge (i.e. semantic memory) is generally preserved and often even enhanced. Although the neural basis of this memory profile remains largely unknown, it has for long been speculated that atypicalities in the functioning of the Hippocampus and areas of the Frontal Lobes may be responsible.

Objectives: To assess, for the first time, the functional integrity of Medial Temporal and Frontal Lobe memory systems in ASD through the use of an established fMRI paradigm.

Methods: Following a paradigm developed by Addis & McAndrews (2006), we asked participants to learn a series of word triads in a 3T scanner. Word-triads were presented for 6 seconds (with 4-8s jittered intervals) and consisted of a category name and two nouns. Either none, one or both of these nouns were examples of the category name and participants were required to indicate the relevant number of category links whilst trying to remember the triads. Immediately after the encoding scan, participants completed a two-alternative forced choice recognition test in a quiet room. In this test, studied triads were presented alongside new triads that included a novel noun, and participants indicated whether they clearly 'remembered', simply 'knew' or 'guessed' which of the two triads they had seen during the earlier scan.

Results: So far, 10 ASD and 10 age and IQ matched typically developed individuals have been tested (12-16 per group are planned). Behavioural results, so far, indicate equivalent forced choice recognition accuracy in the two groups although reports of 'remembering' are significantly attenuated and 'guessing' responses augmented in the ASD group. Preliminary analyses of the fMRI data confirm Addis & McAndrew's (2006) observation of successful encoding effects in the Hippocampus and Inferior Frontal Gyrus (IFG) and although data collection is ongoing the results also suggest that these effects may be attenuated in the ASD group (particularly in the Hippocampus). Our final analysis will assess the extent to which successful encoding effects in the Hippocampus and IFG (and potential group differences thereof) are modulated by the number of category-links in encoded word-triads and by the subjective reports of 'remembering', 'knowing' and 'guessing' of participants during the recognition test. Based on the available literature, we predict atypicalities particularly in hippocampal function in ASD but also in the connectivity between the Hippocampus and Inferior Frontal Lobe.

Conclusions: We will discuss our observations in the context of current cognitive and neurobiological theories of memory in ASD, with a particular focus on the notion that Medial Temporal Lobe dysfunction may constitute a widespread facet of the neuropathology underlying this disorder.

130.026 47 Neural Bases of Inferring Emotional and Perceptual Information From Body Postures in High-Functioning Children with Autism. S. L. Kumar*, M. R. Pennick, E. M. Griffith and R. K. Kana, *University of Alabama at Birmingham*

Background: Information processing in autism is characterized by difficulties in higher cognitive functioning as well as enhancement in low-level visuospatial processing. While a weakness in central coherence may be a debilitating factor in social interaction and social cognition (where the global meaning is usually preferred), it can be an advantage in visuospatial processing, especially in visual search (where ignoring global patterns makes it easier to find embedded targets). Although there have been several neuroimaging studies examining higher cognitive functions in autism, there have been only a few fMRI studies investigating visuospatial processing. This functional MRI study examined the neural bases of visual and social cognition in children with autism.

Objectives: The main focus of this study was to examine the neural bases of visuospatial processing (an area of strength), and social cognition (an area of difficulty) in conjunction in children with autism.

Methods: The stimuli consisted of a series of stick figure characters, made of several geometrical shapes, depicting certain actions. While the participants judged the emotional state of the character in one experimental condition (emotion), they detected the presence of a target geometrical shape in the figure in the other condition (feature). Four high-functioning children (age range: 10-15 years) with autism, and two typical control participants took part in this fMRI study (data collection is in progress). The fMRI data collected from the Siemens 3.0T Allegra scanner at the UAB Civitan International Research Center was analyzed using SPM8.

Results: The preliminary analysis of the functional MRI data revealed a trend in which the participants with autism seem to recruit the same set of regions in both tasks. However, the control participants recruited regions associated with action and emotion processing (the amygdala, left insula, and the orbitofrontal cortex) in the emotion task relative to the feature task. The participants with autism recruited similar areas, most of them associated with visuospatial processing (e.g., superior parietal lobule) in both experimental tasks.

Conclusions: The absence of a difference in activation in participants with autism between the emotion and feature tasks may suggest the use of a common strategy for accomplishing both visuospatial and emotion processing. Control participants, on the other hand, seem to have a different pattern of recruitment for these tasks. Overall, these preliminary findings suggest a difference in the neural route through which children with

autism accomplish reading emotions from body postures.

130.027 48 Neuro-Functional Networks Supporting Cross-Sensory Emotion Processing in Teens with Autism Spectrum Disorder. K. A. Doyle*, J. Goldberg, P. Szatmari and G. Hall, *McMaster University*

Background: The processing of social information involves a network of distributed brain regions, many of which appear to be aberrant in ASD. Because information from the different senses is typically complimentary, cross-sensory integration of sensory input provides information about the environment that is unobtainable from any one sense in isolation (O'Hare, 1991). It has been proposed that the organizational structure of the brain in ASD follows a pattern of high local connectivity and low long-range connectivity (Just et al., 2004). Failure to integrate multi-sensory social-emotional information could be expected to result in considerable social deficit. Objectives: To investigate the neural circuitry underlying the processing of socially important, affective multimodal cues in high functioning teenage boys with ASD. We focused on an age where maturational changes in cortical myelination support faster, superior integration, in order to identify newly established brain networks that support the processing of multimodal cues and detail functional regions that distinguish teens with ASD from healthy controls. Methods: High functioning teenage males with autism (13-19 years old) and matched male controls participated. Stimuli were constructed from simple emotions (happy, sad, angry and no emotion). In advance of the functional Magnetic Resonance Imaging scan, a behavioural test was conducted to establish individual face perception thresholds for visual facial emotion stimuli. Subsequently thresholded stimuli were used in a cross-sensory task that involved the matching of an emotion face and voice combination to an emotion label. This design permitted us to test how successful integration can facilitate the processing of emotion in difficult to detect situations. In the scanner, visual stimuli were projected onto an overhead visor and auditory stimuli were presented using MRI compatible sound isolation headphones. Responses were made via a hand-held response pad. Functional BOLD imaging was done using a gradient-echo planar imaging (EPI) sequence, with 36 axial contiguous slices (3-mm thick, no skip) encompassing the entire cerebrum (repetition time/ echo time [TR/TE] 2500/35 milliseconds, flip angle=90 degrees, field of view [FOV] 24 cm, matrix 64 x 64). An event related design was employed where emotion trials were presented with variable jittered interstimulus intervals. Results: Data analysis is underway, however, preliminary between group results identify greater recruitment of the insula, superior temporal and parietal cortices in typically developing teens. In contrast, teens with autism show greater recruitment of the superior prefrontal cortex. Conclusions: These results suggest, when typically developing teens are processing cross-sensory emotion cues they recruit areas involved in face and emotion processing, integration of emotional state and physical responses to arousal and social relevance. In comparison, teens with autism show greater engagement of regions associated with working memory and problem solving.

130.028 49 No Longer Massively Univariate: Quantifying Individual and Group Differences in White Matter Microstructure in Autism Vs. Typical Development. J. Scott*[1], J. E. Lainhart[2], M. Lazar[3], A. L. Alexander[4] and N. Lange[5], (1)*U.S. Food and Drug Administration*, (2)*University of Utah*, (3)*New York University School of Medicine*, (4)*University of Wisconsin*, (5)*Harvard University*

Background: Massively univariate voxel-based analysis unnecessarily limits the utility of diffusion tensor imaging to probe white matter microstructure (WMM) in autism. This method tests for a regional group difference first at a single voxel by ignoring all of its neighbors and then combines voxel-based statistics by simple averaging, ignoring spatial correlation and heterogeneity within subjects and between groups. Such disregard can increase false positive and false negative rates, yielding misleading conclusions regarding the fiber organization of the autistic brain.

Objectives: We sought to determine if and how spatial correlation and variance heterogeneity affect estimated individual and

group differences in corpus callosum WMM in autism.

Methods: We examined the voxel-wise mean and variance of fractional anisotropy (FA) and a novel full tensor measure (MV) in the genu and splenium in a sample of N=80 children and young adults (mean age 14.1 years) with ASD and N=40 typically-developing matched controls (mean age 15.5 years). We compared results from models that assumed intra-subject, inter-subject and inter-group variances to be equal or unequal across subjects and between groups. All models accounted for inter-voxel correlation in each subject.

Results: After accounting for group mean differences, we found that inter-subject variance was significantly high in splenium FA (_2=6.0, df=1, p=0.01 and genu MV (_2=17.4, df=6, p<0.01). Second, we found that autism subjects had significantly greater intra-subject FA variance in these regions (_2=16.7, df=1, p<0.0001; _2= 44.2, df=1, p<0.0001) and significantly greater MV variance as well (_2= 263.2, df=6, p<0.0001; _2=117.2, df=6, p<0.0001) in autism. Last, we observed substantially more coherent clustering of FA, MV and their group differences by accounting for inter-voxel correlation compared to those derived by a massively univariate approach.

Conclusions: Our results suggest that WMM in the genu and splenium of the adolescent male with high-functioning autism is more heterogeneous than that of his typically developing counterpart. There is a high likelihood of decreased consistency of directional diffusion coherence in the corpus callosum of an individual with autism and between individuals with autism, perhaps due to genetic and/or epigenetic dysregulation in brain development. In addition to the first-order (mean) decreases in directional diffusion coherence between groups reported previously, these second-order (variance) deviations suggest that a variety of disruptions of fiber organization may affect the quality of inter-hemispheric information transfer and perhaps language and social functioning. Our novel method demonstrated that (1) when testing for group differences in WMM, particularly in the corpus callosum and possibly other brain regions, one should acknowledge the correlation and increased variance of voxel-wise tensor measures in autism relative to measures in healthy populations; and (2) the detection of a regional group difference at a single voxel that acknowledges regional voxel-wise correlations outperforms widely-used approaches that ignore them.

130.029 50 Organizational Effects of Fetal Testosterone On Human Corpus Callosum Size and Asymmetry: Potential Implications for Autism Spectrum Conditions. L. R. Chura*[1], M. V. Lombardo[2], E. Ashwin[3], B. Auyeung[4], B. Chakrabarti[2], E. Bullmore[5], R. Holt[1], M. D. Spencer[1] and S. Baron-Cohen[4], (1)*Autism Research Centre, Cambridge University*, (2)*Autism Research Centre, Department of Psychiatry, University of Cambridge*, (3)*Autism Research Centre, University of Cambridge*, (4)*University of Cambridge*, (5)*Brain Mapping Unit, Department of Psychiatry, University of Cambridge*

Background: Previous theory and research in animals has identified the critical role that foetal testosterone (FT) plays in organizing sexually dimorphic brain development. Foetal exposure to elevated levels of testosterone has been implicated as a possible contributory influence in the development of to Autism Spectrum Conditions (ASC) (Baron-Cohen et al., 2004). FT is positively correlated to number of autistic traits in typically developing children (Auyeung et al, 2009) and SNPs in genes related to sex steroid hormones show association with autistic traits and Asperger Syndrome (Chakrabarti et al, 2009). However there are no studies in humans directly testing the organizational effects of FT on structural brain development. Objectives: Here we selected the corpus callosum and neural assymetry because both show sexual dimorphism in the typical brain (Hines, 2003). Aim To investigate the effects of FT on corpus callosum size and asymmetry. Methods: High-resolution structural magnetic resonance images (MRI) of the brain were obtained on n = 28 8—11-year-old boys whose exposure to FT had been measured in utero via amniocentesis. Results: Although there was no relationship between FT and midsaggital corpus callosum size, increasing FT was significantly related to increasing

rightward asymmetry (e.g., Right > Left) of a posterior subsection of the callosum, the isthmus (Chura et al., 2009). Conclusions: Organizational effects of FT on callosal asymmetry may also shape sexual dimorphism in functional and structural brain development, cognition, and behaviour. Ongoing work employing the same technique for callosal measurements is investigating samples of individuals with ASC, their unaffected siblings and unrelated typically developing controls.

130.030 51 Prototype LEARNING IN AUTISM Spectrum Disorders. B. G. Travers*[1], M. Wheelock[1], C. L. Klein[1], L. G. Klinger[1], R. Montague[2] and M. R. Klinger[1], (1)*University of Alabama*, (2)*Baylor College of Medicine*

Background:

Klinger and colleagues (Klinger & Dawson, 2005; Klinger, Klinger, & Pohlig, 2007) proposed that individuals with ASD have impaired categorization abilities that lead to difficulties in learning and generalization. Typically, when individuals encounter natural categories that have "fuzzy" boundaries, they abstract a best example (or prototype) that represents that category and use this prototype to generalize to new experiences. Specifically, prototype formation is a type of implicit learning in which statistical averages are abstracted from complex stimuli (e.g., if you try to think of the most representative table, it will probably be a statistical average of all the tables you have ever seen). Behavioral studies have suggested that prototype formation may be impaired in individuals with ASD (e.g., Gastgeb, Dundas, Minshew, & Strauss, 2009; Gastgeb, Strauss, & Minshew, 2006; Klinger & Dawson; Klinger, Klinger, & Pohlig). In this study, fMRI technology was used to investigate the cognitive and neural responses to prototypes in persons with ASD compared to typically developing individuals.

Objectives:

The present study sought to examine whether different patterns of fMRI-measured brain activation occurred for prototype category learning in persons with ASD compared to typically developing individuals.

Methods:

Fourteen high-functioning children and adolescents with ASD and 14 age and verbal raw matched neurotypical controls participated in this study. The data were collected using a Siemens 3T Allegra fMRI scanner at the Baylor College of Medicine (Houston, TX). In the scanner, participants passively viewed eight drawings of an imaginary animal, whose features varied in size along a scale from one to five. After the viewing, a test phase occurred, in which participants saw more drawings of that animal and were asked to indicate via button press if they had seen that drawing before. The drawings in the test phase included previously seen animals, new animals, and prototype animals (e.g., animals whose features were the mathematical average of the previously seen animals). This procedure was repeated across four sets of imaginary animals.

Results:

The prototype effect was calculated as the proportion of prototype animals selected as "previously seen" minus the proportion of new animals selected as previously seen. This provided of evidence of whether participants viewed the prototype as familiar, suggesting that they had formed this mental representation. Behavioral results showed that typically developing participants showed a larger prototype effect (M=.48) than ASD participants (M=.24). Both groups showed significant prototype learning (TD $t(13) = 7.79$, $p < .001$; ASD $t(13) = 2.92$, $p = .01$). However, the ASD participants showed significantly less prototype learning than typically developing controls, $F(1, 26) = 5.25$, $p = .03$. All imaging data have been collected and preprocessed, but fMRI individual and group contrast analyses are ongoing.

Conclusions:

Behaviorally, prototype learning may be less robust in persons with ASD. We hypothesize that, at the neural level, individuals with ASD may show less activation in areas typically associated with implicit learning (e.g., basal ganglia) during prototype formation tasks. fMRI data analysis will be forthcoming in the next month.

130.031 52 Reduced White Matter Integrity of the Default Mode Network in Children with Autism Spectrum Disorder. D. K. Shukla*[1], B. Keehn[2] and R. A. Müller[1], (1)*San Diego State University*, (2)*San Diego State University / University of California, San Diego*

Background: A few previous studies have suggested reduced functional connectivity within default mode network in children and adults with autism spectrum disorder (ASD), possibly related to impaired self-reference and social cognition. However, anatomical connectivity studies of the default mode network are lacking in ASD.

Objectives: To examine the white matter integrity within the default mode network in children with ASD using probabilistic white matter fiber tracking.

Methods: Diffusion tensor imaging (DTI) data of 19 children with ASD and 17 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. T1-weighted data were also acquired using spoiled gradient-recalled (SPGR) echo pulse sequence. Diffusion tensor tractography was performed using a probabilistic tracking approach from three regions of interest (ROIs) in both hemispheres, identified using Freesurfer parcellation of T1-weighted images: posterior cingulate gyrus (PCC), medial prefrontal cortex (MFC), middle temporal lobe (MTL), and inferior parietal lobe (IPL). Shared tracts for seed pairs (PCC-MFC, PCC-MTL, MFC-IPL) were obtained from single-seed tractography for each ROI and hemisphere. Fractional anisotropy (FA) was calculated to determine the white matter integrity of shared tracts.

Results: Significant group differences were detected for FA of all three region pairs in both hemispheres. No significant group differences in hemispheric asymmetry were found. In the ASD group, FA was significantly lower for the left hemisphere (lh) PCC-MFC (0.27+/-0.008 [mean+/-sem] for ASD vs. 0.29+/-0.005 for TD, p=0.04); lh PCC-MTL (0.28+/-0.007 for ASD vs. 0.30+/-0.005 for TD, p=0.03); lh MFC-IPL (0.27+/-0.007 for ASD vs. 0.29+/-0.005 for TD, p=0.05). Similar results were also found for the right hemisphere (rh): rh PCC-MFC (0.29+/-0.007 for ASD vs. 0.31+/-0.004 for TD, p=0.01); rh PCC-MTL (0.29+/-0.007 for ASD vs. 0.31+/-0.005 for TD, p=0.03); rh MFC-IPL (0.28+/-0.007 for ASD vs. 0.30+/-0.004 for TD, p=0.03).

Conclusions: These results suggest impairment of white matter tracts among regions of the default mode network in children with ASD, consistent with atypical functional connectivity of this network, as previously reported. Convergent functional and anatomical connectivity findings indicate that the default mode network may be one of (potentially many) atypically organized brain networks contributing to sociocommunicative impairments in ASD.

130.032 53 Sex-Related Brain Differences and Heterogeneity in the Autism Spectrum. K. A. Loveland*[1], L. Cirilli[2], D. A. Pearson[1] and J. Bachevalier[2], (1)*University of Texas Medical School at Houston*, (2)*Emory University*

Background: Autism is a neurodevelopmental disorder characterized by social-cognitive differences affecting many areas of functioning. Autism is also highly heterogeneous with a complex genetic and neural basis. Medial temporal lobe structures including amygdala and hippocampus have been identified by imaging, histopathologic, neurologic and neuropsychologic studies as among those affected in Autism Spectrum Disorders (ASD). Research has also linked these structures to the central social cognitive differences of ASD. However, they have not been well studied with respect to other characteristics, such as sex, IQ and changes with age, that may help to explain some of the heterogeneity in ASD.

Objectives: As part of a study of fronto-limbic brain structures and development in ASD, we collected structural Magnetic Resonance Imaging on children and adolescents aged 7 – 18 with (n=58; 49 males) and without (n=52; 38 males) ASD. Regions of Interest (ROIs) for the present study included amygdala, hippocampus, and regions of the corpus callosum, along with anterior

commissure length (AC), Total Brain Volume and Total Brain Surface Area. We examined differences between the two groups in volumes of medial temporal lobe structures, as well as other non-MTL structures and also whether any differences in MTL structure volumes were related to participants' sex, chronological age (CA), verbal or nonverbal IQ (VIQ, NVIQ).

Methods: Participants were grouped using ADI-R and ADOS and stratified by age and IQ. sMRI was collected using a GE 1.5T MR scanner with a thin-slice (0.7 mm) T1-weighted 3D SPGR brain (temporal lobe) sequence. ROIs were traced and volumes calculated using ImageJ software (NIH). All ROI dependent measures except Total Brain Volume with and without ventricles were expressed as a ratio of ROI volume to Total Brain Volume. Group differences were examined using ANCOVA with sex, CA, VIQ and NVIQ as covariates.

Results: Total brain volume differed by sex, $F(1,103)=10.67$, $p=.001$, but not by diagnostic group, CA or IQ. With effects of CA, VIQ and NVIQ controlled, both right and left amygdala volumes for ASD females were higher than those of males, whereas volumes for non-ASD females were lower than those of males [Group x Sex: $F(1,103)=8.39$, $p=.005$]. Total brain surface area of females was also greater than that of males within the ASD group, but this difference was not present in the non-ASD group [Group x Sex, $F(1,103)= 7.26$, $p=.008$]. A statistically significant difference in volume between the ASD and non-ASD groups was found in left but not right hippocampus. In both groups, amygdala and hippocampus volumes (bilaterally) and regions of the posterior corpus callosum were positively associated with CA, whereas total brain surface area, total brain volume, and anterior corpus callosum were not. Bilaterally, hippocampus volumes were positively associated with NVIQ, whereas amygdala volumes were not associated with VIQ or NVIQ.

Conclusions: Males and females with ASD may differ in brain structures in ways not characteristic of similar persons without ASD. Sex-related differences in brain development deserve further exploration in ASD because they may reveal sources of heterogeneity of developmental course and also have implications for treatments.

130.033 54 Structural Abnormalities in School-Aged Children with High Functioning Autism Using Voxel-Based Morphometry.

D. Shook*[1], B. Yerys[2], A. M. Bollich[3], J. James[3], W. D. Gaillard[3], L. Kenworthy[3] and C. J. Vaidya[1], (1)*Georgetown University*, (2)*Children's National Medical Center, George Washington University*, (3)*Children's National Medical Center*

Background:

Previous research on structural abnormalities in Autism Spectrum Disorders (ASD) has largely focused on low-functioning or a broad spectrum of high- and low-functioning adult and adolescent populations. These studies have found reduced temporal, fusiform, and cerebellar grey matter and increases in frontal grey matter in ASD relative to control subjects. One study with school-aged high-functioning children showed increases in prefrontal, supramarginal and post central gyri with a reduction in the parahipppcampal gyrus in ASD relative to control subjects.

Objectives:

To examine differences in gray matter density between high-functioning 7-13 year old ASD children and IQ-matched typically developing controls (TD).

Methods:

15 school-aged TD children and 15 children with ASD matched on age, IQ and gender-ratio (TD: FSIQ = 119, age = 10.4 years, 15 male; ASD: FSIQ = 121, age = 10.2 years, 11 male) were recruited for research studies conducted at Georgetown University. Structural images (MPRAGE) were collected for each subject and processed in SPM8 using the method for optimized voxel based morphometry (VBM). Two-Group t-tests were run between TD and ASD.

Results:

Children with ASD showed reduced grey matter in the right fusiform and left superior temporal gyrus ($p<0.001$, $k=50$). Further, they showed greater grey matter in the right

middle temporal and right middle fusiform gyrus. These abnormalities did not correlate with IQ or ASD symptoms as measured by the Social Responsiveness Scale, ADI or ADOS.

Conclusions:

Our findings converge with prior VBM studies of adults and low-functioning children/adolescents by showing reduced gray matter concentration in regions critical for processing social information. The consistency of differences in gray matter in the fusiform and temporal regions across studies suggests that changes to these regions are independent of age and IQ.

130.034 55 The Neural Correlates of Gaze Perception in Adolescents with Autism Spectrum Disorder (ASD). E. Redcay*[1], J. Cloutier[1], T. Meagher[1], D. R. O'Young[1], B. Joseph[2], P. L. Mavros[1], V. Vogel-Farley[3], J. M. Moran[1], H. Tager-Flusberg[2], C. A. Nelson[3] and J. D. E. Gabrieli[1], (1)*MIT*, (2)*Boston University*, (3)*Children's Hospital Boston*

Background: Faces convey a wealth of nonverbal communicative information. For example, eye gaze shifts can indicate not only the direction of another person's attention but also their intentions and preferences. Behavioral research suggests individuals with autism spectrum disorders (ASD) might be impaired at using such eye gaze shifts to infer another's intention. Despite much research on face processing in ASD, the neural bases underlying gaze perception remain unknown.

Objectives: The current study aimed to identify the neural substrates underlying gaze perception in ASD.

Methods: Functional MRI data were collected from typically developing and ASD adolescents during presentation of neutral faces with either direct or averted eye gaze. Participants were all male and between 14 to 20 years of age. Eye-tracking data was also collected in a separate session to ensure that participants were looking at the eye region of the face and to examine whether gaze direction in the stimulus affected patterns of gaze behavior in participants.

Results: When comparing faces with averted gaze to faces with direct gaze, typical individuals showed activity within the STS, an area important for interpreting intentions from biological motion or implied motion, as well, as the temporal parietal junction (TPJ), which is involved in reasoning about the content of another person's mind. The ASD group, however, did not show differences in either of these social-cognitive areas. Rather, differences between conditions were localized to posterior cortical areas.

Conclusions: These data reveal impairments in the neural bases of gaze perception in adolescents with ASD.

130.035 56 Visuo-Spatial Function Pertaining to the Parietal Region Compared to Verbal Function within the Autism Spectrum. A. Cariello*[1], E. Bigler[1], N. Lange[2], A. L. Alexander[3], A. Froehlich[1], T. Abildskov[4], M. B. DuBray[1] and J. E. Lainhart[1], (1)*University of Utah*, (2)*Harvard University*, (3)*University of Wisconsin*, (4)*Brigham Young University*

Background: Although visuo-spatial function and verbal function are two separate parts of cognition, they are frequently used concurrently when language is used to make reference to spatial objects. The atypical processing of low-level visuo-spatial function and verbal function found in autism has lead researchers to study the interaction between the two. It has been suggested that atypical neural connectivity may account for visuo-spatial processing abnormalities in autism. Objectives: Our goal was to understand more about visuo-spatial processing in autism relative to typical development in these three ways. First, we looked at the discrepancies between visuo-spatial function and verbal IQ between the two groups. Second, in the brain volume and cortical thickness of the parietal regions of autistic brains compared to controls. Finally, we looked at the correlation between brain structures and visuo-spatial function. Methods: 3T MRI T1-weighted images were obtained from 20 high functioning autistic adult males (mean age= 22.8) group matched by age and head circumference to 19 typically developing control male adults (mean age=22.0). A diagnosis of autism was obtained using the ADI and the ADOS. Visuo-spatial function was measured by using the WASI Matrix

Reasoning subtest and the Test of Memory and Learning Abstract Memory subtest. Verbal function was measured by using Verbal IQ of the WASI. Parietal regional brain volumes and cortical thickness were extracted using FreeSurfer software. The comparison was done by two sample t-test, ANOVA and linear regression. Results: While controlling for age, significant autism-control differences between verbal function and visuo-spatial function were found (p range= .003-.006). Significantly decreased cortical thickness was found in the autism group relative to controls in the following parietal subregions: inferior parietal (p= .007), parietal inferior angular (p = .041) and precuneus (p = .021). Significant positive correlations were found between measures of visuo-spatial function and cuneus and parietal regions in the autism group only (p ranges = .456 to .596). Within the controls, negative correlations were found between the same brain measures and visuo-spatial tests (p ranges = -.475 to -.645). Conclusions: We have found statistically significant differences between groups in visuo-spatial function compared to verbal function. The differences found in the cortical thickness of the parietal lobe may indicate abnormal cortical development in individuals with autism. In brain regions found to be important in visuo-spatial function individuals with autism may benefit from increased cortical thickness whereas this relationship may not found within controls.

130.036 57 White Matter Abnormalities in Autism Spectrum Disorders: Evidence of Abnormal Neural Connectivity. R. J. Jou*, N. Mateljevic, C. M. Hudac and K. A. Pelphrey, *Yale University*

Background: Advances in anatomical and functional imaging techniques studying brain-behavior relationships, and the application of these technologies to the study of autism spectrum disorders (ASDs), has resulted in substantial evidence attributing both core and secondary symptoms to abnormalities in brain connectivity. There is preliminary evidence from structural MRI, functional MRI, and diffusion tensor imaging suggesting that the brain phenotype in ASD includes a generalized overabundance of short-range connections (i.e. U-fibers connecting adjacent gyri) with deficiencies of long-range connections (i.e. association fibers connecting different lobes).

Objectives: This study examined structural abnormalities in white matter using structural MRI and diffusion tensor imaging to test the hypothesis that ASDs are characterized by generalized overabundance of short-range connections with deficiencies of long-range connections.

Methods: Subjects included 15 boys with ASD (mean age = 10.5 ±3.7 years) and eight gender- and age-matched controls (mean age = 11.5 ±2.8 years). High-resolution structural MRI and diffusion imaging (directions = 30 and b0 = 5) were obtained using a Siemens 3-Tesla Trio scanner. Structural MRI data was processed and analyzed using the FreeSurfer image analysis suite. FreeSurfer consists of automated tools for reconstruction of the brain from structural MRI data, facilitating the quantification of regional white matter volumes. Cortical and central white matter volumes were taken as representing short-range and long-range connections, respectively. Volumes were entered into a statistical program and comparisons of volumes between groups were be conducted using Student's t test with significance level will be set at $p < 0.05$ (two-tailed). FMRIB Software Library was used to process and analyze diffusion data. Fractional anisotropy was chosen as the primary measure of the structural integrity of axonal fiber tracts. Voxel-wise analysis of multi-subject diffusion data was conducted using Tract-Based Spatial Statistics. Areas of significant difference were computed using Threshold-Free Cluster Enhancement and displayed as p-value images, where $p < 0.05$ corrected for multiple comparisons across space.

Results: There were no significant group differences in age and intracranial volume. A significant decrease in central white matter volume was observed in the ASD group ($p = 0.02$). There was neither a significant difference in cortical white matter volumes nor total cerebral white matter volumes. The ASD group had significant bilateral reductions in fractional anisotropy involving numerous association, commissural, and projection tracts. Affected association tracts included the inferior longitudinal fasciculus, superior

longitudinal fasciculus, inferior fronto-occipital fasciculus, uncinate fasciculus, cingulum, and fornix. Commissural fibers included the corpus callosum (genu, body, and splenium), and both forceps major and minor.

Projection tracts included the anterior thalamic radiation and corticospinal tract. There were no areas of increased fractional anisotropy in the ASD group.

Conclusions: This study provides preliminary evidence of both reduced central white matter volume and reduced fractional anisotropy along numerous long-range fiber tracts in ASDs, suggesting the existence of reduced long-range connectivity. The diffuse distribution of these findings suggests a global abnormality with long-range connections which may not only contribute to both core and associated symptoms, but also the well-known heterogeneity of this spectrum of disorders.

Model Systems Program
130 Cell Culture Models

130.143 164 Homologous Pairing of Chromosome 15q11-q13 Is Associated with Significant Disruption of Gene Expression in Human Maternal Chromosome 15 Microcell Transfered Neurons. M. Meguro-Horike[1], K. N. Leung[2], D. H. Yasui[2], J. M. LaSalle[3] and S. I. Horike*[1], (1)*Kanazawa University*, (2)*UC Davis School of Medicine*, (3)*University of California at Davis*

Background: Autism is a common neurodevelopmental disorder characterized by abnormalities in social, communicative, and behavioral functioning. Although the etiology of autism remains largely unknown, cytogenetic and genetic studies have suggested that autism may be influenced by genomic imprinting of 15q11-q13, through maternal copy number gains of 15q11-q13 occurring in 1-3% of autism cases. In this study, we focused on the homologous pairing of 15q11-q13 in human neuronal cells. Homologous pairing of 15q11-q13 was previously observed to be deficient in Rett Syndrome (RTT), Angelmann Syndrome (AS), and autism brain (Thatcher et al, 2005), and altered in maternal 15 q duplication (idic15) brain (Hogart et al, 2009).

Objectives: Our aim is to understand how the homologous pairing of 15q11-q13 is organized in the mammalian brain and associated with gene expression within the paired regions. Therefore, we investigated the impact of an extra human chromosome 15 on normal maternal to paternal 15q11-q13 interactions in a cell culture model.

Methods: Towards the dissection of the molecular basis of the imprinted gene cluster, we have previously established monochromosomal hybrids containing individual human chromosomes of defined parental origin. Human chromosomes in the monochromosomal hybrids were tagged with pSV2bsr, which confers blasticidin S (BS) resistance, so that the marked chromosomes could be successfully transferred into mammalian cells. In this study, to model 15q11-q13 maternal duplication in a neuronal cell line, a paternal or maternal copy of human chromosome 15 was transferred into the human SH-SY5Y neuronal cells by microcell fusion. Then, FISH analysis was performed using probes to *SNRPN* and *GABRB3* to compare how the homologous alleles of 15q11-q13 are organized in human neuronal cells with a paternal or maternal copy of human chromosome 15.

Results: SH-SY5Y cells show an increase in the percentage of 15q11–q13 paired alleles following induced differentiation with 16 nM PMA. In contrast, homologous pairing of 15q11-q13 was disrupted in human neuronal cells with an extra maternal copy of human chromosome 15. Moreover, gene expression analysis of 15q11-q13 transcripts demonstrated significantly decreased expression of *SNRPN*, *GABRB3*, *CHRNA7* transcripts despite increased maternal dosage.

Conclusions: We observed that homologous pairing of 15q11-q13 was deficient in human neuronal cells with extra copy of human chromosome 15. Interestingly, extra copies of genes are predicted to lead to increased expression, however our study revealed that gene expression can be altered in unexpected ways through epigenetic changes resulting from increased maternal 15q11-13 dosage, similar to what has been previously

observed in a human brain sample with maternal 15q duplication and disrupted homologous pairing. Molecular investigation of gene expression in our autism model cells with an extra copy of 15q11-q13 provides insight into the potential complexities of other copy number variations in autism.

130.144 165 CD8+ T Cell Activation in Children with Autism. A. M. Enstrom*[1], J. Van de Water[2] and P. Ashwood[1], (1)*M.I.N.D. Institute, University of California at Davis*, (2)*University of California at Davis*

Background: Alterations in genes controlling immune responses as well as changes in dynamic cell function have been noted in children with autism. It has long been known that extensive interactions occur between the immune system and neuronal system/brain, and that normal neurodevelopment is contingent upon an appropriate interaction with the immune system. In model systems, it has been shown that abnormal immune function can detrimentally influence early brain development. CD8+ T cells are important in the prevention of infections, the eradication of pathogens and in controlling immune responses. Previous transcriptome studies implicated abnormal expression of genes predominantly expressed by CD8+ T cells in autism, but as yet little to no functional data has been described for these cells. We hypothesized that children with autism have a fundamental defect at the CD8+ T cells immune cell level that leads to abnormalities in immune function noted in many children with autism.

Objectives: Based on our previous reports of gene expression in autism and altered immune cell function, we sought to establish whether CD8+ T cells have abnormal phenotypes and function in autism.

Methods: Peripheral blood mononuclear cells (PBMC) from 16 children with autism and 16 typically developing children between the ages of 2 and 5 years were obtained by density gradient centrifugation. Dynamic cell function was determined by stimulation of PBMC with PMA/ionomycin for 24 hours. Supernatants were collected and analyzed for cytokine production by luminex analysis. Phenotypic analysis of CD8+ T cells were performed by flow cytometry.

Results: The percent of CD8+ T cells that contained the cytolytic proteins, perforin and granzyme B were increased in unstimulated cell cultures from children with autism compared to controls ($p < 0.004$). Following stimulation the number of CD8+ T cells containing cytolytic proteins increased significantly in controls but decreased in children with autism ($p < 0.01$). In addition, following stimulation, surface expression of CD107a, a marker of granule release, was decreased in children with autism compared to controls ($p < 0.003$), suggesting that activation and release of cytolytic proteins due to stimulation was altered in autism compared to controls. Intracellular staining of the inflammatory cytokine interleukin-6 (IL-6) in CD8+ T cells was increased at resting levels in children with autism compared to controls ($p = 0.03$). However, following stimulation intracellular IL-6 and interferon gamma (IFNg) were increased significantly in controls but decreased in children with autism ($p < 0.01$), possibly suggesting an "exhausted" or "maximized" cellular response.

Conclusions: These studies point to specific CD8+ T cell function abnormalities in the blood of individuals with autism. Abnormal CD8+ T cell function may represent an important link between inflammatory processes that have reported in some children with autism, and could point to a specific immune basis for the disorder in many subjects.

130.145 166 Bisphenol-A, An Environmental Risk Factor, Decreases Fluidity and Phosphatidylethanolamine Levels in the Membrane: Potential Role in Autism. V. Chauhan*, K. Kaur and A. Chauhan, *NYS Institute for Basic Research in Developmental Disabilities*

Background: We have previously reported that levels of phosphatidylethanolamine (PE) and membrane fluidity are decreased in the erythrocyte membranes from autism subjects. Bisphenol-A (BPA) is a chemical in many plastic and resin products, including food and drink containers as well as linings of food cans. BPA leaches from containers to food, and it has been found in high amounts in food items including milk and baby food. Its exposure has been suggested to be a

possible causal factor for neurodevelopmental disorders.

Objectives: We studied whether BPA can induce similar effects on membrane as those observed in autistic subjects.

Methods: Lymphoblasts from normal subjects were obtained from Autism Genetic Resource Exchange (AGRE) and incubated with various concentrations of BPA in serum- free medium for 24 h. Membrane fluidity was measured at 37^0C using diphenylhexatraiene (DPH) as a fluorescent probe. Since fluidity of the membrane is related to the temperature, the temperature-dependent effects of BPA on membrane fluidity were also studied at varying temperatures from 10^0C – 50^0C. In order to study the effect of BPA on membrane phospholipids, the cell lipids were extracted with chloroform (C)/methanol (M) (2:1, V/V), organic layer was dried and phospholipids were separated on silica gel 60 plates using C: M: H_2O (65/25/4, V/V) as solvent system. Different phospholipids fractions were quantitated by measuring the inorganic phosphorus.

Results: BPA decreased membrane fluidity of lymphoblasts in a concentration-dependent manner. The effect of BPA on membrane fluidity was observed at all temperatures studied i.e., 10-50 ^{0}C. The measurement of different phospholipids fractions showed that BPA significantly decreases the levels of phosphatidylcholine and phosphatidylethanolamine in the lymphoblasts.

Conclusions: These results suggest that BPA exposure can decrease membrane fluidity and levels of PE. These effects of BPA were similar to those reported previously in the membranes from autistic subjects. It is proposed that BPA exposure may act as an environmental stressor in genetically susceptible individuals resulting in clinical symptoms of autism.

130.146 167 Prenatal Exposure to PBDE47 Alters Motor Behaviors and Spatial Learning in C57BL/6J Mice. R. F. Berman*, T. A. Ta, C. Koenig, M. S. Golub and I. N. Pessah, *University of California at Davis*

Background: Polybrominated diphenyl ethers (PBDEs) are widely used flame retardants found in a variety of products from carpeting to plastics. These compounds are accumulating in the environment and have become persistent world-wide contaminants for human and animal populations. This is of concern because PBDEs, and PBDE47 in particular, can contaminate the fetus by crossing the placental barrier or through breast milk. Therefore, these compounds may represent a serious risk to the developing fetus. Objectives: To examine the effects of low level, chronic, perinatal exposure to PBDE47 on brain development and behavior in C57BL/6J mice. Methods: Female mice were fed one of three doses of PBDE47 (0.03, 0.10 or 1.0 mg/kg/day) or vehicle beginning 4 weeks before mating, throughout gestation, and over the preweaning period for a total of 70 days exposure. Levels of PBDE47 were measured in brain and other tissues of exposed dams and their offspring. Offspring were tested for sensory, motor and cognitive function, and their brains were examined for evidence of neuronal loss using stereological procedures. Results: Dose related elevations of tissue levels of PBDE47 were found in blood, brain, adipose tissue of dams that increased over the course of exposure. Offspring also showed substantial levels of PBDE47 present in their blood and brain when measured on postnatal days 1, 14 and 21. Offspring exposed to PBDE47 at a dose of 0.10 mg/kg/day showed reduced somatic growth over postnatal days 8-18. Behavioral testing of offspring revealed significant motor impairments and altered spatial memory performance. No significant loss of neurons was found in the brains of exposed offspring. Conclusions: Exposure of pregnant dams to PBDE47 results in significant exposure of their offspring, with tissue levels in brain approaching that of the dams. Exposure delayed somatic growth, impaired motor development and resulted in abnormal memory performance. These data demonstrate that perinatal exposure to PBDE47 at low, physiologically relevant levels can alter the normal course of growth and development.

130.147 168 The Presence of Antibodies against Differentiating Neuronal Progenitors in Sera FromChildren with Autism. B.

Mazur-Kolecka*[1], I. L. Cohen[1], E. C. Jenkins[1], E. Marchi[2], W. T. Brown[1] 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: It has been hypothesized that altered brain development during embryogenesis and early postnatal life is responsible for the abnormal behaviors seen in autism. However, the specific pathological mechanisms that influence early development remain unidentified. Because of the presence of autoantibodies against brain tissue in sera from children with autism, damage of the brain-blood barrier and abnormal autoimmune responses were suggested as potential etiologies of autism. Recently we demonstrated that sera from children with autism alter the proliferation and neuronal maturation of human neuronal progenitor cells (hNPCs) in culture. Our study revealed that sera from children with autism immunoreact with neuronal progenitors in the dentate gyrus of the mouse hippocampus.

Objectives: To evaluate sera from children with autism for the presence of autoantibodies directed against human neuronal progenitors at distinct stages of maturation in culture.

Methods: The presence of antibodies against neuronal progenitors was tested in sera collected from control and affected siblings from 4 families, and in sera from unrelated control children (n=14) and children with autism (n=20) aged up to 5 years. Reactions against proliferating hNPCs (day 0); and during neuronal maturation induced in culture (day 3 and day 7) were revealed by immunoblotting using sera diluted 1:250, and by immunocytochemistry using sera diluted 1:100. Cells immunoreactive to sera were identified by 3 color-immunofluorescence using markers of immature progenitors (Sox2, nestin), migrating progenitors (doublecortin), and mature cells (Tuj1, NeuN, GFAP).

Results: Sera from children up to 5 years of age contain antibodies that react with neuronal progenitors during neuronal maturation. As detected by the immunoblotting method, sera most frequently reacted with several proteins with molecular weight of 55 kD, 100-105 kD, 150-160 kD and 210-240 kD. Evident immunoreactivities with multiple bands were detected in 14% of control children and in 35% of children with autism. The intensity of this immunoreaction correlated with the stage of hNPCs maturation. The immunocytochemical method revealed a stronger immunoreaction against hNPCs in sera from children with autism than sera from unaffected siblings. The 3 color-immunofluorescence results suggest that antibodies in sera recognize a subpopulation of neuronal progenitors that express neuronal but not glial markers.

Conclusions: Sera from young children with autism contain antibodies that recognize several proteins of differentiating neuronal progenitors more frequently than controls. This suggests that autoimmune reactions may participate in alterations of early neuronal development. Elimination of specific antibodies against neuronal progenitors may represent a potential treatment strategy in autism.

130.148 169 Chromosomal Engineering of a 15q11-13 Duplication Mouse Model of Autism. T. Takumi*, *Hiroshima University*

Background: Autism is a complex psychiatric illness which has received considerable attention as a developmental brain disorder. Substantial evidence suggests that chromosomal abnormalities contribute to autism risk. The duplication of human chromosome 15q11-13 is known to be the most frequent cytogenetic abnormality in autism.

Objectives: To create a chromosome-engineered mouse model analogous to human 15q11-13 duplication.

Methods: We have modeled this genetic change in mice using chromosome engineering to generate a 6.3-Mb duplication of the conserved linkage group on mouse chromosome 7.

Results: Mice with a paternal duplication display autistic behavioral features such as poor social interaction and stereotypical

behavior, and exhibit abnormal ultrasonic vocalizations. The analysis on a MBII52 snoRNA within these duplicated region reveals that the editing ratio of serotonin 2c receptor (5-HT2cR) pre-mRNA and intracellular Ca^{2+} responses by a 5-HT2cR agonist are altered in the paternally duplicated neurons.

Conclusions: This chromosome-engineered mouse model for autism seems to replicate various aspects of human autistic phenotypes and validates the relevance of the human chromosome abnormality. This model will be a founder mouse for forward genetics of autistic disease and an invaluable tool for its therapeutic development.

130 Comorbidities

130.050 71 Neuroglial and Innate Neuroimmunity Contribution to the Pathogenesis of Autism and Other Neurodevelopmental Disorders. C. A. Pardo*[1], A. Azhagiri[1] and S. Wills[2], (1)*Johns Hopkins University School of Medicine*, (2)*Johns Hopkins University Departement of Neurology*

Background:

Neuroglia, cells of the CNS derived from the neuroectoderm (astroglia and oligodendroglia) and mesoderm (microglia) contribute to the establishment of neuronal networks and brain connectivity. Recent studies have shown the important role of neuroglia and neuroimmune pathways in synaptic function and neuronal homeostasis. Disturbances of neuroglia cells and their activation patterns facilitate the activation of cytokines, chemokines and signaling pathways such as Toll-like receptors (TLRs), activation that may influence neuronal and synaptic function.

Objectives:
Our lab has focused on studies of cytokines/chemokine networks as well as TLRs signaling pathways in the cerebral cortex of brains from children with autism and controls.

Methods:
Proteomic and multiplexed techniques as well as quantitative PCR studies were used to identify the profiles of cytokines, chemokines and TLR pathways in different cortical regions in brain obtained from patients with autism and controls.

Results:
Patterns of neuroglial activation and expression of signaling pathways associated with innate immunity are differentially expressed in the cerebral cortex. Cytokines such as IL-6 and TGF-1 beta as well as the chemokine CCL2 (MCP-1) are prominently overexpressed in selected areas of the cortex such as the anterior cingulated gyrus (ACG) and frontal cortex (FC). Signaling pathways associated with innate immunity such as TLRs, appear also to be selectively expressed across cortical areas. TLR2 and other downstream signaling genes are particularly up-regulated in the ACG as compared with other cortical regions. Interestingly, the ACG appears to be the cortical area with most selective increases of innate neuroimmunity. This selective expression is associated with the magnitude of neuroglia activation and may associated with patterns of neuronal susceptibility and cortical dysfunction.

Conclusions:
Selective expression of cytokines, chemokines and TLRs were observed in cortical brain regions. The ACG appears to be one of the most prominent cortical brain regions with most activation of innate neuroimmunity. The patterns of expression appears to be associated with the magnitude of astroglia and microglia activation and demonstrate the involvement of innate neuro immunity in pathogenic mechanisms in autism.

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130.051 72 Behavioral Improvements with Fever in Children with Autism: Immune Effects On Synaptic Connectivity?. A. W. Zimmerman*, *Kennedy Krieger Institute*

Background:

Frequent clinical observations of rapid but transient functional improvements in autism during fever and illness suggest that immune

factors may affect cortical connectivity. Changes with illness frequently precede the appearance of fever and may persist for several days after fever subsides. No relationship to type of infection, degree of fever or treatment has been found. Additional reports suggest that this phenomenon occurs in some adults as well as children with autism, and in response to pain or external heating.

Objectives: Discuss the basic physiology of fever and possible mechanisms that may explain these findings in autism, including changes in cytokines, chemokines and their receptors, as well as heat shock proteins, cell membrane and synaptic functions.

Methods: Review of study of behavioral changes during fever in children with autism (Curran LK et al, Pediatrics, 2007).

Methods: Review of study of behavioral changes during fever in children with autism (Curran LK et al, Pediatrics, 2007).

Results: Improvements in behavior, language, and social relatedness have been observed to various degrees during fever in a majority of these children.

Conclusions: Responses to fever may provide new insights into underlying immune and synaptic mechanisms in autism.

130.052 73 Biomarkers of Immunological and Metabolic Comorbidities in Autism Spectrum Disorders. J. Bradstreet*[1] and R. F. Palmer[2], (1)*International Child Development Resource Center*, (2)*University of Texas Health Science Center at San Antonio*

Background: Recent published observations have found a consistent pattern of oxidative stress and immunological activation in children with autism spectrum disorders (ASD). Since there is broad consensus in the medical literature that the brain is highly sensitive to oxidative stress and immunological signals, the presence of excessive free radicals and peripheral immune activation would be expected to have potential clinical implications for affected individuals.

Objectives: For several years our population of ASD patients has been evaluated using urinary biomarkers of oxidative stress and immune activation. These include: isoprostane, 8-oxoguanosine (8OHG), 8-hydroxydeoxyguanosine (8OHdG), and neopterin. Urinary porphyrins, isoprostane and neopterin have been previously documented to be significantly elevated in the ASD population relative to controls. The RNA oxidation marker, 8-oxoguanosine has not been published in the autism population, but has been observed clinically to be significantly elevated relative to laboratory norms and appears to correlate with symptom severity within ASD. It is a potential marker of mitochondrial dysfunction. We compared our historical database to a population of neurotypical children.

Methods: A retrospective database review was undertaken to find children with ASD diagnoses for which no prior immunological or antioxidant therapy had been undertaken. Patients were selected from populations in the US, France and Norway which could provide a broad international assessment of the biomarker pattern in the ASD group. After extensive chart review to exclude prior treatment and children without unequivocal ASD, (N=212 ASD children, ages 1 to 8) were selected. These were internally compared within the group for subset evaluations and cross-correlations between the biomarkers as well as to the control population of healthy neurotypical children (N=43) gathered from volunteers in the US and France. Outliers greater than 3SD were excluded from the analysis, resulting in a final study group (N=197). For all specimens, a first morning urinary sample was collected and processed using standard laboratory methods of HPLC and triple quadrupole dual mass spectroscopy.

Results: For all the major variables: 8OHG, 8OHdG, neopterin, uroporphyrin and coproporphyrin, the observed means were significantly higher for the ASD population ($p<0.001$). These data are consistent with previous observations published regarding urinary neopterin, isoprostane and porphyrins. The observed increase in RNA oxidation (8OHG) is a new observation within ASD. Unlike prior reports we did observe significantly higher DNA oxidation in this

group. The observed differences were highest for the population under age 5 for isoprostane ($p < 0.05$), coproporphyrin ($p < 0.001$), and neopterin ($p < 0.001$). In addition, strong correlations existed between markers of oxidation and neopterin as well as coproporphyrin.

Conclusions: This large retrospective controlled evaluation replicates previously published observations of abnormally increased neopterin, isoprostane and coproporphyrin in the ASD population and extends these observations to oxidation of RNA and DNA. It further demonstrates significant correlations of these biomarkers which may have value in biological subtyping as well as in the selection of interventions for these subgroups. The observed oxidation of RNA needs to be further correlated with mitochondrial assessments, and the oxidation of DNA is of obvious concern.

130.053 74 Biopsychosocial Model of ADHD in Autism Spectrum Disorder. K. Gadow*, *State University of New York*

Background: Clinic- and population-based studies indicate that ADHD symptoms are common in ASD. However, it is not clear whether these ADHD symptoms are similar to what is observed in children with ASD.

Objectives: Describes the initial results of programmatic research into a biopsychosocial model of nosology and pathogenesis for ADHD in children with ASD that integrates biomarkers and mental health risk factors with functioning in home and school setting.

Methods: Children with ASD with and without ADHD, their parents, and teachers completed an extensive battery of measures about ADHD and co-occurring behavioral symptoms and psychosocial mental health risk factors and provided DNA samples (parents, child).

Results: Findings indicate that children with and without ADHD exhibit marked differences in co-occurring symptomatology and mental health risk factors as well as differences between ADHD subtypes. ADHD symptoms are associated with social and academic functioning. ADHD also appears to be a distinct behavioral syndrome from other disruptive behavior disorders. Several candidate genes appear to be potential biomarkers for ADHD.

Conclusions: Findings provide initial support for and ADHD syndrome in children with autism that evidences both similarities and differences with ADHD in nonASD samples.

130.054 75 Comorbid Psychopathology in Children with ASD and An Age- and IQ-Matched Control Group. N. Skokauskas* and L. Gallagher, *Trinity College Dublin*

Background:

Comorbid psychiatric disorders complicate the course of ASDs by affecting detection, therapeutic interventions, prognosis and outcome. Despite the recent increase of studies on occurrence of medical and neurological conditions in persons with autism psychiatric comorbidity of ASD is less well examined and previous studies have reported diverse findings. The majority of previous studies did not investigate comorbidity as a primary question and most of them had methodological shortcomings, were not optimally designed and did not address sources of artefacts in detection of comorbidity. The better understand of comorbid psychiatric disorder in ASDs may facilitate more specific treatment potentially limiting negative outcomes.

Objectives: to examine comorbid psychiatric problems in a sample of children with ASD and their parents compared with an age and IQ matched control group and their parents.

Methods: *Subjects*
ASD subjects participating in the Irish Autism Genetics Study were invited to participate. Inclusion criteria for the present study were 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 score greater than 50. Cognitive assessment was based on assessment with the Leiter International Performance Scale-Revised (Leiter-R). Exclusion criteria for the study included known medical causes of autism, exposure to medications in utero known to cause autism, extreme prematurity, presence of the Fragile X anomaly or an abnormal

karyotype. The age, gender and IQ matched control group was collected through Special Schools. Exclusion criteria for this group included children or adolescents with a known clinical diagnosis of ASD.

Assessment Instruments
The Child Behavior Checklist 6-18 (CBCL/6-18) was used to assess behavioral/emotional problems in both groups. Parents reported their own psychological distress using the Brief Symptom Inventory (BSI).
Ethics
Irish Health Service Executive's Ethics Committee approved this study. Parents of the children had all signed informed consent forms prior to participation in the study.

Results:

There were 59 (88%) boys and 8 (12%) girls in the ASD group. Similarly, 57 (85%) of the control group were male and 10 (15%) were female. The groups did not differ significantly on mean age, mean IQ scores, gender, and parents mean age. Children with ASD in comparison to controls were significantly more depressed and withdrawn (CBCL/6-18 Anxious/depressed syndrome, Mean T score 63.99 vs. 54.27), and had more severe social (CBCL/6-18 Social problems syndrome, Mean T score 65.46 vs 55.09) and attention problems (CBCL/6-18 Attention problems syndrome, 77.10 vs 70.07). Almost half of the ASD group met CBCL DSM criteria for clinically significant ADHD (44.78 %) and anxiety (46.2%) problems. Parents of ASD children and controls did not significantly differ on any BSI symptom dimension.

Conclusions:

High rates of clinically significant psychiatric problems were detected in ASD children, with anxiety and ADHD being the most frequently detected syndromes. Parental distress was not associated with the identification of psychological problems in children with ASD.

130.055 76 Autism Spectrum Disorder and Cri Du Chat Syndrome. D. R. E. Emerich[1], C. S. Paula*[2], R. C. R. Rimério[1] and M. C. Teixeira[1], (1)*Mackenzie P University*, (2)*Universidade Presbiteriana Mackenzie*

Background:

Cri du Chat syndrome is a rare genetic disorder due to a missing part of chromosome 5 and the main symptoms are: behavioral problems, severe cognitive, speech, and motor delays. The diagnosis of this syndrome is complex and it requires standardized assessment tools with good sensitivity and specificity. The presence of autistic symptoms in Cri du Chat syndrome seems to be frequent. Thus, studies which help professionals discriminate individuals with autism spectrum disorder from individuals with Cri du Chat syndrome are important.

Objectives:

To investigate the presence of autistic symptoms in a sample of patients with Cri du Chat syndrome.

Methods:

(1) subjects: a sample of 10 patients with clinical and molecular-cytogenetic diagnosis of Cri du Chat syndrome. (2) measurements: all subjects were evaluated according to the Brazilian version of the Autism Screening Questionnaire (ASQ). In addition, their behaviors were video recorded to measure frequency and duration of adaptive responses (imitation, cooperation, following rules) and non-adaptive responses (stereotypes, aggression and self-injury).

Results: Pearson's Correlation Coefficient showed positive correlations between the score of the ASQ: (1) non-adaptive behavior of the repetitive and stereotyped use of objects ($p = 0.043$), (2) aggression directed toward objects ($p = 0.002$) and (3) self-injury ($p = 0.004$). Negative correlations were observed between the total score of the ASQ and (1) adaptive behavior of imitation and ($p = 0.032$) cooperation and (2) following rules ($p = 0.013$).

Conclusions:

In this sample, higher scores on the ASQ scale were correlated with higher frequency of non-adaptive behavior. Thus, more severe cases of individuals with Cri du chat

syndrome have similar behavior of individuals with autism spectrum disorder. These results have clinical implications because professionals must be prepared to differentiate patients with autism spectrum disorder than patients with Cri du chat syndrome.

130.056 77 Characteristics of Anxiety in Children with Co-Occurring Autism Spectrum and Anxiety Disorders. F. Cruz*, A. Pulido, L. Ampolos, K. La Marca, R. McNally Keehn and A. J. Lincoln, *Alliant International University*

Background: Anxiety symptoms have long been considered an associated feature of autism spectrum disorder (ASD). Several studies have demonstrated that children with ASD evidence higher levels of clinically significant anxiety compared to their typically developing peers (e.g., Russell & Sofronoff, 2005) and children with other intellectual and language disabilities (e.g., Gillot, Furniss, & Walter, 2001). Although high rates of anxiety in this population are well documented, little is known about the differential pattern of anxiety disorders. Furthermore, evidence regarding agreement between parent and child perceptions of anxiety symptoms in children with ASD is lacking. Finally, no studies to date have examined the relationship between anxiety symptoms and ASD symptom severity.
Objectives: The aims of this study were threefold: 1) to examine the differential pattern of anxiety and other psychiatric symptoms among children with ASD and untreated co-occurring anxiety, 2) to determine the relationship between parent and child reported symptoms of anxiety in children with ASD, and 3) to explore the relationship between anxiety symptoms and ASD symptom severity.
Methods: Participants are twenty-two 7 – 14 year-old children with a diagnosis of ASD, at least one anxiety disorder diagnosis, and intellectual and language abilities ≥ 70. ASD diagnoses were confirmed using the ADOS and ADI-R. Anxiety disorder diagnoses were confirmed using the Anxiety Disorders Interview Schedule - Parent Version (ADIS-P). Ratings of anxiety symptoms were measured using both parent and child versions of the Multidimensional Anxiety Scale for Children (MASC; MASC-P) and Spence Children's Anxiety Scale (SCAS; SCAS-P).
Results: Within a sample of children with co-occurring ASD and anxiety diagnoses, 82% of children met criteria for Generalized Anxiety Disorder (GAD), 73% met criteria for Specific Phobia, 68% met criteria for Social Phobia, 64% met criteria for Separation Anxiety Disorder (SAD), and 9% met criteria for Obsessive Compulsive Disorder (OCD). Two or more anxiety diagnoses were present in 96% of the sample. Additionally, 77% met criteria for at least one additional non-anxiety psychiatric diagnosis (Attention Deficit Hyperactivity Disorder, Major Depressive Disorder, or Oppositional Defiant Disorder). The relationship between parent and child reported anxiety symptoms was not significant (r=.20 - .31, p > .05). There was a significant positive relationship between autism symptom severity and total anxiety symptoms, as measured by ADOS Social and Communication Total and SCAS-P Total scores respectively (r=.47, p= .03).
Conclusions: Results suggest that among children with ASD and clinically significant anxiety, generalized anxiety, specific phobia, social phobia, and separation anxiety disorders were most prevalent. Further, a majority of children had more than one anxiety disorder as well as additional non-anxiety psychiatric disorders. Agreement among child and parent ratings of anxiety symptoms was low, suggesting a difference in perceptions of the child's untreated anxiety symptoms. Finally, higher levels of anxiety appear to be related to autism symptom severity in children. Further research investigating the relationship between anxiety symptoms and the severity of ASD symptoms in children with and without anxiety diagnoses is warranted. This research could elucidate whether anxiety may be an inherent feature of ASD.

130.057 78 Depressive Symptoms in Children with Autism Spectrum Disorder. L. Thornton* and G. Benson, *Cheshire and Wirral Partnership NHS Trust*

Background: The detection of depression in children with autism spectrum disorder (ASD) can be problematic, even for experienced child mental health clinicians. An awareness of the presentation of depressive features in ASD is therefore important.

Objectives: This study describes the prevalence of parent-reported depressive symptoms in children with high functioning ASD, and the associations with autistic features, non-affective comorbidity, and competencies.

Methods: This is a retrospective study of 90 children (76 boys,14 girls; age range 5-16 years; mean age 9.9 years) referred to an autism assessment clinic and subsequently diagnosed as having a high functioning ASD. Data derived from the CBCL, ADI-R, and ADOS were analysed.

Results: Thirty four children (38%) had a CBCL Affective Problems score in the clinical range, with 94% having significantly impaired competencies. In addition,there were high levels of comorbidity, with 88% having an additional DSM-oriented Scale score in the clinical range.

For the whole sample, Affective Problems were significantly correlated with higher levels of anxiety, more ADOS social affect impairments, and reduced activity competence ($p<.01$).

When compared with the rest of the sample, Affective Problems cases were particularly discriminated by higher levels of 'tiredness' (47% vs 2%),'self-harm' (53% vs 7%),'lack of enjoyment' (68% vs 21%),'depression' (71% vs 25%),'suicidal talk' (47% vs 9%), and 'sleep problems' (65% vs 27%) ($p<.0001$). In addition,the group had significantly higher ADI-R social and communication symptoms ($p<.01$), and more ADOS social affect impairments ($p<.05$).

Conclusions: Clinically significant levels of impairing depressive symptoms were common in this clinical sample of children with ASD. Although individual affective symptoms discriminated children with depression, the clinical picture was complicated by the frequent coexistence of non-affective symptoms. In addition, depressive symptoms may affect parental-reporting and clinical observations of autistic behaviours, further complicating accurate diagnostic assesment.

This study emphasises the need to enquire about the specific features of depression when assessing children with suspected ASD, and to be particularly alert to the presence of suicidal thoughts and self-harm. This approach is essential for the early detection and treatment of depressive disorders.

130.058 79 A Large Scale Study of the Psychometric Characteristics of the Ibr Modified Overt Aggression Scale: Findings and Evidence for Increased Self-Destructive Behaviors in Adult Females with Autism Spectrum Disorder.

I. Cohen*[1], J. A. Tsiouris[1], M. J. Flory[1], S. Kim[1], R. L. Freedland[1], G. Heaney[1], J. Pettinger[2] and W. T. Brown[1], (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*NYS OMRDD*

Background:

Aggressive behaviors toward self and others are reported to be relatively common problems in persons with intellectual disabilities (ID), have major impacts on the family, and seriously affect the ability of such individuals to reside in more "normalizing" environments. In order to begin to study the biological bases of some of these behaviors, we carried out a survey using a modification of the Overt Aggression Scale (OAS) (Yudofsky, et al 1986). We added new items to assess self-deprecating statements and included information on antecedents and consequences of aggressive behaviors, clinical diagnoses, and known etiologies of ID to better define our samples. We named this version the IBR (Institute for Basic Research) Modified Overt Aggression Scale or IBR-MOAS. Due to this modification it was important to ensure it had adequate reliability and validity.

Objectives:

To document both the reliability and validity of the aggression scale of the IBR-MOAS using a sample of over 2,000 people. Validity studies included developmental validity (showing variations in scores with age and ID level), diagnostic validity, and construct validity. Diagnostically, we tested whether females show more self-injury, as reported by Crocker et al. (2006) , and whether this effect would be stronger in those females who also have an autism spectrum

disorder, controlling for level of intellectual disability.

Methods:

Two sets of samples were ascertained for this study. The first sample consisted of 3,547 people community-based people who received services from OMRDD between 2006 and 2007. The second set consisted of a sample of 25 people who were seen in 2008 at the George A. Jervis Clinic because of problems with aggressiveness toward self and/or others. Forms completed on this set were used for determining inter-rater and two-week test-retest reliability of the Aggression Scale of the IBR-MOAS. A Likert measure of the frequency of occurrence of each of the aggression items during the past year was developed as follows: 0 = Never (never happens); 1 = Rarely (averages about once a year to once a month); 2 = Sometimes (averages about several times a month to several times a week); 3 = Often (averages about daily to several times a day); and U (Used to happen but not this past year). For the present analyses, the U rating was coded as equivalent to Never. Unlike the OAS and its modified versions, a weighted scoring system was not used.

Results:

Reliability ranged from good to excellent. Aggression toward others and objects was highest in the youngest adults, in those in the moderate to severe range of ID, and in those with an autism spectrum diagnosis. Self-injury was highest in those in the severe to profound range of ID and in those with autism, particularly the females. Females with autism were also more likely to make the most self-deprecating statements.

Conclusions:

Our data suggest that adult females with autism are a unique group and support the notion that mood and anxiety disorders play a role in self-destructive behaviors in this population.

130.059 80 Case Report: Event Related Potentials in An Adolescent with Autism Prior to Onset of Schizophrenia. L. L. Sears*, E. M. Sokhadze, G. Mathai and T. Erwin, *University of Louisville*

Background: Although identification of schizophrenia in persons with autism can be difficult, several research studies have suggested a link between these disorders based on genetic and biologic evidence. Of note is the high prevalence of pervasive developmental disorders in subjects who later display features of schizophrenia (Rapoport et al., JAACAP, 2009, 48:10-18). Since it is unclear what may predispose certain individuals with autism to develop schizophrenia, further study is needed including identification of potential neurobiologic markers (Toal et al., BJP, 2009, 194:418-425). Establishing predictive measures will enhance our understanding of the etiology of psychosis in autism and impact treatment and intervention for subjects with autism and co-morbid psychiatric disorders.
Objectives: To identify potential biologic markers for schizophrenia risk in autism we retrospectively evaluated event related potentials (ERPs) on a novelty oddball task completed prior to a subject with high-functioning autism (HFA) developing clinical features of schizophrenia. The individual displayed onset of delusions, disorganized behavior and worsening adaptive skills with diminished motivation and blunted affect several months after completing the ERP study. No medical conditions were identified that may have produced the psychosis.
Methods: We collected ERPs from the18-year-old male subject with HFA during a novelty oddball task and compared findings for the same task with 11 subjects with HFA but no positive symptoms of a psychotic disorder. All subjects met Autism Diagnostic Interview-Revised criteria for autism.
Results: The subject with autism who developed schizophrenia had increased amplitude of P3a, P3b and N170 waves for both novel and target stimuli compared to subjects with autism without positive symptoms of schizophrenia. Locations where differences were found on the novelty oddball task include frontal, centro-parietal, and parieto-occipital brain regions.
Conclusions: Increased amplitude in ERPs during a novelty-processing task suggests

differences in cognitive processing and brain function in a subject with HFA who later developed schizophrenia compared to HFA subjects without positive symptoms of psychosis. While the negative signs found in schizophrenia are common in autism this ERP finding may be relevant for understanding the onset of the positive symptoms of a psychotic disorder such as delusions and hallucinations. Further study of neuropsychological and biologic differences in persons with autism developing psychosis is needed to better address the complexity of these individuals for differential diagnosis and to better understand the etiology and treatment of both disorders.

130.060 81 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[2] and T. Rovito Gomez[1], (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*Institute of Professional Practice*

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 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 in this group and non-PDD diagnosed cases.

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 indicate moderate to strong associations between birth measures (e.g., body length, birth weight, visual asymmetry) and neurobehavioral assessments (e.g., atypical looking preferences to higher amounts of stimulation) performed before 12 months of age with a variety of later PDDBI domain scores including: SENSORY (sensory seeking-type behaviors); AROUSE (hyper- and hypoactivity); 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) in the PDD group. The smaller the infant, the greater the SENSORY and AROUSE scores. Preference for high frequency visual stimulation at 4 months was strongly correlated with later PDDBI measures of autism severity and early measures of visual asymmetry modulate this effect.

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.

130.061 82 Anxiety and Depression in Children with HFASDs: Symptom Levels and Source Differences. C. Lopata*[1], J. A. Toomey[2], J. D. Fox[3], M. A. Volker[4] and M. L. Thomeer[1], (1)*Canisius College*, (2)*Summit Educational Resources*, (3)*Autistic Services*, (4)*University at Buffalo, SUNY*

Background: Children with high-functioning ASDs (HFASDs) are reportedly at risk for psychiatric symptoms including depression and anxiety. While some studies have documented significant symptom elevations (e.g., Gadow et al., 2005), others have noted no elevations (e.g., Solomon et al., 2004). Interpretation of findings across studies is confounded by use of different data sources (parent-, teacher-, and/or child-reports). While source differences have been observed, there has been little systematic study of how child-reports align with parent-reports (Weisbrot et al., 2005). Such examination is necessary due to concerns regarding the ability of individuals with HFASDs to express internalized states (Ghaziuddin et al., 2002). Ongoing research is also warranted as studies have been characterized by small and poorly characterized samples, comparisons with normative data, and/or lack of controls for sample characteristics.

Objectives: This study examined: (1) anxiety and depression symptoms in children with HFASDs compared to matched controls using child self-reports and parent-ratings; and (2) source differences (child vs. parent) within the two condition groups (HFASD vs. control).

Methods: The sample included 40 children ages 7-13 with a HFASD (AD, HFA, or PDD-NOS) and 40 typical-controls matched on age, gender, and ethnicity. Participants in the HFASD group participated in a multiple-gate screening; inclusion criteria included a short-form IQ composite > 70; receptive or expressive language score ≥ 80; and score meeting ASD criteria on the ADI-R. Matched-controls were recruited using flyers.

Symptoms were assessed using the Depression and Anxiety subscales of the Behavior Assessment System for Children 2 – Parent Rating Scales (BASC2-PRS) and Self-Report of Personality (BASC2-SRP).

Results: The two groups did not significantly differ on important demographic variables. A significant between-group multivariate effect was found based on parent reports; follow-up univariate analyses indicated significant between-group differences for both depression (F[1,78] = 34.78, p < .001, d = 1.10) and anxiety (F[1,78] = 13.05, p = .001, d = .75)). No significant multivariate effect was found based on child self-reports. Within-condition source comparisons (parent vs. child) revealed a significant multivariate effect for the HFASD group only, with follow-up univariate analyses indicating significant source-differences for both depression (F[1,78] = 29.07, p < .001, d = 1.04) and anxiety (F[1,78] = 7.01, p = .010, d = .57). Correlations between parent- and child-reports were significant only for depression in the HFASD group (r = .315).

Conclusions: Results indicated significant depression and anxiety symptom elevations for children with HFASDs based on parent ratings. Children with HFASDs reported symptom levels similar to controls. A significant discrepancy was found between parent and child ratings for the HFASD group only, with parent ratings significantly higher for depression and anxiety. A low but significant correlation between parent and child ratings of depression in the HFASD group suggested that the children reported symptoms in a manner that to some degree paralleled parent ratings. Despite this positive association, mean score differences reflected a substantial discrepancy in magnitude of depressive symptoms by rater. Implications will be described.

130.062 83 Cognition in ADHD and Autism. H. M. Geurts*, *University of Amsterdam*

Background: ADHD and Autism are both heterogeneous, lifelong neurobiological developmental disorders, which have an enormous impact on all developmental domains. Recently research regarding the etiology of these neurodevelopmental disorders is increasingly moving towards determining intermediate phenotypes that

will characterize the heterogenic nature of these disorders, instead of trying to pinpoint which single cognitive construct or brain anomaly underlies all related characteristics. The question is whether there is indeed enough knowledge to select these potential intermediate cognitive phenotypes.

Objectives: To give an overview of studies showing the cognitive overlap and differences between ADHD and autism and discuss whether cognitive profiles might be potential intermediate phenotypes.

Methods: Two examples of one cognitive domain, i.e., cognitive control, will be given to illustrate the type of studies that are executed to study ADHD and autism in tandem. Children with ADHD will be directly compared with children on interference control and response variability.

Results: There are various cognitive domains were both disorders overlap in their cognitive deficits, however in some domains ASD and ADHD are clearly distinct. The two studies show that by detailed analyses differences between the two disorders can be detected while on first sight there seems to be a large overlap.

Conclusions: More detailed comparisons on cognitive domains between ADHD and autism are needed to determine which cognitive domains are potential intermediate phenotypes that help us in understanding the overlap. However, while inhibitory control might indeed be a potential intermediate phenotype, this seems not to be the case for intra-individual variability.

130.063 84 The Relationship Between Prenatal Stressors, Autism Diagnosis, and Autism Severity. K. D. Ward*, K. C. Salava and E. R. Hahn, *Furman University*

Background:

A growing body of literature points to a relationship between prenatal exposure to stress and an increased risk of autism spectrum disorders (e.g., Kinney, Munir, Crowley, & Miller, 2008). Mothers of autistic children report significantly more relationship conflicts and stressful life events during pregnancy compared to controls (Beversdorf et al., 2005; Ward, 1990). Inspection of medical records also reveals that mother of autistic children are more likely to experience obstetric complications (e.g., Burd , Severud, Kerbeshian, & Klug, 1999; Glasson et al., 2004). Two critical points during gestation appear to be especially critical: between months 5 and 6, and in the two weeks just before birth. Women who faced significant stress at either of these two times were especially likely to give birth to a child who would later receive an autism diagnosis (Kinney, Miller, Crowley, Huang, & Gerber, 2008; Torrey, Hersh, & McCabe, 1975).

Objectives:

The primary goal of the current research was to investigate in detail the relationship between retrospective reports of prenatal stress and autism. We compared the prevalence of self-reported stressors during pregnancy for mothers of children with autism and neurotypical controls. Additionally, we asked whether certain types of stressful events were reported more frequently by mothers of children with autism. A final question was whether the quantity or quality of stressful events was related to the severity of autistic behaviors.

Methods:

Twelve mothers of male children (range = 3 and 6 years) with a medical diagnosis of autism participated (ASD). Data was also collected from mothers of 12 neurotypical males who were age-matched to the male children with autism (NT). Mother-child dyads visited the lab for one session. Mothers completed a modified version of the Childhood Autism Rating Scale (CARS) to assess the presence and severity of their child's autistic symptoms. Next, the mother was asked to complete a self-report measure that included questions about family demographic information, child autism history, and events during pregnancy.

Results:

Consistent with previous research, we found that ASD mothers reported more stressors during pregnancy (M= 3.13) compared to NT mothers (M= 1.57). We further found that stressors related to pregnancy and health

concerns were overrepresented in the ASD sample compared to the NT participants. Finally, the number of reported stressors during pregnancy was strongly correlated with children's score on the CARS (r = .55) among ASD participants. In contrast, there was a substantially weaker relationship between stressors and CARS score for NT participants (r = .21).

Conclusions:

The preliminary results support previous studies that have found a potential relationship between prenatal exposure to stress and an increased risk for autism. Our research extends this work by examining the occurrence of specific types of stressors. In our sample, health-related concerns appear to be largely responsible for the differences in reported stressors. Our results also suggest that the number of stressors experienced prenatally is related to the severity of autism. The biochemical pathways by which stress may undermine neurotypical development are considered.

130.064 85 Psychiatric Symptoms and Comorbidities in Children with a History of Autism Who Achieve An "Optimal Outcome". K. E. Tyson*[1], E. Troyb[1], M. A. Rosenthal[1], M. Helt[1], I. M. Eigsti[1], M. L. Barton[1], L. Naigles[1], E. A. Kelley[2], A. Orinstein[1], M. C. Stevens[3], R. T. Schultz[4] and D. A. Fein[1], (1)*University of Connecticut*, (2)*Queen's University*, (3)*Institute of Living, Hartford Hospital / Yale University*, (4)*Children's Hospital of Philadelphia and the University of Pennsylvania*

Background: A study is currently following children who have a history of autism spectrum disorder (ASD), but who no longer meet diagnostic criteria for such a disorder. These children have achieved social and language skills within the average range for their ages and receive little or no school support. Several recent studies suggest that this small subset of children, once diagnosed with ASD, achieve an "optimal outcome" (Sutera et al., 2007, Kelley et al., 2006, and Helt et al., 2008).

Objectives: The current study examines the lifetime prevalence of psychiatric disorders (other than ASD) in these "optimal outcome" (OO) children as compared to typically developing (TD) children and children with high-functioning autism (HFA). The study also looks at the occurrence of psychiatric symptoms in these children, whether or not these symptoms are part of a full-fledged diagnosis.

Methods: We compared prevalence rates of psychiatric symptoms and disorders in 19 TD children (mean age = 13.5), 20 HFA children (mean age = 12.8), and 28 OO children (mean age = 13.0). Groups did not differ in gender (p = .42), age (p = .77), or WASI full-scale IQ (p = .35). We administered the *Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version* (K-SADS-PL) to children's parents to ascertain current and lifetime rates of at-threshold psychiatric symptoms, as well as of specific disorders, across the three groups. Only lifetime rates are examined in the present study.

The K-SADS-PL asks whether a child has any broad symptoms of a psychiatric disorder before proceeding to more fine-grained questions about the disorder. Non-parametric Fisher's Exact tests assessed differences across groups in lifetime presence of psychiatric symptoms and diagnoses.

Results: There were differences among the three groups in the frequency of at least one lifetime symptom of several disorders. Compared to TD children, the OO children showed greater frequency of at least one lifetime symptom of ADHD (p<.01), ODD (p<.01), or specific phobia (p<.01). Significantly more HFA than TD children showed at least one lifetime symptom of ADHD (p<.001), social phobia (p<.001), or depression (p<.01). In addition, significantly more HFA than OO children evidenced at least one lifetime symptom of generalized anxiety disorder (p<.001); there was no such difference between the HFA and TD groups.

Frequencies of lifetime psychiatric diagnoses, as determined by the K-SADS-PL supplementary interviews, were also analyzed. Significantly more OO than TD children met criteria for a lifetime diagnosis of ADHD (p<.001) or specific phobia (p<.01). Furthermore, significantly more HFA than TD children met criteria for a lifetime diagnosis of ADHD (p<.001). Compared to OO children,

more HFA children also met criteria for a lifetime diagnosis of ODD ($p<.01$).

Conclusions: Although the OO children in this study appear to have experienced less lifetime psychopathology than the HFA group, the OO children displayed significantly more lifetime psychiatric symptoms and comorbid diagnoses than TD children. These findings suggest that these OO children, though evidencing fewer lifetime symptoms than HFA children, may retain or develop certain psychiatric symptoms after losing an ASD diagnosis.

130.065 86 Exploring the Relationship Between the Neuromodulator Adenosine and Behavioral Symptoms of Autism. S. A. Masino*[1], M. Kawamura[1], J. Svedova[1], L. M. Plotkin[1], F. J. DiMario[2] and I. M. Eigsti[3], (1)*Trinity College*, (2)*Connecticut Children's Medical Center*, (3)*University of Connecticut*

Background: The neuromodulator adenosine is an endogenous sleep promoter, neuroprotector and anticonvulsant, and people with autism often suffer from sleep disruption and/or seizures. Unfortunately, measuring plasma adenosine is not informative, measuring brain adenosine is not practical, and direct administration of adenosine or adenosine receptor agonists results in significant peripheral side effects. Recent efforts to regulate adenosine in the brain have yielded some success. To our knowledge, dysregulation of adenosine has neither been proposed nor tested with respect to the symptoms of autism.

Objectives: Based on published research (primarily with animal models), specific physiological stimuli are expected to increase brain adenosine. We sought to determine if changing adenosine would influence specific behaviors. We hypothesized that in addition to established beneficial physiological effects of adenosine, such as reducing seizures, increasing adenosine would decrease behavioral symptoms of autism. In contrast, adenosine-neutral or adenosine-decreasing activities would not be expected to improve behavioral symptoms of autism.

Methods: To test this relationship between adenosine and autism, we developed a customized parent-based questionnaire to assess child participation in activities expected to influence adenosine, and the behavioral changes that follow these experiences. For each type of activity, we established both adenosine-increasing and adenosine-neutral or decreasing questions. Within a defined time window after each event, parents reported changes in nine domains (social and communicative skills, repetitive or perseverative activities, eye contact, social interest, sound sensitivity, sleep, anxiety, adapting to transitions and aggressive behavior) using a 5-point Likert scale ("lots of decline," "some decline," "no noticeable change," "some improvement," "lots of improvement").

Results: The results of this questionnaire demonstrate significantly better behavior associated with events predicted to increase rather than decrease or have no influence on adenosine. There were no age-related effects, suggesting that the adenosine-related functional effect is independent of developmental level; there was also no effect of gender. Although this initial report relies on parental observation, parents were naive to any study hypotheses and all conditions were pre-assigned.

Conclusions: Pilot data from an internet-based parent survey customized to explore the relationship between autism and adenosine indicate a significant relationship between events predicted to increase adenosine and parental observations of behavioral symptoms of autism. Abnormalities in purine metabolism have been observed in autism, but have not been linked to core symptoms. Ultimately, understanding the relationship between adenosine and autism could help simultaneously to prevent seizures, improve sleep and reduce social and behavioral dysfunction. Importantly, a meaningful physiological relationship between adenosine and symptoms of autism opens new therapeutic strategies for Autism Spectrum Disorders.

130.066 87 Low Ferritin in Children with ASD: Association with Pica and ADHD Symptoms. K. A. Johnson*, J. Roesser, S. Hyman, L. Cole, A. Diehl, C. Murray and T. Smith, *University of Rochester*

Background: Low ferritin has been associated with nighttime waking due to restless leg syndrome in children with autism spectrum disorders (ASD). Two small studies have documented low ferritin levels in children with ASD (Dosman 2007; Latif 2002). Neither of these studies examined pica or ADHD symptoms, although iron deficiency has been related to these (Konofal 2007) in children without ASD. Children with ASD may be at greater risk for low iron stores because of dietary selectivity. This preliminary analysis examines the potential association of ferritin as a measure of decreased iron stores with pica and the behavioral symptomatology of ADHD.

Objectives:

This study will test the hypotheses that:

1). Children with ASD are at risk for iron deficiency as documented by low ferritin levels

2). Low ferritin levels will be associated with the presence of pica

3). Low ferritin levels will correlate with increased scores on the ADHD index and attention subscale of the CBCL

Methods: The Autism Treatment Network (ATN) is a network of 14 academic centers that follow a common assessment protocol to establish a standard of medical care for children with ASD. The clinical charts of 100 children with ASD (ages 2-17) recruited to the University of Rochester ATN site were reviewed for ferritin status. Twenty-four children with ferritin levels and Complete Blood Count drawn in clinical care were identified. Data collected included a standardized parent report of pica, the (CBCL) Child Behavior Checklist (Achenbach 1991) and cognitive levels (Mullen Scales of Early Learning or the Stanford-Binet 5th edition).

Results: The children had a mean age of 7 years 1 month (33 months-13 years 7 months). The mean ferritin level was 25.5ng/mL. Ten children (41.7%) had ferritin levels below the laboratory normal range. Eight of the 24 children (33%) had symptoms of pica. The mean ferritin level for children with pica (24ng/mL) was more than six points below the ferritin level for children without pica (30.7ng/mL) but did not reach clinical significance (p=.41) by t test. However, in a post-hoc exploratory analysis, children with IQ scores below 70 were more likely to have pica (p=0.039). Ferritin levels were not correlated with the ADHD index (p=.402) or attention subscale (p=0.946) on the CBCL. Further, ferritin levels were not correlated with anemia as measured by hemoglobin (p=0.205).

Conclusions: In this small preliminary study, over 40% of the children with ASD were found to have ferritin levels below the normal range. Pica was not associated with ferritin level as a measure of iron status, but was associated with lower cognitive level. No relationship was found between the ferritin level and the ADHD index or attention subscale on the CBCL. The participants in this study may have been selected for laboratory testing because of behavioral or dietary concerns on the part of the clinician. Since children with ASD have limited diets and high rates of pica, evaluation of a larger sample with data related to dietary intake is indicated.

130.067 88 Anxiety Symptoms in Children with Autism Spectrum Disorders and Their Siblings. R. A. Libove*[1], J. Hallmayer[2], J. M. Phillips[2], K. J. Parker[2] and A. Y. Hardan[1], (1)*Stanford University School of Medicine/Lucile Packard Children's Hospital*, (2)*Stanford University*

Background: Anxiety symptoms are often co-occurring and debilitating conditions in children with autism spectrum disorders (ASD). However little is known about the characteristics and severity of anxiety in siblings of children with ASD.
Objectives: The purpose of this investigation is to examine anxiety symptoms in a well-characterized sample of children with ASD and to determine if any anxiety symptoms are present in their siblings.
Methods: Participants included children with ASD, their siblings and neurotypical control children between the age of 3 and 12 years. Autism spectrum diagnosis was based on the Autism Diagnostic Observation Schedule (ADOS), Autism Diagnostic Interview Revised

(ADI-R) and expert clinical opinion. Parents completed several behavioral measures assessing anxiety symptoms including the Spence Children's Preschool Anxiety Scale (SCPAS) or Spence Children's Anxiety Scale (SCAS), the Early Childhood Inventory- 4 (ECI-4) or Child Symptom Inventory-4 (CSI-4), and the age appropriate version of the Child Behavior Checklist (CBCL). Analysis of variance (ANOVA) and post hoc comparisons were performed to examine group differences on these parent report anxiety measures. Results: To date, behavioral data on anxiety symptom measures have been collected on 22 children with ASD (mean age: 8.7 ± 2.0), 15 siblings (8.4 ± 2.1) and 20 controls (9.2 ± 1.8). When comparing these 3 groups, preliminary analyses revealed a significant main effect of group on the anxiety domains ($F=1.978$; $p=.007$). These findings were due to differences between the ASD and control groups and the ASD and sibling groups. There were significant differences between the groups on the SCPAS/ SCAS subscales total ($F=7.547$, $p=.001$) as well as Obsessive Compulsive Disorder (OCD) ($F=7.776$, $p=.001$), Injury Fears ($F=5.594$, $p=.006$), Separation Anxiety ($F=6.156$, $p=.004$) and Panic ($F=4.788$, $p=.012$) subscales. Dimensional scoring of the ECI-4 /CSI-4 revealed significant differences on Generalized Anxiety Disorder (GAD) ($F=13.437$, $p<.001$), Specific Phobia ($F=7.119$, $p=.002$), Compulsions ($F=3.583$, $p=.035$) and on the anxiety subscales total ($F=12.870$, $p<.001$). As expected the T-scores on all of the anxiety domains of the CBCL were also statistically significant including Anxiety Problems ($F=14.721$, $p<.001$), Anxious/Depressed ($p=.008$) and Obsessive Compulsive Problems ($p=.001$). In contrast, Social Anxiety domains on the SCAS/SCPAS and CSI-4/ECI-4 were not significant. Post hoc comparisons revealed that all these findings were due primarily to differences between the ASD and control groups and the ASD and sibling groups. No differences were observed between the sibling group and controls.
Conclusions: These preliminary data suggest that many anxiety symptom domains are elevated in a small sample of children with ASD when compared to control children. However, there appears to be no significant difference in anxiety symptoms in siblings of children with autism.

130.068 89 Increased Mid-Gestational IFN-g, IL-4, and IL-5 in Mothers Giving Birth to a Child with Autism. P. E. Goines*[1], D. Braunschweig[2], C. Yoshida[3], J. K. Grether[4], R. L. Hansen[2], M. Kharrazi[5], P. Ashwood[6], J. Van de Water[2] and L. A. Croen[3], (1)*University of California, Davis*, (2)*University of California at Davis*, (3)*Kaiser Permanente*, (4)*California Department of Public Health*, (5)*Genetic Disease Branch, California Department of Health Services*, (6)*M.I.N.D. Institute, University of California at Davis*

Background: Some mothers of children with autism demonstrate immunological differences from mothers of typically developing children, which include autoimmune, allergic, and asthmatic phenomena. Skewed maternal immune function during pregnancy can negatively impact fetal development. Therefore, autism spectrum disorders may be related to prenatal exposures involving the maternal immune system.

Objectives: To characterize mid-gestational serum cytokine profiles in mothers of children with autism compared to mothers of control children.

Methods: Blood samples were collected from pregnant women during 15-19 weeks of gestation. The mothers included in this study gave birth to: 1) a child with autism (AU, n=84), 2) a child with a developmental delay but not autism (DD, n=49), or 3) a child with no known developmental disability (general population, GP; n=159). Serum cytokine profiles were determined using Luminex technology. Mean maternal cytokine levels were compared with a t-test. Multivariable logistic regression was used to estimate odds ratios (OR_{adj}) and 95% confidence intervals (CI) for log-transformed cytokine values, adjusting for maternal age, race, ethnicity, birth country of mother, gestational age, and maternal weight at blood draw.

Results: Mothers whose child was subsequently diagnosed with autism (M-AU) had significantly increased mid-gestational levels of serum IFN-_ (mean (pg/ml): 9.28 vs. 3.44, $P=0.01$; OR_{adj}= 1.52, 95% CI 1.19-1.93), IL-4 (mean: 10.31 vs. 5.16, $P=0.01$;

O R_{adj} =1.51, 95% CI 1.12-2.03), and IL-5 (mean: 7.27 vs. 3.43, P=0.04; OR_{adj}=1.45, 95% CI 1.07-1.98) compared with mothers of children from the general population (M-GP). Findings were similar for early onset and regressive autism, as well as autism with and without mental retardation. Additionally, there was a significant positive correlation between IFN-_, IL-4, and IL-5 levels, such that mothers with high levels of IFN-_ also had high levels of IL-4 and IL-5. This correlation was most dramatic in the M-AU population (r = 0.72-95 in M-AU, r = 0.38-0.77 in M-GP).

Conclusions: We report elevated serum IFN-_, IL-4, and IL-5 during pregnancy in women giving birth to a child with autism. This cytokine profile is observed in individuals with allergy and asthma disorders. Our findings in the peripheral blood therefore agree with previous epidemiological data, which indicate that mothers whose child was subsequently diagnosed with autism have a higher occurrence of mid-gestational allergy and asthma. The maternal immune system is involved in many aspects of pregnancy and fetal development, and is uniquely regulated during gestation to maintain a favorable environment for the fetus. Inappropriate maternal immune responses have been associated with various obstetrical and developmental complications. Further investigation is needed to characterize the relationship between the observed maternal immunological phenotype and autism.

130.069 90 Nutrient Intake, Gastrointestinal Symptoms and Intestinal Microflora in Children with Autism Spectrum Disorder. M. Geraghty*, A. E. Lane, L. Wang, J. E. Wall, J. Altenburger and K. Klug, *The Ohio State University*

Background: Although the etiology of ASD has yet to be fully elucidated, a variety of gastrointestinal (GI) symptoms have been described in this population. Nutrient intake is often compromised in children with autism, for a myriad of reasons. The incidence of gastrointestinal problems has been documented as 30-40% and in some studies up to 80%. Abnormal intestinal microflora has been reported in some children with ASD. Is it possible there is a clinical "gastrointestinal phenotype" to be described in these children?

Objectives: The objectives of this study were to: Indentify nutrient intake deficiencies in children with ASD; Describe gastrointestinal symptoms in children with ASD; Characterize (via molecular techniques) the stool microflora (beneficial and pathogenic) in children with ASD; and Analyze for relationships among these three variables to explore trends for a possible clinical phenotype for further hypothesis testing.

Methods: Twenty-four children with ASD and 12 typical children were recruited for this pilot study. Nutrient Intake, Gastrointestinal Symptoms, and stool microflora were measured in the ASD children. Stool samples from children with ASD were age and gender-matched with samples from typical children. Three day food records were collected and analyzed using the Food Processor Nutrient Analysis Software, 2009 (ESHA Research, Salem, OR). The degree to which the children experienced the various symptoms (bloating, flatulence, abdominal pain, diarrhea, headache) was recorded by placing an "X" on a 5 cm. line numbered 0-5 on a record sheet, with 0= none and 5 = severe. Stool was collected and handled as described in a recently published OSU protocol which demonstrated improved PCR—*Polymerase chain reaction* - quality community DNA extraction. The DNA extraction called for the repeated bead-beating plus column (RBB+C) method. For *Bifidobacteria*, *Lactobacilli*, and *Clostridia,* the specific primers for each real-time PCR assay were used.

Results: A deficient nutrient intake was considered as such for <80% of the Dietary Reference Intake (DRI) of the specific vitamin or mineral. Following is the *percentage of the children* for who had deficient intakes for each nutrient: Vitamin A- 67%; Biotin-63%;Calcium 37%; Choline-96%; Folic acid-25%)Vitamin D, 54%; Vitamin E- 67%, Vitamin K-92%; Magnesium-42%; Manganese-63%; and Potassium-71%. Forty-six percent (11/24) of the children regularly experienced at least one gastrointestinal symptom, with ***Bloating, Flatulence,*** and ***Constipation*** being reported

more frequently as 2.5-4.0 (moderately severe), and ***Abdominal Pain*** and ***Diarrhea*** reported as mild (1.0-2.0). Preliminary molecular characterization of stool reveals a statistically significant lower count of *Lactobacilli* (P= 0.0081) in the children with ASD vs. typical children, and no difference in the *Bifidobacteria* enumeration. Pathogenic bacteria are currently being analyzed. Relationships among the variables will be statistically tested.

Conclusions: The majority of children with ASD have compromised nutrient intakes. Half of the children regularly experience gastrointestinal symptoms, with bloating, flatulence, and constipation being the most severe. The beneficial bacteria, *Lactobacilli,* is significantly lower in the gastrointestinal tracts of children with autism in this study. Relationships among the variables, implications, and preliminary discussions regarding possible clinical phenotypes will be further explored.

130.070 91 Autism Symptoms in ADHD. A. M. Reiersen*, *Washington University School of Medicine*

Background: DSM-IV prohibits the diagnosis of ADHD if symptoms occur only during the course of an autism spectrum disorder. However, clinic- and population-based studies indicate that autistic symptoms are common in ADHD.

Objectives: To give an overview of studies showing evidence of elevated autistic symptoms in ADHD and discuss implications of these findings.

Methods: Relevant published studies are discussed and new epidemiological data from Missouri population-based twin and large sibship samples are presented.

Results: Clinic and population-based studies indicate that autistic symptoms are common in ADHD, particularly for individuals with high levels of both inattentive and hyperactive-impulsive symptoms (combined type ADHD). Progress is being made in distinguishing autistic-like social impairment from social difficulties that may be a direct result of ADHD symptoms. Consistent with the concept of Deficits in Attention, Motor control and Perception (DAMP), individuals with the combination of ADHD and motor coordination difficulties may be particularly likely to exhibit autistic symptoms. The relationship between ADHD and autism symptoms may be stronger for adolescents and young adults than for young children. Emerging evidence suggests some genes can influence both ADHD and autistic symptoms.

Conclusions: Although co-diagnosis of ADHD and autism spectrum disorders has been discouraged, it appears important to assess and treat autistic symptoms in children, adolescents, and young adults with ADHD. Evaluation for autistic symptoms may also be important in defining phenotypes for genetic studies of ADHD.

130.071 92 Screening for Autism Spectrum Disorders in Epilepsy and Tuberous Sclerosis Complex with the SRS and SCQ. Y. Granader*[1], H. Bender[2], R. Nass[3] and W. MacAllister[2], (1)*Yeshiva University & New York University Comprehensive Epilepsy Center*, (2)*New York University Comprehensive Epilepsy Center*, (3)*New York University*

Background: Screening for autism spectrum disorders (ASDs) is of considerable utility in settings where children and adolescents with epilepsy are evaluated. For example, epilepsy occurs in approximately 5-38 percent of individuals with ASDs and in tuberous sclerosis complex (TSC), a disorder typically associated with epilepsy, ASD occurs in approximately 25-50 percent of cases. Rapid detection of ASDs will lead to earlier treatment and improved outcomes. The Social Responsiveness Scale (SRS) and the Social Communication Questionnaire (SCQ) are two commonly administered instruments used to screen for ASDs.

Objectives: The present analysis investigates the utility of the SRS and SCQ in detecting ASDs in children with TSC and epilepsy versus children with epilepsy only.

Methods: 21 patients with TSC (12 males and nine females, ages 5-18, mean = 10.10, SD = 4.30) and 50 patients with epilepsy (26 males and 24 females, ages 4-17, mean = 10.32, SD = 4.27) were assessed. Parents completed SRS and SCQ forms. An independent samples t-test compared mean scores on the SRS and SCQ of the patients

with TSC and patients with epilepsy. Chi-square analyses assessed the classification rates of ASD for the SRS and SCQ scores across the patient populations.

Results: The mean SRS total T-score for patients with epilepsy was 63.44, SD = 13.61 (range = 41-92) and the mean SRS total T-score for patients with TSC was 69.67, SD = 17.39 (range = 42-98). There was no significant mean score difference between these patient populations on this measure (t = 1.618, p = .110) means of these two patient populations.
30% of patients with epilepsy had SRS total T-scores that were above the cutoff for ASD, whereas 52.3% of patients with TSC had SRS total T-scores that were above the cutoff. The chi-square test did not reveal any significant differences in the frequency at which epilepsy and TSC patients were classified as ASD.
The mean SCQ total for patients with epilepsy was was 8.24, SD = 5.71 (range = 0-25) and the mean SCQ total for patients with TSC was 13.10, SD = 7.54 (range = 2-28). Scores were significantly greater for TSC patients (t = 2.967, p <.005).
10% of patients with epilepsy had SCQ total scores above the cutoff for ASDs, whereas 42.8% of patients with TSC had SCQ total scores that were above the cutoff. Pearson's chi-square was significant (8.450, p<.005).

Conclusions: Only scores on the SCQ significantly differed between epilepsy and TSC groups. The SRS may be overestimating autism in this sample of children with epilepsy not due to TSC.

130.072 93 Using the Anxiety Disorders Interview Schedule to Assess Social Phobia in Autistic Adolescents. N. L. Kreiser*, C. Pugliese and S. White, *Virginia Polytechnic Institute and State University*

Background: Social anxiety is a commonly reported problem among higher functioning adolescents with autism spectrum disorders (ASD) (Kuusikko et al., 2008; Bellini, 2004). There is no 'best practice' approach for assessing social anxiety, or diagnosing comorbid Social Phobia (SoP), in people with ASD. Accurate clinical diagnosis of social anxiety is essential to effective treatment delivery. The Anxiety Disorders Interview Schedule (ADIS; Silverman & Albano, 1996) is a widely used, empirically supported clinician-rated diagnostic interview. Despite its application in studies of children and teens with ASD (Wood et al., 2008; White et al., 2009; Reaven et al., 2009), little is known about its psychometric properties with this population. This study evaluated the convergent and divergent validity of the ADIS as a tool for assessing SoP in adolescents with ASD. Objectives: The purpose of this study was to evaluate the utility of the ADIS SoP module for assessing social anxiety in ASD. Methods: Twenty-two adolescents (12-17 years; 4 females) with confirmed ASD diagnoses (via ADOS; Lord et al., 2002, and ADI-R; Lord et al., 1994) and comorbid anxiety disorders were administered the ADIS upon entry into a treatment study. Interviewers trained to reliability administered the ADIS jointly to parent and adolescent. SoP diagnoses were based on the clinician's severity rating (CSR) and clinical interview. Of the 22 participants, 18 had SoP, either as a primary or secondary diagnosis. Parents completed measures of anxiety (MASC-P; March, 1997, ASI-4; Gadow & Sprafkin, 1998) and social ability (SRS; Constantino & Gruber, 2005), teachers completed measures of social ability (SRS), and youth completed a self-report measure of anxiety (MASC-C; March, 1997). Results: Intraclass correlation was used to evaluate agreement among the three raters of the ADIS – clinician, parent, and child. Inter-rater ratings were acceptable (ICC=.802) indicating that parent, child, and clinician ratings of SoP on the ADIS were largely consistent. Kendall tau correlations were calculated in order to measure convergent and divergent validity of the ADIS with other measures. In support of divergent validity, SoP scores on the ADIS were not correlated with verbal IQ (tau=-.037), with measures of social functioning (tau=.214 to .323) or global anxiety (tau=.073). No evidence was found to support convergent validity of the ADIS: SoP scores on the ADIS did not correlate with social anxiety ratings (tau=.063 to .139). Conclusions: Although the results suggest that the ADIS measures something distinct from core ASD symptoms, these results yield inconclusive evidence for its convergent validity. Scores on the ADIS are not confounded with ability to report

symptoms or lack of social skills. Additionally, scores from parent, child, and clinician ratings are consistent. However, clinician rated ADIS scores did not converge with other commonly used measures of social anxiety. Interpretation is difficult because we do not have a universal 'gold standard' for measuring social anxiety in ASD. Future studies must continue to develop valid and psychometrically sound measures of social anxiety, as it is uniquely expressed in ASD, to aid clinical decision-making.

130.073 94 Intestinal Inflammation, Impaired Carbohydrate Metabolism and Transport, and Microbial Dysbiosis in Autism. B. L. Williams*[1], M. Hornig[1], T. Buie[2], M. L. Bauman[3], A. Bennett[1], O. Jabado[1], C. Street[1], D. L. Hirschberg[1] and W. I. Lipkin[1], (1)*Columbia University*, (2)*Massachusetts General Hospital*, (3)*MassGeneral Hosptial for Children/Harvard Medical School; Boston University School of Medicine*

Background: Many children with autism have gastrointestinal (GI) disturbances that affect their quality of life. Although some of these children have been investigated through GI immunopathology, we are not aware of molecular studies to characterize host gene expression or survey microflora using pyrosequencing methods.

Objectives: The objective of this study was to survey host gene expression and microflora in intestinal biopsies from children with autistic disorder and gastrointestinal complaints (AUT-GI) vs children with gastrointestinal complaints alone (Control-GI).

Methods: Transcription profiling was pursued by cDNA microarray using RNA extracted from ileal biopsies (4 per patient) of 15 male AUT-GI and 7 age-matched, male Control-GI patients. Pathway analysis was performed using Ingenuity Pathway Analysis and GO Ontology. Changes in gene expression were confirmed by quantitative real-time PCR. Intestinal microbiota were investigated in ileal and cecal biopsies from AUT-GI and Control-GI children using amplicon-based, bar-coded pyrosequencing of the V2 region of bacterial 16S rRNA gene. Taxonomic classification of 525,519 bacterial sequences was accomplished using the Ribosomal Database Project classifier tool. Differences in microbiota between the two groups were further evaluated and confirmed using Bacteroidete-, Firmicute-, and Sutterella-specific real-time PCR.

Results: Microarray and pathway analysis revealed significant changes in genes involved in carbohydrate metabolism and transport and inflammation in ileal biopsies from AUT-GI as compared to Control-GI subjects. Real-time PCR confirmed significant decreases in the AUT-GI group in the primary brush border disaccharidases, sucrase isomaltase ($p=0.0013$), maltase glucoamylase ($p=0.0027$), and lactase ($p=0.0316$) as well as in two enterocyte hexose transporters, sodium glucose co-transporter 1 ($p=0.0082$) and glucose transporter 2 ($p=0.0101$). In contrast, increases were confirmed for inflammation-related genes in AUT-GI subjects: complement component 1, q subcomponent, A chain ($p=0.0022$), resistin ($p=0.0316$), CD163 ($p=0.0150$), tumor necrosis factor-like weak inducer of apoptosis ($p=0.015$), and interleukin 17F ($p=0.0220$). No significant group differences were observed for the enterocyte-specific marker, villin. In conjunction with changes in intestinal gene expression, bacterial content differed between the AUT-GI and Control-GI groups: pyrosequencing and real-time PCR revealed lower levels of Bacteroidetes (ileum: 50% reduction, $p=0.0027$; cecum: 25% reduction, $p=0.0220$, and higher Firmicute/Bacteroidete ratios in AUT-GI children (ileum: $p=0.0006$; cecum: $p=0.0220$). High levels of *Sutterella* species were found in 47% of AUT-GI biopsies (7/15), whereas Sutterella was not detected in any Control-GI biopsies (0/7; ileum: $p = 0.0220$; cecum: $p = 0.0368$).

Conclusions: We describe a distinctive syndrome in autistic children wherein gastrointestinal dysfunction is associated with altered gene expression reflecting intestinal inflammation, impaired carbohydrate metabolism and transport, and dysbiosis. These findings may provide insights into pathogenesis and enable new strategies for therapeutic intervention.

130.074 95 Autistic Symptoms in a Traumatized Child: A Natural Experiment in Trauma and Resilience– Part II. B. Siegel*[1], A.

Bernard[2], E. C. Ihle[3] and E. Marco[1], (1)*UC San Francisco*, (2)*University of Denver*, (3)*UCSF*

Background:

Research on anxiety disorders in Autistic Spectrum Disorders (ASD) has focused primarily on anxiety as a possible co-morbid phenotypic trait. Few studies examine anxiety as a result of traumatic experiences the child with autism may have, though there is much research on post-traumatic anxiety in non-ASD children. This results in a lack of professional knowledge about how to recognize or treat PTSD in children with ASDs. Last year, we reported a case of PTSD surmised in a 4:7 year-old boy (PL) diagnosed with ASD at 3:1 and confirmed at 4:2 (Bernard & Siegel, 2009). PL's signs of ASD had spontaneously and substantially remitted by 4:7 (falling below all cutoffs on the ADOS). We speculated that the pattern of ASD diagnoses related to having undergone 60 invasive general anesthesia procedures followed by two days of complete eye patching to treat retinoblastoma between age 0:9-4:0 years of age, followed by remission. This report follows the same subject to age 5:7. He has returned to meeting criteria for ASD. The proximal cause is renewed traumatic experiences: At 5:2, a new cancer and further invasive medical procedures began, and continue. This natural A-B-A design allows us to further explore the relationship between signs of ASD and environmental stressors.

Objectives:

The goal of this case study is to add to the literature about recognizing PTSD in the ASD population.

Methods:

At age 5:7, PL underwent clinical evaluation for ASD, cognitive functioning and PTSD. Previous evaluations of PL at ages 3:1, 4:2, and 4:7 years included comprehensive diagnostic interviews, cognitive evaluations, PTSD evaluation, ADOS, and ADI-R. He has now been clinically reassessed at 5:7. PL's narrow, restricted interests and social responsiveness have waxed and waned dramatically when he has been on and off cancer treatment.

Results:

During assessments at 4:2 and 5:7 while in cancer treatment, PL met criteria for Autistic Disorder. At 4:2, he lacked spontaneous communication. He read upcoming items from the WPPSI manual out loud, but refused to respond to any items. He labeled areas of his house as familiar street intersections, and evidenced distress when announcing the intersection where the clinic for retinoblastoma treatment was. At 4:7, when in remission, his language was spontaneous and functional (though slightly echolalic) and his social behaviors markedly improved. Then, at 5:7 when cancer treatments had re-started, PL's repetitive interests and behaviors (e.g., drawing maps of parts of Asia, countries bordering the Aegean Sea, adding numbers by 17 or 144) were very marked and he only spoke when queried repeatedly about his drawings.

Conclusions:

The stress of medical trauma can exacerbate ASD symptoms in a preschool age child. PL's case suggests a need for trauma screening and anxiety assessment in this population, as well as development of empirically-supported treatment methods for psychiatric co-morbidities such as anxiety that may be non-neurodevelopmental in origin.

130.075 96 A Twin Study of Anxiety in Autism Spectrum Disorders: Investigating Prevalence and Associations with the Autistic Triad. V. Hallett*[1], A. Ronald[2], E. Colvert[3], E. Woodhouse[1], N. Gillan[3], S. Lietz[1], P. Bolton[1] and F. Happé[3], (1)*Institute of Psychiatry, King's College London*, (2)*Birkbeck College, University of London*, (3)*Institute of Psychiatry, KCL*

Background: Children with autism spectrum disorders (ASD) commonly experience significant difficulties with anxiety, particularly social anxiety, panic and obsessive compulsive behaviours (White et al, 2009). However, despite the debilitating impact of these symptoms, little is known about how they are associated with the core diagnostic impairments within ASD: social interaction problems, communication deficits and the presence of repetitive behaviours and

interests. Prior studies of the prevalence of anxiety within ASD have often relied on data from a single informant and have used small samples that are not representative of the full autism spectrum.

Objectives: The current study aimed to further our understanding of the overlap between ASD and anxiety by using a large population-based twin sample, gold-standard diagnostic tools for ASD and both parent and self-report measures of anxiety.

Methods: The study forms part of the Twins Early Development Study (TEDS), a longitudinal investigation of approximately 16,000 twin pairs born between 1994 and 1996. Within the Social Relationships Study, we visited 120 of these twin pairs, now aged 13-15, where one or both of the children were diagnosed or suspected of having ASD. These twins were representative of the full autism spectrum. 75 comparison families were also visited, with no history of ASD. The Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview-Revised (ADI-R) were used to determine the diagnostic status of each twin with suspected or diagnosed ASD and their cotwin. In addition, we obtained parent and self-report ratings of anxiety (using the Revised Child Anxiety and Depression Scale); which included measures of panic, social anxiety, obsessive compulsive symptoms (OCD), general anxiety and separation distress.

Results: Rates of parent-reported anxiety were significantly increased in individuals with ASD, compared to controls ($p<0.05$). This was true for all 5 subtypes of anxiety. OCD symptoms were the most frequently observed difficulties in the ASD group, followed by symptoms of panic and social anxiety. In general, cotwins of ASD probands scored at a level that was comparable to the control group. Children with ASD, control children and cotwins were very similar with regard to their self-reported levels of anxiety. The only exception was social anxiety, where children with ASD rated themselves as significantly more anxious than controls (although not cotwins). In the ASD group, symptoms of anxiety were most strongly associated with communication difficulties and also repetitive behaviours and interests.

Conclusions: Our results supported previous findings that children with ASD experience elevated levels of anxiety; particularly symptoms of OCD and panic disorder. However, this was only observable using parent-ratings, suggesting that the children themselves may find it difficult to introspect about their anxiety difficulties. Investigating the associations between anxiety and specific aspects of ASD may help to guide timing and targeting of anxiety interventions. For example, focused intervention on communication may help reduce anxiety in ASD by making interactions less stressful and increasing available coping strategies in high anxiety situations.

130.076 97 Clinical Genetic Clues to the Origins and Outcomes of Autism Spectrum Disorders. E. Lopez*[1], L. Kasmara[1], M. J. Hildebrand[1], P. Carrion[1], L. Swinton[1], C. Tyson[2], M. A. Hrynchak[2], J. J. A. Holden[3], E. Rajcan-Separovic[4] and S. M. Lewis[5], (1)*BC Child & Family Research Institute, University of British Columbia*, (2)*Royal Columbian Hospital*, (3)*ASPIRE, Queen's University*, (4)*Molecular Cytogenetic and Array Research Lab, ASPIRE & the BC Child & Family Research Institute*, (5)*University of British Columbia*

Background: The Autism Spectrum Disorders (ASDs) are the most common childhood developmental disorder. Despite high prevalence (>1/150 births) and clear evidence that early interventions can improve the adverse developmental and behavioural sequelae, ASDs are often not recognized until children reach 3 years of age or older. The population of individuals with ASDs is extremely heterogeneous in regards to clinical presentation, concurrent disorders, co-morbidities and developmental outcomes. In some (up to 40%) cases, ASD are recognized as a component of a specific medical, genetic or chromosomal disorder, and/or occur in association with identifiable teratogenic embryopathies. In most others, no specific genetic or medical etiologic diagnosis is apparent. Affected children can have seizures, co-existing psychiatric disorders, intellectual disability, immune, gastrointestinal disturbances, and major or minor physical anomalies that often occur as clusters of signs and symptoms (i.e., show

patterns), suggesting syndromic relationships to each other and to ASDs.
Objectives: By identifying early, reliable biomarkers and mechanisms of ASD susceptibility, etiology and co-morbidity, we aim to enable earlier individualized treatments for improved outcomes, individual function and full quality of life for affected individuals. Our research program targets largely unexplored clusters/syndromic physiologic co-morbidities of ASDs and is designed to address the overall hypothesis that they serve as clues for understanding critical health similarities and differences among individuals with ASD.
Methods: To narrow our focus to the most informative co-morbidities serving as embryological antecedents of ASD susceptibility and/or etiology, we applied a series of standardized clinical genetic tools that allow for the selection of specific genetic, medical and teratogenic conditions known to co-exist with ASDs amongst a randomly selected cohort of > 450 individuals with an ADOS-G and ADI-R confirmed ASD.
All individuals received comprehensive clinical genetics consultation including review of family, medical, psychiatric and developmental history with thorough dysmorphology exam, including 3D craniofacial and selective EEG and neurostructural imaging. Clinical investigations included Fragile X, karyotype, subtelomeric, and targeted FISH testing of autism-associated loci at 2q37, 7q11, 15q11, 22q11, 22q13 in all subjects. Targeted biochemical studies screened for ASD-associated inborn errors of metabolism, including mitochondrial or other neuropathies coincident with ASD. Samples were also taken for the purpose of high resolution CGH-microarray analysis in separate studies.
Results: Data were analyzed to identify and compare *essential* (non-syndromic/nondysmorphic) or *complex* (syndromic/dysmorphic) ASD subgroups that clearly differed in etiology, co-morbidities, outcome and genetic measures. Comprehensive clinical genetic assessments revealed syndromic co-morbidities encompassing intellectual disability (*ID*), craniofacial, systemic, growth and neuroclinical anomalies [seizures, hearing, vision, psychiatric] within ASD subgroups commonly predictive of ASD-associated genetic, chromosomal, genomic, syndromic and non-syndromic disorders.
Conclusions: By identifying several cases sharing the same phenotypic pattern of symptoms, co-morbidities and/or clinical genetic/syndromic contributors to ASDs, we can begin to generate HealthCare Watches to facilitate optimal anticipatory management and functional outcomes for individuals and families living with ASDs. Our findings aim to set the standard for Clinical Genetic and Child Health Services critical to recognizing and managing brain and body features/co-morbidities of autism to improve individualized therapies and management over the life course.

130.077 98 Microbial Translocation as a Factor for Immune Activation in Autism. C. A. Pardo*[1], S. J. Spence[2], M. Kimura[1], A. Thurm[2], L. C. Lee[3] and S. E. Swedo[2], (1)*Johns Hopkins University School of Medicine*, (2)*National Institute of Mental Health, National Institutes of Health*, (3)*Johns Hopkins Bloomberg School of Public Health*

Background:
Microbial translocation (MT) results from permeation of bacteria or microbial byproducts from the lumen of mucosal barriers such as the gastrointestinal (GI), respiratory or urinary tract into the bloodstream. MT is thought to result from enteropathies and inflammatory disorders of the GI tract that increase permeability of the mucosa or a "leaky gut". In turn, MT is postulated to produce systemic immune activation which results in dysfunction of the central nervous system (CNS). Autistic individuals have been reported to have increased rates of GI abnormalities, including increased mucosal permeability, leading some to postulate that at least some individuals with autism may develop the neurodevelopmental symptoms as a secondary manifestation of MT resulting from a "leaky gut".
Objectives:
To assess the role of MT in patterns of immune activation and evaluate MT serum markers among children with autism (AUT) and typically developing controls (TYP) and to examine the relationship of MT to developmental regression by comparing those with a history of regression (AUT-R) to those without a regression history (AUT-NR).

Methods:
Evidence for MT was examined in the sera from 57 children with autism, [23 AUT-R (mean age 4.38 yrs) and 34 AUT- NR (mean age 4.29 yrs)], and 33 TYP child (mean age 3.5 yrs)] All were participants in a longitudinal study of clinical and immunological factors associated with autism. 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. Markers for MT included lipopolysacharide (LPS - a component of Gram negative bacteria cell walls), LPS-binding protein (LBP) and anti-endotoxin core immunoglobulins IgG and IgM. Circulating levels of MT markers were determined in sera: LPS were determined by the limulus amebocyte lysate assay and LBP and anti-endotoxin core IgG and IgM antibodies were quantified with ELISA assays. Wilcoxon's signed-rank test was used for statistical analysis of significance.

Results:
No significant differences in circulating levels of LPS were observed between the AUT and TYP groups ($p=0.161$); or between the AUT-R and AUT-NR groups ($p=0.974$). LBP levels did not differ significantly between the AUT and TYP groups ($p=0.056$ with trend towards TYP>AUT) or AUT-R vs. AUT-NR group ($p=0.24$).Similarly, the anti-endotoxin core IgG and IgM antibodies levels showed no significant differences between the AUT and TYP groups ($p=0.913$ and 0.418 respectively)

Conclusions:
Circulating levels of MT markers did not differ significantly between children with autism and age-matched typical controls, nor did a history of regression correspond to evidence of circulating MT markers. These observations suggest that MT is not a common physiopathological response in children with autism and fail to provide support the hypothesis of "leaky gut" associated with autistic symptomatology.

130 Neuropathology

130.037 58 Brain Levels of Methionine Synthase MRNA Are Decreased in Autism. R. Deth* and C. Muratore, *Northeastern University*

Background: Methionine synthase (MS) uses folate-derived methyl groups to convert homocysteine to methionine, and its activity is highly sensitive to oxidative stress, which accompanies inflammation. Lower MS activity diverts homocysteine to the synthesis of cysteine and glutathione, and also inhibits methylation reactions, including DNA methylation. Thus MS activity serves as the link between redox status and epigenetic regulation of development. A number of studies have documented oxidative stress in autism, including the presence of brain neuroinflammation.

Objectives: 1. To evaluate age-dependent trends in MS mRNA status in postmortem samples of human cortex. 2. To evaluate MS mRNA status in cortex of autistic subjects *vs.* age-matched controls.

Methods: Standard PCR and qRT-PCR were carried out using primers targeted to cobalamin-binding and cap domains of MS. Amplified MS transcript levels were normalized to GAPDH levels.

Results: In control subjects the MS mRNA level displayed a dramatic age-dependent decrease across the lifespan, amounting to a more than 1000-fold reduction from 28 weeks of fetal gestation to 84 yrs of age. From fetal to 18 yrs the decrease in mRNA was rapid, while a slower decrease prevailed thereafter. In autistic subjects (4-30 yrs of age), MS mRNA levels were significantly reduced, and the decrease was greatest for the youngest individuals. The normally present initial phase of decrease was absent, due to the premature occurence of low levels. This pattern is consistent with an adpative response to oxidative stress which can accompany neuroinflammation.

Conclusions: Our studies demonstrate that the level of MS mRNA in the brain is high during fetal development and gradually decreases with age. This decrease is likely to be important for the normal progression of development, via its influence over DNA and histone methylation. MS mRNA levels in the cortex are abnormally low in autism, which is likely to reflect the presence of oxidative stress. Therapies which counteract oxidative

stress and promote methylation may be a useful strategy in treating autism.

130.038 59 Fetal Microglia Become Activated Following Maternal Immune Challenge. L. Pratt*[1], N. M. Ponzio[2], L. Ni[3], I. Sheng[1] and G. M. Jonakait[3], (1)*Rutgers University/Newark*, (2)*UMDNJ - New Jersey Medical School*, (3)*Rutgers University/Newark and New Jersey Institute of Technology*

Background: Prenatal maternal infection and its accompanying immune response are increasingly recognized as an environmental risk factor for neurodevelopmental disorders such as autism. In mice mid-gestation administration of a viral mimic, polyinosinic:polycytidylic acid (PolyI:C), produces aberrant behavior in the adult offspring. However, though many studies have established an association between prenatal infection and abnormalities in the adult, little work has focused on the mechanisms and events occurring in the fetal brain. We hypothesize that microglia mediate the effects of the maternal immune response in the fetal brain. At mid-gestation in the mouse, microglia are migrating into the brain and are becoming abundant throughout the parenchyma. They are strategically located alongside the cortical-organizing Cajal-Retzius cells in the marginal zone and are notable inhabitants of the ganglionic eminence and thalamus. Microglia in the adult brain can become activated in response to trauma after which they secrete inflammatory cytokines. These cytokines, if elaborated in the fetal brain, could skew brain development altering the differentiation and/or migration of neurons generated there.

Objectives: Though brain cytokines have been measured, a direct investigation of the response of fetal microglia to maternal inflammation is lacking. We will determine whether they are activated and evaluate their cytokine production in control conditions and in response to maternal immune activation.

Methods: In order to study fetal microglia, we have used mice genetically engineered to express EGFP in place of the fractalkine receptor in monocytic derivatives, including microglia ($CX3CR1^{tim1Litt}$). We have developed a protocol that employs a process of both mechanical and enzymatic digestion of fetal brain tissue followed by separation using CD11b magnetic beads. Microglia identification is confirmed by examination of fluorescent cells. With this method we have been able to isolate enriched populations of microglia directly from the fetal mouse brain. Expression of cytokines by the fetal microglia from Poly (I:C)-treated dams was compared by real-time PCR to those of saline-injected dams. Immunohistochemistry was used to examine expression of transcription factors in relation to microglial populations.

Results: We found that microglia from dams injected with 10 mg/kg Poly (I:C) on embryonic day E12.5 produced greater amounts of IL-6 mRNA whereas those from saline-injected dams produced higher levels of IL-10 mRNA. A careful time course showed peak production of these cytokines at E16 though levels remained altered through E18, the last time point measured. There were no detectable differences in the production of IFN_, IL-1_ or TNF_ between the two groups. Immunohistochemistry showed changes in foxp2 expression in the ganglionic eminence.

Conclusions: Our work demonstrates that fetal microglia can be activated and suggests that their cytokine profile can be altered as a result of maternal immune activation. Therefore, microglia may play an active role in altering normal brain development resulting in the structural and behavioral effects observed in the adult.

130.039 60 Morphine and Gluten/Casein-Derived Opiate Peptides Inhibit Cysteine Uptake and Decrease Glutathione in Human Neuronal Cells: Implications for the Redox/Methylation Theory of Autism. M. S. Trivedi*, N. Hodgson and R. Deth, *Northeastern University*

Background:

Parents, support groups and several clinical studies report improvement in behavioral symptoms when autistic children are treated with a gluten-free/casein-free dietary intervention. Opiod derivatives of these food products, namely _-casomorphin (_-CM) and gliadinomorphin (GM) are absorbed from a "leaky gut" and may activate opiate receptors in brain. Morphine has been linked with oxidative imbalances during the development of addiction, and oxidative stress is believed to be a significant etiological factor for

autism. We therefore hypothesized that opiates and food-derived opiate peptides might promote oxidative stress in neurons, leading to exacerbated behavioral symptoms.

Objectives:

1. To observe the acute and chronic effects of morphine and food-derived opiate peptides, as well as the opiate antagonist naltrexone, on cysteine uptake in cultured human neuronal cells.

2. To measure the effect of these drugs on cellular levels of sulfur-containing metabolites, including glutathione (GSH), a major antioxidant.

Methods:

Cellular [^{35}S]-Cysteine Uptake:

SH-SY5Y neuroblastoma cells were grown to confluence in six-well plates in _-MEM media containing 10% FBS and 1% penicillin-streptomycin. Cells were pre-treated with drugs for the specified time and [^{35}S]-cysteine uptake was measured. Non-transported [^{35}S]-cysteine was subtracted from total CPM for each sample and values were normalized to protein content.

HPLC Determination of Intracellular Thiols:

SH-SY5Y cells were pre-treated with drugs prior to addition of ice-cold perchloric acid. After sonication, centrifugation and filtration, the protein-free cell extract was analyzed via HPLC with electrochemical detection to measure thiol levels. Results were normalised to protein content.

Results:

Acute treatment with morphine decreased [^{35}S]-cysteine uptake by 70% ($p<0.001$), while _-CM and GM decreased uptake by 40% ($p<0.05$). Naltrexone blocked both of these effects, indicating involvement of opiate receptors. Long-term treatment with each of the opiates caused a complex pattern of inhibition and recovery of [^{35}S]-cysteine uptake activity, ultimately resulting in a sustained inhibition at 24 and 48 hrs.

_-CM and GM acutely lowered the cellular glutathione level (52% and 62%, respectively), while the level of homocysteine was acutely increased (50% and 44%, respectively). Glutathione levels recovered during the ensuing 8 hrs, although homocysteine levels decreased. Both glutathione and homocysteine levels were reduced at 24 and 48 hrs.

Together these results indicate that opiates acutely inhibit cysteine uptake in neuronal cells, resulting in an increase of homocysteine transsulfuration to cysteine and glutathione. However, this pathway is gradually exhausted, leading to decreased levels of intracellular levels of thiol metabolites, including glutathione. The long-term decrease in glutathione can contribute to oxidative stress.

Conclusions:

This is the first study to demonstrate inhibitory effects of food-derived opiod peptides on redox status and provides mechanistic support for the "Gut-Brain Hypothesis". It reveals a rationale for the beneficial effect of a GF/CF dietary intervention in the treatment of autistic children, and may have general relevance for inflammatory bowel disorders in which gluten and/or casein intolerance plays a role.

130.040 61 Neuronal Growth Delay within the Claustrum of Autistic Subjects. S. Y. Ma*[1], I. Kuchna[1], K. Nowicki[1], J. Wegiel[1], H. Imaki[1], I. Cohen[2], E. London[2], M. Flory[2], W. T. Brown[3], T. Wisniewski[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*, (3)*NYS Institute for Basic Research*

Background: The claustrum ontogeny and morphology indicate a pallial and subpallial origin and explains why the claustrum receives inputs from multiple cortical areas, integrates the multiple inputs into a new signal, and redirects sensory information throughout the striatum and thalamus. Involvement in sensorimotor integration and cognition suggests that the claustrum plays a role in higher order functionality enabling the organism to rapidly adapt to the subtleties and nuances of an ever changing environment (Edelstein and Denaro 2004).

The severely compromised ability to adapt characteristic of autism suggests that these high order functions are not processed properly and that developmental alterations of the claustrum may contribute to the autistic phenotype.

Objectives: The aim of this study was to test the hypothesis that claustrum development is modified and to characterize the type of structural changes employing unbiased morphometric methods.

Methods: Brain hemispheres of 13 autistic and 14 control subjects 4 to 64 years of age were fixed in 10% formalin, dehydrated and embedded in celloidin. The fractionator method was used to determine the number of neurons, the Cavalieri method to estimate the volume of the claustrum, and Nucleator method to determine the volume of neurons and neuronal nuclei.

Results: In subjects 4 to 23 years of age both the claustrum and the prepiriform claustrum were characterized by developmental delays. Volume of the claustrum was reduced by 30% on average, and the total number of neurons by 29% whereas the numerical density was not modified. The volume of neurons in this younger group of autistic subjects was reduced by 32% and the volume of neuronal nuclei was proportionally less (by 31%).

Conclusions: The claustrum showed a similar range of developmental delay to the structures interacting with the claustrum including the entorhinal cortex, several striatal subdivisions and the thalamus as shown in our other studies. These results support the hypothesis that developmental delay of the claustrum may contribute to the rigidity of behaviors and the lack of ability to adapt to a changing environment seen in autism.

130.041 62 The Anatomy and Aging of the Amygdala-Hippocampal Complex in Autism Spectrum Disorder. D. Murphy*, *Institute of Psychiatry*

Background: It has been proposed that people with autism spectrum disorder (ASD) have abnormal morphometry and development of the amygdala-hippocampal complex (AHC). However, previous reports of AHC in ASD are inconsistent – perhaps because they included people from different parts of the spectrum, of variable ages and health characteristics. Moreover nobody has investigated the genetic and biochemical influences on differences in AHC.

Objectives: We carried out two related studies of people with ASD (defined as scoring above cut-off on the Autism Diagnostic Interview, Revised (ADI-R)). In the first we investigated the anatomy, and age-related differences, in the AHC of 32 healthy individuals with ASD aged 9 – 68 years, and 32 healthy matched controls. In the second we investigated if variation in genes which regulate glutamate and GABA contribute to differences in development. Specifically we examined if genetic variation in Glutamic Acid Decarboxylase (GAD) 65 modulates the anatomy of entorhinal cortex.

Methods: MRI

Results: Individuals with AS had a significantly larger raw bulk volume of amygdala ($p < 0.01$), and when corrected for whole brain size ($p < 0.01$). Also there was a significant difference in age-related effects with controls, but not individuals with AS, having a significant age-related increase (respectively; $r = 0.486$, $p < 0.01$, $r = 0.007$, $p = 0.97$). There were no significant differences in volume or age-related effects in hippocampus. Lastly, we found a significant association between variation in GAD65 and increase in volume.

Conclusions: Young people with ASD have a significant difference in volume and aging of the AHC, and this not simply accounted for by a generalised difference in brain. Genes which modulate the concentration of glutamate and GABA may play a crucial part in the abnormal developmental process.

130.042 63 Corticostriatal Circuitry and Inhibitory Control in Autism: Findings From Diffusion Tensor Imaging Tractography. M. Langen*[1], P. Johnston[2], A. Leemans[3], C. Ecker[2], E. Daly[2], C. M. Murphy[2], M. Catani[2], F. dell'Acqua[2], S. Durston[1], H. van Engeland[1], D. G. Murphy[2] and M. R. C. -. A. I. M. S. Consortium[4], (1)*Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht*, (2)*Institute of Psychiatry, King's College London*, (3)*University Medical*

Center Utrecht, (4)*Institute of Psychiatry, London; University of Oxford; University of Cambridge*

Background:
Repetitive behaviour and inhibitory control deficits are core features of autism; and it has been suggested that they result from differences in the anatomy of striatum; and/or the 'connectivity' of subcortical regions to cortex. There are few studies, however, that have measured the micro-structural organisation of white matter tracts connecting striatum and cerebral cortex.
Objectives:
To investigate differences in bulk volume of striatum and microstructural integrity of corticostriatal white matter in people with autism; and their association with repetitive behaviour and inhibitory control.
Methods:
We compared the bulk volume of striatum (caudate nucleus, putamen and nucleus accumbens) and white matter integrity of corticostriatal tracts using (respectively) sMRI and tract specific DTI measures in 21 adults with autism and 22 controls. We also assessed performance on a cognitive inhibition (go/nogo) task.
Results:
Bulk volume of striatal structures did not differ between groups. However, adults with autism had a significantly smaller total brain white matter volume, lower fractional anisotropy of white matter tracts connecting putamen to frontal cortical areas, and worse performance on the go/nogo task. Also, performance on the go/nogo task was significantly related to anatomical variation when both groups were combined; but not within the autism group alone.
Conclusions:
Autism is associated with differences in the anatomy of corticostriatal white matter tracts.

130.043 64 Brain Region-Specific Nurotrophin Changes in Autism. E. M. Sajdel-Sulkowska*, *Harvard Medical School, Harvard Institute of Medicine, BWH*

Background: We have previously reported increased oxidative stress and neurotrophin-3 (NT-3) levels in autistic cerebella. Furthermore, an increase in oxidative stress markers 3-nitrotyrosine (3-NT) and NT-3 showed brain region-specific distribution.

Objectives: The focus of the current study was to determine the levels of brain-derived neurotrophic factor (BDNF) and compare its expression to NT-3 levels across regions of autistic and control brains.

Methods: The levels of NT-3 and BDNF were measured by ELISA in homogenates prepared from frozen 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) and in cerebellar homogenates of 5 control and 6 autistic cases matched for age and PMI.

Results: Cerebellar NT-3 and BDNF levels were increased in autistic cerebella. NT-3 was increased by 40.3% from 561.8 pg/g in control to 788.1 pg/g in autism ($p=0.034$). Similarly, cerebellar BDNF levels were increased by 54.2% from 346.6 pg/g in controls to 534.5 pg/g in autism ($p=0.047$). Both NT-3 and BDNF were increased in BA46. In contrast, both neurotrophins were decreased in BA11 and BA22. In the hippocampus, NT-3 levels were increased while the BDNF levels were decreased.

Conclusions: Our results provide evidence of both over- and under-expression of neurotrophic factors, NT-3 and BDNF, in selected brain regions in autism. The increase is most evident in brain areas associated with attention and working memory, motor coordination, and integration of sensory perception (BA46 and cerebellum). Under-expression of NT-3 and BDNF is evident in BA11 and BA22 (Werickes's area) - brain areas associated with speech processing, decision making, emotional and cognitive processing, learning and social behavior. These two areas also showed the greatest increase in levels of the oxidative stress marker 3-NT, a pattern consistent with clinical manifestations of autism. Since NT-3 and BDNF are critical for growth, differentiation, and survival of neurons, their region-specific deficiency could contribute to the focal nature of autistic pathology resulting in the autistic phenotype. Clearly, further characterization of oxidative stress and neurotrophin levels across brain regions is necessary to increase our understanding of

autistic pathology and to devise means of its prevention and treatment.

130.044 65 Epigenetic Investigations of 15q11-13 Using Autism Post-Mortem Brain. J. M. LaSalle*[1], H. A. Scoles[1], K. N. Leung[1], W. Powell[1], A. Hogart[2], R. Nagarajan[1], M. Martin[1] and D. Schroeder[1], (1)*UC Davis School of Medicine*, (2)*UC Davis*

Background: Autism is an increasingly common disorder of complex etiology, affected by multiple genetic and environmental influences. Epigenetic mechanisms act at the interface of genetic and environmental risk factors in autism. Methylation of CpG dinucleotides and methyl-specific binding proteins are part of an epigenetic pathway essential for parental imprinting and chromatin dynamics during normal brain development. Autism has several phenotypic features in common with the neurodevelopmental disorders with altered epigenetic pathways. Rett syndrome (RTT) is an X-linked pervasive developmental disorder caused by mutations in *MECP2*, which encodes methyl-CpG-binding protein 2 (MeCP2). Prader-Willi (PWS), Angelman (AS), and 15q duplication syndromes are imprinted disorders caused by paternal or maternal 15q11-13 deficiency or duplication, respectively. Copy number variants within 15q11-13 are also associated with a spectrum of neurodevelopmental disorders, including autism, schizophrenia, and epilepsy. Human brain samples are required for further understanding the complex interaction between genetics and epigenetics in 15q11-13 because 1) many of the neurologically relevant genes within 15q11-13 are expressed exclusively in brain, 2) there are distinct tissue-specific patterns of DNA methylation and parental imprinting not observed in blood, and 3) a mouse model of 15q duplication syndrome shows the opposite parental inheritance pattern as the human disease.

Objectives: To perform integrated analyses of genetic, epigenetic, and environmental differences that effect transcript levels of 15q11-13 genes in autism brain.

Methods: Frozen samples of cerebrum and cerebellum from individuals with autism, 15q duplication, PWS, AS, RTT, and Down syndrome were obtained from the Autism Tissue Program, the NICHD Brain and Tissue Bank for Developmental Disorders, and Harvard Brain Tissue Resource Center. DNA, RNA, and protein were isolated and additional tissue fixed and arrayed in tissue microarrays. DNA methylation analyses were performed by bisulfite sequencing, and transcript levels were assessed by quantitative RT-PCR. Immunofluorescence on tissue microarrays was quantitated by laser scanning cytometry for MeCP2 and global DNA methylation. Fluorescence in situ hybridization was performed to investigate chromatin organization and homologous pairing of 15q11-13 alleles.

Results: Epigenetic alteration in autism human brain samples have included reduced MeCP2 due to increased *MECP2* promoter methylation in males, reduced 15q11-13 $GABA_A$ receptor subunit *GABRB3* due to reduced homologous pairing and loss of biallelic expression, and altered global levels of DNA methylation. Epigenetic differences also exist within brain samples with maternal chromosome 15 duplication syndrome, with a subset showing gene expression and DNA methylation not predicted from additional maternal copies.

Conclusions: These results suggest that multiple genetic and epigenetic alterations contribute to 15q11-13 gene dysregulation in autism. The use of human brain samples is critical to further understanding mechanistic explanations and therapeutic solutions.

130.045 66 Dystrophy with Calcification within Brains of Autistic and Control Subjects. I. Kuchna*[1], K. Nowicki[1], H. Imaki[1], J. Wegiel[1], S. Y. Ma[1], E. Marchi[1], I. Cohen[2], E. London[2], W. T. Brown[3], T. Wisniewski[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*, (3)*NYS Institute for Basic Research*

Background: Intracranial calcifications are observed in many diseases including those with viral and bacterial infections, vascular pathology, toxic injury, brain tumors, teratomas, lissencephaly, in children with Fahr's disease, and very often in parasitic infections (Rabbitt et al 1969).

Objectives: Our neuropathological studies of autistic subjects brains have revealed the presence of dystrophic changes with calcification. The aim of this study was to determine the prevalence of this type of encephalopathy in autistic and control cohorts.

Methods: The brain hemispheres of 13 autistic and 14 control subjects 4 to 64 years of age were fixed in 10% formalin, dehydrated and embedded in celloidin and cut into 200 _m- or 50 _m-thick coronal serial sections

Results: Dystrophy with calcification was found in all of the 13 autistic and 14 control brains examined. Dystrophic changes disrupt the continuity of the cortical ribbon and white matter in the frontal, temporal and occipital lobes but only on the lateral side of the brain. The pathology spreads from the leptomeningeal vessels to the cortex and white matter and was detectable by postmortem MRI and histopathological examination. Microscopic examination revealed linear dystrophic lesions free of neurons but with signs of neuronal degeneration at the border between the dystrophic and normal cortex. There was no sign of activation of astrocytes or macrophages within the dystrophic and adjacent brain tissue. The dominant component of the dystrophic lesions was calcium deposits.

Conclusions: Similar morphology of lesions in control and autistic subjects 4 to 64 years of age suggests that dystrophic calcifications undergo relatively limited modifications with age. However, the presence of degenerated neurons and vessels with degenerated smooth muscle cells in the border zone between the lesion and cortex suggests the process of brain tissue damage continues to progress decades after the original causative events. Multifocal dystrophy with calcification in all the examined brains of autistic and control subjects reflects a common pathological mechanism with yet undetermined subclinical or clinical manifestations.

130.046 67 Sensory Filtering Abnormalities in Autism Spectrum Disorder (ASD). J. M. Baruth*, E. M. Sokhadze, L. L. Sears and M. F. Casanova, *University of Louisville*

Background: Individuals with Autism Spectrum Disorder (ASD) often have atypical reactions to the sensory environment. Sensory abnormalities generally associated with ASD are indicated by hypersensitivity and an extraordinary interest in certain sensations. In fact, it has been suggested that altered inhibitory control of sensory intake in ASD may cause sensory overload leading to avoidance of external stimulation. Sensory overload in individuals with ASD can impair functioning, raise physiological stress, and adversely affect social interaction. Since all senses appear involved in the sensory abnormalities of ASD, an underlying cortical pathology is inferred. It has been suggested that sensory abnormalities in ASD may be due to a lack of cortical inhibitory tone in cortical minicolumns--specifically a reduction in peripheral neuropil space. A disturbance in inhibitory function of the brain to irrelevant sensory input, i.e. an impaired ability to suppress evoked potentials elicited by task-irrelevant distracters, has been called 'sensory filtering'.

Objectives: We wanted to test the hypothesis of a sensory filtering deficit in ASD by investigating event-related potentials elicited by task-irrelevant, illusory Kanizsa figures and non-Kanizsa distracter stimuli in a visual oddball task.

Methods: A 128 channel electroencephalographic (EEG) system was used on 15 high-functioning children and young adults with autism spectrum disorder (ASD) and 15 age-matched, typically developing control subjects. Subjects were required to respond with a button-press to rare (25% probability) Kanizsa squares (targets) among Kanizsa triangles (rare non-target distracters, 25% probability) and non-Kanizsa figures (standards, 50% probability) presented on a 15" display. EEG data were segmented off-line into 1000 ms epochs spanning 200 ms pre- to 800 ms post-stimulus onset. Data were digitally screened for artifacts and sorted by condition and averaged to create ERPs.

Results: Participants with ASD had significantly increased P50 amplitudes to non-target Kanizsa stimuli compared to controls at both parieto-occipital and frontal regions-of-interest (ROI). N100 amplitudes were significantly more negative to target stimuli over frontal ROI, and N100 latencies to target stimuli were significantly prolonged over both frontal and parieto-occipital ROI. Also, individuals with ASD had equally augmented P200 amplitudes to all stimuli over frontal ROI with a lack of stimulus discrimination, and had significantly more commission and omission errors in motor responses to target stimuli.

Conclusions: As our results indicate, individuals with ASD failed to suppress task-irrelevant sensory stimuli at pre-attentive stages of visual processing compared to controls. We found difficulty in sensory filtering at pre-attentive (P50) stages disrupted stimulus discrimination in early attentive (N100), later attentive (P200), and behavioral stages (motor responses to targets), i.e. longer latencies to target stimuli at the stage of the parieto-occipital N100, lack of stimulus discrimination at the frontal P200 stage, and a significantly higher rate of error at the stage of motor responses. A sensory filtering deficit in individuals with ASD may impair functioning, raise physiological stress, and adversely affect social interaction. Further research on sensory filtering abnormalities in ASD may lead to earlier diagnosis and intervention by defining electrophysiological endophenotypes in infants and young children at a higher risk of developing ASD.

130.047 68 Inflammatory Cytokines, Bcl2 and Cathepsin D Are Abnormally Regulated in Lymphoblasts of Autistic Subjects.
X. Li*, A. Sheikh, G. Wen, W. T. Brown and M. Malik, *NYS Institute for Basic Research in Developmental Disabilities*

Background:

Autism is a severe neuro-developmental disorder of childhood characterized by impairments in social interaction, deficits in verbal and non-verbal communication, and restricted repetitive and stereotyped patterns of behavior and interests. Susceptibility to autism is clearly attributable to genetic factors, but the etiology of this disorder is unknown, and no biomarkers have yet been proven to be characteristic of autism. Recently, a number of studies have shown that inflammatory cytokines are elevated in the serum, cerebrospinal fluid and brain of autistic subjects. Several studies also implicate the apoptosis-related protein Bcl-2 and p53 as being involved in autism. In addition, it has been suggested that the apoptosis induced by cytokines TNF-_ and IFN-_ may be mediated by cathepsin D, which is the predominant lysosomal aspartic acid protease abundantly expressed in the brain.

Objectives: The aim of this study is to determine whether inflammatory cytokines and apoptosis related protein Bcl2 are abnormally regualted in the lymphoblast of autistic subjects and whether cathepsin D is involved in the modulation of the inflammatory and apoptotic processes in autism.

Methods: Lymphoblasts of 6 autistic subjects (mean age 8.4 ±0.27 yrs) and 6 age-matched normal controls (mean age 7.0 ±0.91 yrs) were included in this study. Subjects fit the diagnostic criteria for autism 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, Invitrogen's Multiplex Bead Immunoassays was used to determine the levels of the different cytokines in lymphoblast. Western Blot Analyses were used to detect the protein expression levels of Bcl2 and cathepsin D. Northern Blot analysis and EM Immuno-gold labeling were used to detect the RNA and protein levels of cathepsin D in lymphoblast.

Results:

We found that cytokines TNF-_ and IL-6 were significantly elevated in the lymphoblasts of autistic subjects as compared to controls,

while anti-apoptotic Bcl2 protein expression was significantly reduced. In addition, our study shows that cathepsin D mRNA and protein expression levels were significantly increased in lymphoblasts of autistic subjects as compared to controls.

Conclusions:

These findings strongly suggest that there is increased inflammation and apoptosis present in autistic lymphoblasts. The elevated activation of cathepsin D in autistic lymphoblasts indicates that cathepsin D may be involved in the regulation of cytokine induced apoptosis in autism.

130.049 70 Repetitive and Stereotyped Behaviors in Autism Are Driven by Abnormal Development of the Striatum but Not of the Substantia Nigra. K. Nowicki*[1], T. Wisniewski[1], I. Kuchna[1], J. Wegiel[1], H. Imaki[1], S. Y. Ma[1], I. Cohen[2], E. London[2], M. Flory[2], W. T. Brown[2] 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: Repetitive and stereotyped behaviors defined as recurring, nonfunctional activities or interests that occur regularly and interfere with daily functioning are defining signs of autism (Gabriels et al., 2005). Several studies have implicated the role of basal ganglia and fronto-striatal circuitry in the pathophysiology of autism, related especially to repetitive and stereotyped behaviors.

Objectives: The aim of this morphometric study was to determine whether the developmental trajectories of neurons within the dorsal, ventral and lateral parts of the substania nigra, the source of dopaminergic innervation of the human striatum, are similar to the pattern of development of four striatal subdivisions including the caudate, putamen, nucleus accumbens and globus pallidus.

Methods: We applied the Nucleator method to detect patterns of developmental changes of neuronal soma and nuclear volume within five subdivisions of the nigro-striatal system in the brains of 12 subjects with idiopathic autism and 12 age-matched controls.

Results: Volume of neurons within the three subdivisions of the substantia nigra, including the dorsal, ventral and lateral parts innervating four parts of the striatum was almost identical in the autistic and control subjects both 4 to 8 years of age and >8 years of age.

However, in the brains of autistic children 4 to 8 years of age we found a significant delay of neuron growth with the volume of cell body smaller than in control subjects by 22% in the caudate nucleus (0.025*), by 21% in the putamen ($p<0.042$*), by 31% in the globus pallidus ($p<0.008$**) and by 37% in the nucleus accumbens ($p<0.004$**). The volume of neuron nucleus was also significantly reduced. No significant difference between the volume of neuronal soma and nucleus in autistic and control subjects >8 years of age suggests that a correction of neuronal growth occurs in late childhood and adulthood.

Conclusions:

The observed pattern indicates a normal development of neurons producing dopamine but a delayed development of striatal neurons. It suggests that development of the nigro-striatal system is desynchronized and that the repetitive and stereotyped behaviors in autism are driven by delayed development of neurons within the striatum but not in the substantia nigra.

Mandell Program

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130.078 99 Parents of Preschoolers with ASD: Stress, Burnout, and Social Support During 3-Month ABA Training. V. A. Bruce*, M. N. Gragg, K. Stefanovich and A. Tiede, *University of Windsor*

Background: Past literature suggests that parents who are more involved in their children's ABA programs experience more stress. Other research has found that stress is lower when parents have more social support. Less research has focused on changes in parents' experiences over time during training to implement ABA interventions with their children.

Objectives: To determine if parents' stress, burnout, belief in ABA, family empowerment, and social support change from an introductory workshop until the end of a 3-month training program.

Methods: Eight parents of preschoolers with ASD completed measures (Perceived Stress Scale, Burnout Measure, Belief in the Efficacy of ABA, Family Empowerment Scale, and Multidimensional Support Scale) at an introductory workshop, and at the end of each month of a 3-month ABA training program. After the introductory workshop, parents were selected to participate in the program based on their motivation, social support, and ability to learn new skills. The program involved 15 hours per week of intensive training. Of the participants selected, 75% were female and 75% were married; mean age was 29.4 years. Most of their children were male (75%), ranged from two to four years old, and were currently receiving additional interventions (75%), such as speech therapy.

Results: Preliminary results indicated that these selected parents' mean level of stress was average, and overall burnout was at the very low level at the introductory workshop. Neither overall stress nor overall burnout increased during the course of training. One parent reported above average stress at the introductory workshop, however, this parent's stress level did not increase during training. In addition, two parents were at the burnout level at the introductory workshop. Although one parent's level of burnout increased over training, the other parent's level of burnout decreased. Both family empowerment and belief in the efficacy of ABA were high at the introductory workshop and stayed high during the course of training; overall, parents in this study reported feeling above average levels of empowerment compared to parents of children with disabilities. On average, parents reported high levels of social support from family and friends, other parents of children with ASD, and professionals; they also reported being highly satisfied with the amount of social support they received from each of these sources.

Conclusions: Past literature has found that parents experience high levels of stress during ABA training programs when assessed at one time point. This study found that parents' stress was average at the start of the program and did not increase as they were trained to implement intensive interventions with their children. This could be due to parents being highly satisfied with the social support they experienced during training. Thus, future training programs should strive to provide a highly supportive atmosphere for parents. It should be noted that strict selection criteria were used for the present study and most parents had higher levels of education and lower income than average for Ontario, Canada. Specific case studies will be presented to demonstrate changes in individual participants over time. Data collection is ongoing.

130.079 100 Pilot Study of Minocycline Treatment for Autism. S. E. Swedo*[1], A. W. Buckley[1], A. Thurm[1], L. C. Lee[2], A. Azhagiri[3] and C. A. Pardo[4], (1)*National Institute of Mental Health, National Institutes of Health*, (2)*Johns Hopkins Bloomberg School of Public Health*, (3)*Jonhs Hopkins University School of Medicine*, (4)*Johns Hopkins University School of Medicine*

Background:

Minocycline is a member of the tetracycline class of antibiotics that has been found to have beneficial effects on neuroinflammation, microglial activation and neuroprotection in disorders such as multiple sclerosis, Parkinson's disease and neuroAIDS. The CNS effects of minocycline appear to be facilitated by modulation of microglial activation and regulation of critical factors in inflammatory pathways such as matrix metalloproteinases (MMPs), nitric oxide production, and apoptotic cell death.

Because microglial activation and neuroinflammation have been reported to be associated with autism, we hypothesized that minocycline might be of value in the treatment of children with autism, particularly if they had a history of developmental regression – a potential marker of the onset of neuroinflammation.

Objectives:

To evaluate the effects of minocycline treatment on autistic symptomatology and markers of neuroinflammation

Methods:
IRB approval was received for an open-label preliminary trial of 6 months of minocycline therapy (1.4 mg/kg) in 10 children (8 boys, 2 girls; mean age 7.58yrs; range 3-12 yrs). CSF, serum and plasma were obtained before and at the end of minocycline treatment (1 child withdrew at 3 months and CSF was obtained then). All subjects met ADOS, ADI-R and DSM-IV criteria for autism. Developmental regression was an inclusionary requirement with loss of social skills and/or language occurring at 18.4 months, on average (range 12 to 28 mos). Symptom severity was rated at baseline and monthly intervals using the Clinical Global Impression Severity Scale (CGI-S) and change was recorded with the CGI-Improvement (CGI-I) scale. In addition, adaptive functioning was measured using the Vineland Adaptive Behavior Scale, 2nd edition, with a mean composite score at baseline of 57.8 (SD 8.6).

Results:
Clinical improvements were negligible, with CGI-S scores remaining stable and only 2 of 10 children demonstrating "minimal improvement" on the CGI-I. The Vineland composite scores also showed little or no change. In contrast to the clinical findings, the laboratory assays demonstrated significant changes in the expression profile of the proform of BDNF (p=0.042) and HGF (p=0.028) in CSF and the proform of BDNF (p=0.028) and IL-8 (p=0.047) in serum when pre- and post-treatment levels of these proteins were compared. No significant changes were observed in chemokines such as CCL2 (MCP-1) or cytokines such as TNF-_, CD40L, IL-6, IFN-_ and IL-1_. No significant pre- and post-treatment changes were seen in the profiles of markers of microbial translocation or MMPs, although there was a trend towards change in MMP7, one of the MMPs that appears to be a target of the effects of minocycline.

Conclusions:
No significant clinical effects were seen in this small group of children with autism in response to minocycline treatment. However, changes in the pre-/post-treatment profiles of the proform of BDNF in CSF and blood, HGF in CSF and IL8 in serum, suggest that minocycline may have effects in the CNS by modulating the production of neurotropic growth factors. Larger studies are needed to determine if minocycline treatment could be helpful for children with autism, and particularly for those with baseline evidence of neuroinflammation.

130.080 101 Prediction of Differential Treatment Outcomes of ASD After EIBI. J. Knapp*, A. Sinoff, T. Frazier and A. Newman, *Cleveland Clinic*

Background: Predicting differential treatment outcomes in young children with Autism Spectrum Disorder (ASD) can lead to improved treatment planning. This is particularly important given the growing ASD population and limited access to treatment programs for many children. Previous research suggests that initial ability (IQ), language, and attention - but not the initial severity of repetitive behaviors - predict greater language gains and better outcomes of early intensive behavioral intervention (EIBI) (Howlin et. al., 2009; Bopp et. al. 2009). However, studies have not agreed as to the most important predictors, few studies have examined the incremental validity of multiple predictors, and no studies have predicted level of educational treatment support after EIBI – an important outcome for short-term treatment planning.
Objectives: To determine which combination of baseline variables (autism symptoms, functional skills, and/or language) is effective in predicting level of educational support after EIBI.
Methods: Participants included 51 children (44 male; 7 female; mean age at baseline = 43.24 months) who graduated from an EIBI program. Youth received an average of two years (Median=22 months) of 1:1 instruction based on the principles of Applied Behavior Analysis (ABA) as well as at least one hour per week of speech and language therapy. Language was assessed using the Preschool Language Scale-4th Edition (PLS-4), Receptive One-Word Picture Vocabulary Test (ROWPVT) and Expressive One-Word Picture Vocabulary Test (EOWPVT). Adaptive functioning was determined using the Vineland Adaptive Behavior Scales-Second Edition (VABS-II) and the Childhood Autism Rating Scale (CARS) was used to obtain a rating of autism severity. Level of support at program exit was coded as minimal or significant by a

psychologist blinded to youths test scores. Hierarchical logistic regression analyses were computed with Preschool Language Scales-4 Total scores, VABS-II scales, and CARS scores as predictors of level of support at exit.
Results: PLS-4 total standard score was entered as the initial predictor because this measure showed the largest bivariate correlation with level of support at exit (n (50), r = -.74, p=<.001). CARS scores and VABS-II Daily Living and Motor Skills measures were individually added in the next step of these regressions based upon their strong bivariate correlations. Results of these hierarchical regressions indicated that adding each of the three baseline predictors individually (CARS, VABS-II Daily Living and Motor Scales) significantly and substantially improved the prediction of level of support at exit beyond baseline PLS-4 Total scores ($\_R^2$= .082 - .173; p=.003 - .050). Adding all three predictors simultaneously in Step 2 resulted in a significant and substantial increase in predicted variance beyond baseline PLS-4 Total scores ($\_R^2$= .271; p=.017).
Conclusions: Initial language ability, autism severity, daily living skills, and motor skills provided the best prediction of level of support after exit of EIBI. This information can help treatment professionals and families in their decision making on maximizing EIBI efforts and future educational needs.

130.081 102 Promoting Imitation and Joint Attention in Preschoolers with Autism Spectrum Disorder. P. Warreyn* and H. Roeyers, *Ghent University*

Background: In typical development, imitation and joint attention are both present in the first year of life. For the preverbal child, they have a significant social-communicative function, and they seem to be longitudinally related to later language and theory of mind development. In preschoolers with autism spectrum disorder (ASD), both imitation and joint attention are impaired. Given the importance of these abilities for present as well as future functioning, imitation and joint attention have been identified as important treatment goals.

Objectives: The objective of the current study was to improve imitation and joint attention in preschoolers with ASD, with a combination of naturalistic and behavioural techniques.

Methods: Eighteen pairs of children (aged 4 – 7 years) participated in the study. Each pair was matched as precisely as possible on chronological and language age, total IQ, gender and pre-test imitation and joint attention scores. Of each pair, one child was randomly assigned to the treatment condition, the other child received care as usual.
The intervention was developed for use in the Flemish rehabilitation centres, where children with developmental-, learning-, and/or behaviour disorders are treated in a non-residential setting. The program consisted of 24 30-minute sessions, with a pace of two sessions per week. Each session comprised both imitation and joint attention exercises, with gradually increasing difficulty over the sessions. The intervention was delivered by the child's usual therapist (either a psychologist or a speech-language therapist). The sessions replaced part of the child's care as usual so both groups of children received a comparable total amount of therapy.
Pre- en post-testing was done by research assistants. This testing included measures of gestural, verbal, procedural and symbolic imitation, and initiating as well as following imperative and declarative joint attention. In addition to these scores, a total imitation- and joint attention score were calculated.

Results: The treatment group's joint attention skills improved significantly more between pre- and post-testing than those of the control group (F(1,34)=9.341, p<.01). For imitation, both groups together obtained higher scores on the post-test than on the pre-test (F(1,34=16.635, p<.001). The treatment group, however, made a significant gain in imitation scores between pre and post (t(17)=-3.976, p<.001), while this was not the case in the control group (t(17)=-1.860, p=n.s.).

Conclusions: The results of our study suggest that it is possible to improve joint attention as well as imitation skills with a limited number of treatment sessions. While our

treatment was clearly more effective in promoting joint attention than standard care, both groups seemed to have improved their imitation skills at post-testing. However, this improvement only reached statistical significance in the treatment group. Upon inquiry it appeared that imitation was also an explicit treatment goal for most children who received care as usual. Although this seemed to be somewhat effective, our results suggest that the current treatment had a stronger effect on these children's imitation skills. In sum, the current intervention seems to be a promising approach to improve both imitation and joint attention in preschoolers with ASD.

130.082 103 Psychotropic Medication Use in Autism Spectrum Disorders (ASD): An Autism Treatment Network Study. P. Manning*[1], E. Anagnostou[2], A. M. Reynolds[3], L. Cole[4], R. McCoy[5], D. Treadwell-Deering[6], A. Whitaker[7], J. M. Perrin[8] and D. L. Coury[9], (1)*Cincinnati Children's Hospital Medical Center*, (2)*Bloorview Research Institute, Bloorview Kids Rehab*, (3)*The Children's Hospital/University of Colorado Denver*, (4)*University of Rochester*, (5)*Oregon Health & Sciences University*, (6)*Baylor College of Medicine*, (7)*Columbia University Medical Center*, (8)*MassGeneral Hospital for Children*, (9)*Nationwide Children's Hospital*

Background: Children with autism spectrum disorders increasingly receive psychotropic medications. Rapid growth in pharmacologic treatment of target behaviors in ASD has occurred despite few medications having proven effectiveness or approval for use for these symptoms.

Objectives: To describe the scope of psychotropic medication use in ASD.
Methods: The study population consisted of children and adolescents ages 2 -18 years entered in the Autism Treatment Network (ATN) Registry. The ATN collects data on children with ASD (autism, Asperger disorder, or PDD-NOS) at 14 sites across the US and Canada. Psychotropic medication use was established by both parent and clinician report of use and entry into the registry.
Results: Medication data were available on 415 children. Of these, 112 (27%) were taking at least one psychotropic medication. Of the 48 children under the age of 3, 2 (4%) were taking at least one psychotropic medication. Of the 184 children between the ages of 3 and 5, 21 (11%) were taking at least one psychotropic medication and 4 (2%) taking two or more. Of the 131 children between the ages of 6 and 10, 58 (44%) were taking at least one psychotropic medication with 29 (22%) taking two or more medications and 4 (3%) taking four or more medications. Of the 52 children older than 10 years, 31 (60%) were taking at least one psychotropic medication with 23 of these (74% of children on medication, 44% overall) on two or more medications. Of the total 112 children receiving psychotropic medication, 52 (46%) were on two or more medications. Most commonly prescribed medications were risperidone, alpha agonists, methylphenidate, SSRI, amphetamine and atomoxetine. Most common reasons for medications were hyperactivity, repetitive behaviors, irritability and attentional concerns.

Psychotropic Medication Use

	<3yo n=48	3-5 n=184	6-10 n=131	>10yo n=52
None	46 (96%)	163 (89%)	73 (56%)	21 (40%)
1	2 (4%)	17 (9%)	29 (22%)	8 (15%)
2 or more	0	4 (2%)	29 (22%)	23 (44%)

Conclusions: Prescription of psychotropic medications is common in ASD, and prescription of multiple medications is also common. Children at different ages show different treatment patterns.

130.083 104 Social Robots Encourage Social Engagement in Children with ASD. E. Kim[1], D. Leyzberg[1], B. Scassellati*[1] and R. Paul[2], (1)*Yale University*, (2)*Yale University School of Medicine*

Background: Even high-functioning individuals with ASD with strong language skills show difficulties in engaging successfully in conversational interactions. Robots have been demonstrated to provide increased motivation and prolonged

engagement. Feedback from a robot may be appealing and motivating in social skills therapy for children with ASD.

Objectives: The present study: (1) compares the social behaviors observed in children before and after interaction with a socially expressive dinosaur robot; (2) compares the effects of robot interaction in children with ASD with those from a typically developing population; (3) assesses the feasibility of using a robot as a therapeutic tool in order to capitalize on any improvement in social behavior seen in the robot context.

Methods: Participants were 9-12 years of age and were divided into two groups: (1) 17 high-functioning individuals with IQ in the normal range but within ASD range on ADOS and ADI-R, as judged by two experienced clinicians; (2) 12 typically-developing individuals with IQ in the normal range and SCQ scores < 6. There were no significant differences in age, verbal or performance IQ between the groups. Participants took part in a 15-minute task that was divided into three phases, each approximately 5 minutes in length: a pre-task interview, a robot interaction task, and a post-task interview. During the pre- and post-task interviews, an examiner engaged the child in naturalistic conversation. The interviews included probes designed to provoke responses on specialized interests, interest in others, eliciting encouragement, and contingency. The robot task asked participants to help a commercial toy dinosaur robot (Pleo, from UGobe Inc.) to cross a playmat containing painted rivers and mountains. Participants were asked to "help Pleo get over his fear of water. Talk to him to encourage him whenever he comes to a stream to help him find the courage to cross over the water." Interactions were video recorded and scored by independent raters.

Results: Participants with ASD spent more time in face-to-face orientation to the interviewer following interaction with the robot than they did preceding it (paired one-sided t-test, df=16, p=0.04). This difference was not significant for participants in the control group. The difference in time spent in face-to-face orientation increased after interaction with the robot, significantly more for chidren with ASD than for children with TD (paired one-sided t-test, df=16, p=.05).

Conclusions: Following a session in which children with ASD were encouraged to speak to a dinosaur robot, they exhibited increases in social behavior directed toward the examiner. These trends are not seen for children in the control group, and cannot be explained by familiarization, as this interaction followed a battery of similar tests with the same experimenter. These results suggest that engaging in "social interaction" with a robot may promote social behaviors with others in children with ASD. The use of robots in interventions aimed to improve social communication in speakers with ASD may be indicated.

130.084 105 The Classroom Practice Inventory: Psychometric Evaluation of a Rating Scale of Early Intervention Practices for Children with Autism Spectrum Disorders. L. Sperry*[1], K. Hume[2], M. McBee[2], B. Boyd[3], A. Gutierrez[4], S. Odom[5] and M. Alessandri[4], (1)*University of Colorado Denver*, (2)*Frank Porter Graham Child Development Institute, University of North Carolina, Chapel Hill*, (3)*University of North Carolina at Chapel Hill*, (4)*University of Miami*, (5)*University of North Carolina*

Background: Comprehensive treatment models are psychosocial or behavioral interventions that target multiple developmental domains. These models often are implemented in classroom settings for individuals with ASD. Though educators may self-identify with a specific model, it is likely that they use additional classroom practices and strategies that may or may not be complementary to the comprehensive model. There is a lack of empirically validated tools to accurately measure the use of those additional practices. The purpose of this study was to empirically validate the Classroom Practice Inventory (CPI), a tool designed to capture teacher's self-report of classroom practices used with preschool-aged children with ASD.

Objectives: The goals were to (1) determine if the CPI was a reliable measure and could discriminate between the comprehensive treatment models of TEACCH or LEAP as well as discriminate those models from an eclectic, non-model specific treatment

approach ("Business as Usual or BAU") based on the classroom practices endorsed by those teachers, (2) provide descriptive information on the types of practices teachers reported they used across model types, and (3) explore variables that predict teachers' selection of specific classroom practices.

Methods: 24 teachers across 3 states (9=TEACCH, 6=LEAP, 9=BAU) completed the CPI at the beginning and end of the school year as part of a larger study. In addition, data related to number of years teaching and highest level of education attained were collected. The reliability of the measure was determined by examining test-retest reliability and internal consistency. Discriminant analysis was conducted to identify the classroom practices on the CPI that best discriminated between classroom types. Regression analyses were conducted to determine which demographic variables predicted teachers' use of specific classroom practices.

Preliminary Results:

Test-retest reliability for pre/post-test time points was M = .80 (.29-.95 across 10 subscales)

Internal consistency was examined using Cronbach's alpha and was .77.

Discriminant analyses revealed two canonical variates. Canonical variate 1 significantly discriminated the three models from each other based on the practices endorsed by teachers. The practices that discriminated the models included Floortime and social stories (endorsed most by BAU teachers) as well as discrete trial training and peer-mediated instruction (endorsed most by LEAP teachers). Canonical variate 2 significantly separated LEAP from BAU and LEAP from TEACCH.

Regression models indicated that number of years teaching children with autism and education level were not significant predictors of teachers' selection of classroom practices. Only two practices, structured teaching and social stories were negatively associated with years teaching (structured teaching, -.145, $p < .05$) and level of education (social stories, -1.61, $p < .05$).

Conclusions: We found that the CPI is a psychometrically robust measure and discriminates between intervention models. Both the development of this measure and the analysis of its psychometric properties are valuable contributions to classroom-based intervention research for children with ASD. Adequately describing and measuring additional practices in use during treatment evaluation is critical to explain intervention effects.

130.085 106 The Effects of Olanzapine On QTc in Children with Autistic Disorder. M. Ghaffari*, S. H. West, R. P. Malone, H. H. Hardison, M. A. Delaney, M. Lech and A. Fuscellaro, *Drexel University College of Medicine*

Background: Antipsychotics are the best-studied drugs for reducing disruptive symptoms such as irritability, hyperactivity, and mood lability in children with autistic disorder. A safety concern with antipsychotics is that administration can be associated with prolongation of the QTc, an electrocardiographic measure of ventricular depolarization and re-polarization. QTc prolongation of greater than 60 msec from baseline or an absolute QTc of greater than 500 msec have been associated with ventricular arrhythmias and sudden death. Olanzapine has not been shown to prolong QTc in adults (Czekalla et al, 2001; Welch & Chue, 2000). However, the effect of olanzapine on this important index is not well studied in children.

Objectives: To examine the effect of olanzapine on QTc in a population of children with autism who participated in a clinical trial of olanzapine monotherapy.

Methods: Patients were 35 children (26 males), aged 3-11.9 years (mean, 6.3 ± 2), diagnosed with autistic disorder. The study included a six-week randomized, double-blind, placebo-controlled phase, followed by a six-week open treatment phase. Responders at the end of the 6 week open treatment phase continued to receive open olanzapine for an additional 20 week (32 weeks total study drug exposure). Concomitant medication use was not permitted during the

study. Electrocardiograms (ECG) were obtained at baseline, week 12, and week 32. They were obtained in a fasting state between 9 and 10 AM, when drug was at its trough level. To investigate whether there were any QTc increases associated with olanzapine administration, paired t-tests were performed comparing the QTcs obtained at baseline to the QTcs obtained at weeks 12 and 32.

Results: The mean QTc was 409.3 ± 19.1 msec at baseline, 407.3 ± 25.2 msec at week 12, and 411.3 ± 40.1 msec at week 32. Thus the change in QTc from baseline to week 12 was -2.1 ± 29 msec ($t = 0.42$, $df = 34$, $p = 0.68$). The mean QTc change from baseline to week 32 was 2.28 ± 42.7 msec ($t = -0.226$, $df = 17$, $p = 0.824$). No child had a QTc greater than 500 msec during this study. One child with a baseline QTc of 388 msec had an increase of ≥ 60 msec at weeks 12 and 32 compared to baseline. His maximum QTc was 452 msec at week 32.

Conclusions: The results of this study suggest that olanzapine monotherapy does not significantly affect the QTc when administered to children with autism.

References**:**
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130.086 107 The Impact of Multisystemic Therapy on Youths with Autism Spectrum Disorder. D. V. Wagner*[1], S. M. Kanne[2], M. O. Mazurek[3], J. E. Farmer[4] and C. M. Borduin[5], (1)*University of Missouri, Columbia*, (2)*Thompson Center for Autism and Neurodevelopmental Disorders*, (3)*University of Missouri - Columbia*, (4)*University of Missouri*, (5)*University of Missouri-Columbia*

Background: Parents of youths with Autism Spectrum Disorder (ASD) report a multitude of individual and family problems, including high levels of stress, maladaptive coping patterns, depressive symptoms, substance use, and frequent conflict. In addition, many youths with ASD engage in problematic behaviors (e.g., interpersonal aggression) that have been linked with negative outcomes for other family members. Multisystemic therapy (MST; Borduin & Henggeler, 1990) is an intensive, family- and community-based treatment that has been evaluated in multiple randomized clinical trials with youths exhibiting severe behavioral problems, including antisocial behavior. MST has demonstrated improved family functioning, improved caregiver and youth mental health, and reduced youth problem behaviors relative to comparison treatments and services (Henggeler, Schoenwald, Borduin, Rowland, & Cunningham, 2009). Furthermore, adaptations of the MST model have demonstrated promising results for other clinical populations (e.g., youths with type-1 diabetes, youths with HIV). We believe that MST may represent an effective treatment in reducing severe behavioral problems and improving family and peer relations in youths with ASD.

Objectives: The primary goal of this pilot study is to evaluate the effects of MST on youths diagnosed with ASD and their families. More specifically, we are examining the impact of MST on relevant individual (i.e., behavior problems, peer relations), parent (i.e., parenting stress, marital conflict), and family (i.e., conflict, warmth) variables.

Methods: Participants include youths (11-17 years of age; approximate N = 8) who have (a) a diagnosis of ASD that has been confirmed by the Autism Diagnostic Observation Schedule or the Autism Diagnostic Interview-Revised within the past 6 months and (b) severe behavior problems (e.g. physical aggression towards another person, property destruction) during the past 3 months. Youths and their families who consent to participate in MST complete a multiagent, multimethod assessment battery designed to assess functioning across individuals and systems using family (e.g., Family Adaptability and Cohesion Evaluation Scales-II), youth (e.g., Vineland-II), parent (e.g. Parenting Stress Index-Short Form), sibling (e.g. Child Behavior Checklist), and teacher (Teacher Report Form) measures at pre- and post-treatment assessments.

Results: Scores from self-report, other-report, and observational measures will be compared pre- and post- treatment with

respect to the following variables: youth autism traits, youth peer relations, youth adaptive functioning (in home, school, and community settings), youth behavior problems, parent social support, parent symptoms, parent stress, parent marital satisfaction, and family relations.

Conclusions: The results of this ongoing pilot study will have implications for the continued adaptation and validation of the MST model for ASD youths who exhibit severe behavior problems. This study represents a step towards a more comprehensive approach to ASD treatment that is designed to improve both adolescent and family functioning and is intended to lead toward a larger randomized clinical trial in which we plan to examine treatment outcomes and mechanisms of change with this population.

130.087 108 The Parental Experience of a Home-Based Joint Attention Intervention for Preschoolers with Autism. S. Ferguson*, *University of Canberra (ACT)*

Background:

Many parents report that receiving a diagnosis of autism for their young child is one of the most distressing events in their lives. At this very vulnerable time they feel pressured to immediately begin an intervention regime. They can receive very conflicting advice about the efficacy of various approaches. Many interventions require the parent to hand over responsibility to other agencies, like early intervention preschools, therapists, autism experts or teams of workers. Parents can become marginalized into the role of the "funders" of programs, rather than the instigators. This model can disempower parents who need to be the life long educators, therapists and advocates for their child.

This study looked at the implementation of a home based intervention for families with a preschool aged child with autism. It used a parent training paradigm, and focused on developing joint attention skills, using both behavioural and developmental, play based strategies. Methods of training were both psycho-educational and experiential. Parents were given notes on autism, interventions, and the rationale for targeting joint attention, as a pivotal skill to teach these children.

Objectives:

The first objective of this study was to explore the efficacy of training parents to teach joint attention skills to their children with autism using this model. The next objective was to measure the effects of that teaching on the children's cognitive, adaptive, behavioural and language development. The final objective was to explore the experience of this intervention for parents, and to measure its effects on parental stress and feelings of competency.

Methods:

Six families with a three to four year old child, recently diagnosed with autism, were recruited from the local autism advisors. They completed 20 intervention sessions with the researcher. Initial sessions were intensive, and clinic based, then they ran weekly, in the home for the last 10 weeks. Each session involved a 10 minute, videoed, semi structured play between the child and the parent; a table based skill teaching session, a floor play session and a discussion of how to embed the skill into routines. Notes were given weekly.

The experimental design was a single subject repeated design. Pre and post measures included a range of cognitive, behavioural, adaptive and language standardized assessments of the child. Parent assessment included the Parenting Stress Index II, and a semi structured interview conducted at the end of the program. Pre and post assessments will be statistically analysed for significant change and the interviews will be transcribed and analysed for recurrent themes. The videos will be coded for changes over time in skill acquisition, in both the parents and the children.

Results:

Data is being processed at the moment and preliminary results will be presented at the conference.

Conclusions:

This study will give a clearer picture of the usefulness of a time limited, skill targeted, parent training program, not only for facilitating a child with autism's development, but also for fostering parental wellbeing, and feelings of competence.

130.088 109 Understanding Treatment Response in a Pivotal Response Treatments-Based Program for Children with Autistic Spectrum Disorder. K. Fossum[1], I. M. Smith*[2] and S. E. Bryson[3], (1)*Dalhousie University*, (2)*Dalhousie University & IWK Health Centre*, (3)*Dalhousie University/IWK Health Centre*

Background: Comprehensive treatments that start early and are based on the principles of Applied Behaviour Analysis (ABA) substantially improve outcomes in just under 50% of children with autistic spectrum disorders (ASD). The remaining 50% of children display varying levels of response to treatment, ranging from very little or no change to modest gains. Understanding this variable response to treatment in ASD requires examining the impact of a variety of important factors (e.g., child, family and environmental variables) on treatment outcomes.

Objectives: The overall objective of the current study is to examine specific child factors that may help to explain the variable response to treatment in a group of children with ASD enrolled in the early intensive behavioural intervention (EIBI) program in Nova Scotia, Canada. The program is based on Pivotal Response Treatment (PRT), and is supplemented by Positive Behavioural Support (PBS) practices. Key program components include parent training, one-to-one therapist-led intervention for up to 15 hours per week, and monitoring of treatment fidelity for both parents and therapists.

Methods: Data were collected for 29 children with ASD. The mean age for the total sample of children was 51.21 months (*SD* = 10.09) at the start of intervention. Initial cognitive ability, as measured by the Merrill-Palmer-Revised Scales of Development (M-P-R) Cognitive scale standard score was 51.97 (SD = 27.81). Baseline video data were collected of the children interacting with trained therapists in play situations. These videos were coded for the presence of six child variables that are empirically and/or theoretically linked to outcomes in PRT-based intervention (i.e., toy contact, avoidance, approach, stereotyped and repetitive vocalizations and non-verbal behaviours and affect). The degree to which children displayed these behaviours was examined in relation to language outcomes after 6 months of therapist- and parent-delivered PRT.

Results: Preliminary analysis (n = 6) examining child factors predictive of response to PRT indicated that children's appropriate toy contact at baseline was significantly positively correlated with expressive language at 6 mo (r = .97, p < .006), controlling for initial language level. In addition, avoidance behaviour was negatively correlated with language, though not significantly in this small preliminary sample (r = -.41, *ns*). Additional data will be presented for the total sample (n = 29).

Conclusions: Pre-treatment levels of toy contact, avoidance, approach, stereotyped and repetitive vocalizations and non-verbal behaviours, and child affect may predict the variable response to PRT-based intervention in children with ASD. Ultimately, these variables may point to important initial intervention targets for children who do not display optimal response to PRT.

130.089 110 Use of Complementary and Alternative Medicine (CAM) in Children with Autism Spectrum Disorders (ASD): An Autism Treatment Network (ATN) Study. D. L. Coury*[1], E. Anagnostou[2] and P. Manning[3], (1)*Nationwide Children's Hospital*, (2)*Bloorview Research Institute, Bloorview Kids Rehab*, (3)*Cincinnati Children's Hospital Medical Center*

Background:

Complementary and alternative medicine (CAM) treatments are becoming widely used as an adjunct to conventional medical treatment for many conditions. CAM treatments are often recommended by several ASD advocacy organizations as potential components of an overall treatment plan and families of children with ASD may be exposed to CAM treatments through various media outlets.

Objectives:

The objective of this study is to determine the frequency of CAM treatments in a large ASD registry, and identify factors associated with the use of CAM treatments.

Methods:

Children and adolescents with a diagnosis of ASD (autism, Asperger disorder, or PDD-NOS) confirmed by ADOS, age 2 – 18 years were enrolled into the Autism Treatment Network (ATN) Registry which collects data on children with ASD at 14 sites across the US and Canada. Upon entry into the registry, parents completed a medical history questionnaire including use of CAM treatments, GI symptom inventory, Child Sleep Health Questionnaire (CSHQ), and demographic data.

Results: 201 (17%) of 1,212 children were on special diets. Of the 201 children, 53% were on a casein free diet, 53% were on an "other diet". 19% of children diagnosed with Autism, 7% of children diagnosed with Asperger's, and 14% of children diagnosed with PDD/NOS were on a special diet (P = 0.004 on chi-squared test.)We examined the relationship between GI and sleep problems and special diet use. Using a p-value of 0.001 as evidence of an association (Bonferroni adjusted for multiple looks) children with GI problems were more likely to be on any special diet and specifically were more likely to be on casein free/gluten free, no processed sugars, and "other" diets. No significant association was found for sleep problems. Approximately 21% of children received one or more complementary alternative treatments. 22% of children diagnosed with Autism, 20% of children diagnosed with Asperger's, and 19% of children diagnosed with PDD/NOS received one or more CAM treatments. The most common treatment across the three diagnoses was taking other types of vitamins. 12% of children are taking 2 or more CAM treatments. Children with GI problems were more likely to be on any CAM treatment and specifically were more likely to have been treated with digestive enzymes, other vitamins or probiotics. Chelation was used by 4% and hyperbaric oxygen treatment by 3% of those reporting CAM use, each accounting for less than 1% of all children in the ATN registry.

Conclusions:

CAM treatments for children with ASD are common. Children with autism were more likely to be receiving special diets than children with Asperger's or PDD-NOS. Children with GI symptoms were more likely to be receiving CAM treatments in the form of special diets, digestive enzymes, other vitamins or probiotics. Health care providers should be aware of CAM use in patients with ASD and help families monitor their child's response to these treatments.

130.090 111 Using Computer Aided Instruction to Improve Motivation and Learning. C. Whalen*, *Jigsaw Learning*

Background: There are several studies showing promise for Computer Assisted Instruction (CAI) in teaching a variety of skills to children with Autism Spectrum Disorders (ASD). TeachTown: Basics (TT-B) is a CAI program that focusses on individualized instruction of academic (receptive and expressive vocabulary), social (recognizing emotions, eyegaze tracking) and functional (auditory memory for multistep directions) skills. TeachTown includes a manual for implementing naturalistic off-computer or 'Connection' activities (TT-CA) which are closely aligned with TT-B content.

Objectives: We tested whether instruction via TT-B of a range of academic, social, and functional activities skills would improve learning relative to off computer learning (TT-CA) in ASD students. Individualized learning was measured by analyzing both within and between subject data in preschool and K-1 special education classrooms in a large public school district in Los Angeles.

Methods: 47 preschool and K-1 students in ASD classrooms participated in both on- (TT-B) and off- (TT-CA) computer activities. TT-B was implemented over 3 months for an average of 20 minutes a day (includes a range of 13-24 minutes). TT-CA were conducted for 20 minutes a day, by an education professional both in small groups

and 1:1, as per instruction from a manual. Within and between subjects' comparisons were conducted to evaluate the difference between on and off computer learning. Children in the within subjects' design received both 'treatments' for 3 months at a time; half were included in TT-B first and the other half participated in off-computer tasks first.

Results: In a comparison with students in the TT-CA, the TT-B students showed more improvement overall on language and cognitive outcome measures including measures of expressive and receptive vocabulary (PPVT and EVT) and broader measures of social, academic, language and memory using the Briganz. In addition, TT-B students demonstrated significant progress overall in the program. Students who used TT-B for more time per day demonstrated larger gains within the software and in outcome measures. When analyzing within subject data, we found that students made more progress overall while using the TT-B, compared to when they only engaged in TT-CA. Students who completed TT-B first continued to make progress 6 months after first using the program. The most improvement was shown in auditory memory and social skills, with smaller gains in language and academics. Furthermore, we found improved attention, spontaneous language, affect, and joint attention, for students using TT-B compared to TT-CA.

Conclusions: These findings offer possibilities for the use of CAI for contributing to the remediation of deficits for children with ASD. It provides an affordable intervention option that is both motivating and effective even when compared with teacher led instruction. The individualized nature of the lessons, the data portability and ease of use for home and school communication will be discussed. This presentation will include all data analyses from both between and within subject comparisons along with a brief demo of the program, and video clips of participating students.

130.091 112 Using the Vineland - II to Screen for Psychopathology in Individuals with Autism. K. Wells*, A. Perry, J. M. Bebko and N. Luthra, *York University*

Background:

Although the focus of the Vineland Adaptive Behavior Scales – Second Edition (Vineland – II; Sparrow, Cicchetti, & Balla, 2005) is obviously adaptive skills, it also includes an optional maladaptive domain, consisting of four sections: internalizing, externalizing, critical items, and other. The scale produces three standard scores: internalizing, externalizing, and the Maladaptive Behavior Index. The authors describe this section as a screening tool that may be used to determine the need for further behavioural evaluation. However, the manual provides substantially less information on the maladaptive index as compared to the adaptive sections of the scale.

The Vineland – II manual does provide a comparison of maladaptive scores from the normative sample with verbal and nonverbal children and adolescents with autism. The results suggest that individuals with autism exhibit higher levels of maladaptive behaviour across all scales. The difference between the sample with autism and the normative group was greatest on the internalizing section. According to the authors the higher scores are due, in part, to the fact that a number of the internalizing items are characteristic of autism. The externalizing section scores are also higher among those with autism than the normative sample, but are still within the average range. The authors suggest that this is because many of the items within the externalizing scale are social in nature.

Objectives:

The information about the Maladaptive domain provided in the Vineland – II manual suggests that the characterization of internalizing and externalizing behaviours may not be appropriate for individuals with autism, due to the nature and characteristics associated with the disorder. The intent of this study is to analyze the individual items within the Maladaptive domain in order to determine a more appropriate framework for screening maladaptive behaviour in individuals with autism using the Vineland – II.

Methods:

This was a file review study across multiple sites for individuals with autism in Toronto, Ontario, Canada. All measures were given within the context of routine clinical assessments by a team of trained clinicians. The Vineland – II was used as the measure of adaptive and maladaptive behaviours. In addition, measures of cognitive skills (Mullen Scales of Early Learning or The Stanford Binet Intelligence Scales – Fifth Edition), and severity of autism (Childhood Autism Rating Scale) were also administered to the participants.

Results:

Over 120 children, adolescents, and adults with autism and developmental disabilities participated in this study. Data analyses are currently underway. A factor analysis of the items within the maladaptive section of the Vineland – II will be performed as a means of determining whether or not the current construction of the scale is valid for individuals with autism and how maladaptive factor scores are related to participant characteristics, such as age, cognitive level, and severity of autism.

Conclusions:

Conclusions will focus on the conceptualization and clinical implications of the results regarding the use of the Maladaptive domain within this population, including possible misinterpretations of the scale and how the maladaptive section of the Vineland – II may be better utilized for individuals with developmental disabilities and autism.

130.092 113 Visual Attention to Faces Among Preschool Children with Autism Spectrum Disorders: Preliminary Findings From a Randomized Control Trial of a Parent Training Program. D. Ostfield*[1], L. Tidmarsh[2], E. Fombonne[1] and K. Cornish[3], (1)*McGill University*, (2)*Fraser Health Authority*, (3)*Monash University*

Background:

Theorists of typical development have empirically documented a developmental trajectory of dyadic behaviours supporting the acquisition of joint attention and referential communication. In autism, early-onset difficulties in dyadic engagement, particularly the ability to process information from faces, may deprive children with an ASD of social learning opportunities critical to joint attention. Given that joint attention delays are typical of autism, it is vital to understand the nature of these difficulties and their amenability to change.

Objectives:

To determine whether behavioural changes occur in children's gaze perception skills following the More than Words (MTW; Sussman, 1999) parent-training program using a novel, computerized task as an outcome measure of treatment effectiveness. MTW is a 12-week program that teaches parents how to use natural opportunities to socially engage their child in a manner that adheres to their child's interest or activity by fostering the dyadic coordination of shared attention.

Methods:

Fourteen children (mean CA= 34.07 months; SD = 6.16 months) newly diagnosed with either Autistic Disorder (n=12) or Pervasive Development Disorder not otherwise specified (n=2; diagnosis based on ADOS/ADI) were assigned to either a parent training (PT, n = 7) or waiting-list control (CT; n = 7) group based on a matched-pair, random assignment procedure. At the pre-intervention assessment there were no significant group differences in either developmental or social functioning. Groups were similar in terms of age, gender, ethnic distribution, languages spoken in the home, and the number of children attending daycare or receiving behaviour intervention services. Children's perception of different gaze directions was measured using the *Eye Gaze Preference Task* (EGPT). During the EGPT, a central probe engages the child's attention before each experimental slide. The display then changes to 1 of 4 conditions: eyes closed, direct gaze, or gaze averted to the left or right. Participants passively view 2 blocks of 16 randomly presented faces. Separate videos of the participant's face and computer screen were recorded and viewed

simultaneously to code children's fixation patterns. Inter-rater reliability was established.

Results:

A pattern emerged across the course of treatment among children whose parents participated in MTW, which fell short of significance but was in the expected direction. Children whose parents received the training demonstrated greater mean increases according to specific gaze directions in their orienting responses (direct: *M* = 8.43, *SD* = 11.85; averted: *M* = 7.28, *SD* = 10.73) and percentage of total fixation time (direct: *M* = 9.04, *SD* = 15.6; averted: *M* = 7.73, *SD* = 8.88). There were no observed post-treatment gains among children in the control group across performance variables (orienting responses direct: *M* = .43, *SD* = 9.69, averted: *M* = -.43, *SD* = 9.91; percentage of total fixation time direct: *M* = -1.05, *SD* = 10.88, averted: *M* = 1.64, *SD* = 12.11).

Conclusions:

Data reported lead to tentative suggestions that the MTW program may support developmental gains in children's dyadic social responses. The exploratory data warrants replication among a larger sample of children with comparisons to alternative treatment approaches.

130.093 114 Metabolic Effects of Olanzapine in Children with Autistic Disorder. R. P. Malone*, M. Ghaffari, S. H. West, H. H. Hardison, M. A. Delaney, M. Lech and A. Fuscellaro, *Drexel University College of Medicine*

Background: Antipsychotics are the best-studied drugs for reducing symptoms in children with autistic disorder. A safety concern with antipsychotics is that administration can be associated with increase in metabolic parameters such as weight, body mass index (BMI), fasting glucose, and fasting lipids (triglycerides, total cholesterol, HDL, LDL). Increase in metabolic parameters has been associated with increased risk of cardiovascular disease and diabetes.

Objectives: This study examines the effect of olanzapine on metabolic parameters in a population of children with autism who participated in a clinical trial of olanzapine.
Methods: Patients were 33 children (25 males, 8 females), aged 3-11.9 years (mean, 6.58 ± 2), diagnosed with autistic disorder. The sample included 24 Caucasians, 8 African Americans, and one Asian. The study included a six-week randomized, double-blind, placebo-controlled phase, followed by a six-week open treatment phase. Responders at the end of the 6 week open treatment phase continued to receive open olanzapine for an additional 20 week (32 weeks total study drug exposure). Safety measures included weekly BMI and laboratory studies were obtained at baseline and week 12. Paired t-tests were performed comparing week 12 and baseline values to identify any significant olanzapine associated increases in BMI z-score, fasting glucose, and lipids. The CDC [1] BMI criteria were used to categorize children as obese ($\geq 95^{th}$ percentile for BMI), overweight ($85^{th} \leq x < 95^{th}$ percentile), healthy ($5^{th} \leq x < 85^{th}$), and underweight ($< 5^{th}$ percentile).
Results: At baseline, 70.3% of children were at a healthy weight, 21.6% were overweight, 2.7% were obese, and 5.4% were underweight. By week 12, 42.4% were healthy weight, 21.2% were overweight, and 36.4% were obese. Paired t-tests comparing the BMI *z*-score from baseline and week 12 showed a mean increase of 0.85 ± 0.5 which was significant ($t = 9.8$, $df = 32$, $p = 0.0000$). There was no clinically significant change in fasting glucose. There was also no systematic change in any of the fasting lipid parameters. For example, at baseline, six subjects had elevated triglycerides (TG), but by week 12, two of these subjects experienced normalization in their levels while four subjects with normal TG levels at baseline experienced an elevation. Overall, the mean increase for fasting triglycerides was 1.8 mg/dL which did not reach statistical significance. Mean total cholesterol increased by 3.8 mg/dL from baseline to week 12, not statistically or clinically significant. Mean changes in HDL and LDL were 0.2 mg/dL and 4.5 mg/dL, respectively; neither reached statistical or clinical significance.
Conclusions: The results of this study

suggest olanzapine significantly increases BMI when administered to children with autism. Other clinically significant effects on metabolic parameters were not found in this twelve week study.

Reference:

1. www.cdc.gov

130.094 115 Parents of Preschoolers with ASD: Weekly Changes in Feelings of Competency throughout Twelve-Week ABA Training. D. D. Barrie*, M. N. Gragg, T. M. Carey, B. E. Drouillard and J. L. Scammell, *University of Windsor*

Background:

There is considerable research supporting the effectiveness of Applied Behaviour Analysis (ABA) for improving intellectual, social, emotional, and adaptive functioning of children with Autism Spectrum Disorders (ASD). 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 earlier treatment for their children is critical. Many parents want training to implement ABA with their own children, thereby providing behavioural interventions earlier. However, research findings investigating parent experiences while implementing in-home ABA programs have been mixed. Some studies have found that parents experience higher stress, while others report improved parental outcomes in feelings of empowerment, self-esteem, and social support. However, many of these studies have only measured parental experiences at one point in time and parents' perceptions of their experience and competencies may change over time.

Objectives:

To examine weekly changes in parents' perceptions of their training experiences and competencies throughout a 12-week intensive ABA training program.

Methods:

Participants were 14 parents/caregivers of preschool children with ASD (86% mothers), with a mean age of 35.4 years (range 26 – 49.5). All had some college education or more, and average family income was $60,577 (Canadian). Their children (86% boys) ranged in age from 28 to 51 months; 10 had diagnoses of Autistic Disorder and 4 had diagnoses of PDD-NOS. Participants completed intensive 12-week ABA training at a ASD preschool. Each week, participants completed a 17-question survey rating their perceptions of training over the past week (e.g., "How much did you understand the tasks in your child's program?" "How independent were you in carrying out your child's program?" "To what extent do you feel in control of your child's ABA program?")

Results:

The six most positively rated items by parents were instructor effectiveness (13 parents), instructor support (11 parents), effectiveness of ABA in improving outcomes (11 parents), enjoyment of the training program (10 parents), their contribution to their children's therapy (9 parents), and their understanding of the ABA concepts covered (8 parents). The four least positively rated items were the challenge of implementing their children's program (14 parents), the stress of the training program (14 parents), effort taken to complete homework assignments (12 parents), and the difficulty of carrying out ABA tasks (11 parents). Overall, parents' ratings of their experiences and competencies became more positive over the 12-week training program. Parent ratings were temporarily less positive at times of transition; around Week 4 parents started working independently with another child, and around Week 9 parents began teaching ABA to their support persons.

Conclusions:

Parents' perceptions of their experiences and competencies became more positive over the course of the 12-week ABA training program. Although parents found the training to be challenging and stressful, they perceived their instructors as effective and supportive. They felt positive about their ability to contribute to their children's therapy and enjoyed the training experience. Data collection is ongoing.

130.095 116 Pilot Study of Mind Reading and in-Vivo Rehearsal for Children with HFASDs. M. L. Thomeer*[1], J. D. Rodgers[2], C. Lopata[1], M. A. Volker[2] and J. A. Toomey[3], (1)*Canisius College*, (2)*University at Buffalo, SUNY*, (3)*Summit Educational Resources*

Background: Research suggests that individuals with high-functioning ASDs (HFASDs) can exhibit a range of facial- and vocal-emotion decoding difficulties (Golan et al., 2006; Lindner & Rosén, 2006). Computer software interventions have been proposed to address this deficit, including *Mind Reading* (*MR;* Baron-Cohen et al., 2004). LaCava et al. (2007) evaluated *MR*'s effectiveness with 8 children with HFASDs (M=10.5 hours per person). Pre-post comparisons indicated significant improvements in emotion recognition; however facial improvements were limited to tasks from *MR*. Although promising, LaCava et al. noted the need for studies that include measures of broader social performance. Additional limitations included no reporting of effect sizes, IQ, or language data, and lack of diagnostic confirmation using a diagnostic instrument.

Objectives: This pilot evaluated a manualized administration of *Mind Reading* (*MR*) and in-vivo rehearsal for its: (1) effect on emotion recognition and social behaviors of children with HFASDs; and (2) overall feasibility.

Methods: *Participants.* Eleven participants, ages 7-12 with HFASDs were screened using a multiple-gate procedure. Inclusion criteria included a short-form IQ composite > 70; receptive or expressive language score ≥ 80; and score meeting ASD criteria on the ADI-R.

Outcome measures. Social Responsiveness Scale (SRS; 65-item rating scale assessing ASD features and social behaviors); *Emotion Recognition and Display Survey* (ERDS; 54-item researcher-developed rating scale assessing *decoding* and *encoding* of 27 *MR* emotions). Participant and parent satisfaction was assessed via eight-item satisfaction surveys. Feasibility was evaluated using the *MR* chronometer that tracked *MR* time and satisfaction surveys.

Procedures. The manualized *MR* and in-vivo rehearsal protocol was administered during 12 staff-supervised 90-minute sessions. Children completed *MR* exercises (Emotions Library, Learning Center, etc.) and in-vivo rehearsal according to a pre-established schedule and protocol. Children earned *MR* generated computer-based rewards and earned points for following rules, identifying and displaying emotions, and exhibiting pro-social behaviors.

Results: Parent ratings indicated a significant pre-post decrease in SRS scores (t(10)=4.073, p<.0167, d=.65) and significant increases on the ERDS emotion recognition (t(10)=3.004, p<.0167, d=.95) and display of emotions scores (t(10)=5.185, p<.0167, d=1.70). Exploratory comparisons on the SRS indicated significant decreases for 3 of 5 subscales (*Social Awareness* (t(10)=2.970, p<.01, d=.58); *Social Communication* (t(10)=2.972, p<.01, d=.70); and *Social Motivation* (t(10)=2.861, p<.01, d=.77). Effect sizes (SRS and ERDS) were medium-to-large. *MR* usage time approximated the 16-hour projected time (M=15.87 hours). Average parent satisfaction rating was 55.33 out of 56 and child satisfaction was 43.89 out of 56.

Conclusions: Results indicated that completion of the manualized *MR* and in-vivo rehearsal protocol was associated with significantly higher post-intervention ratings of emotion decoding and encoding, and lower ratings of ASD-related social problems particularly in the areas of social awareness, communication, and motivation. The findings also suggest the children's newly-learned skills generalized to some extent and may have affected other social behaviors (collateral improvements as captured by the SRS). Support for feasibility was reflected in high satisfaction ratings and participant usage of *MR*. Limitations and implications will be described.

130.096 117 Role of Complementary & Alternative Medicine (CAM) Using Acupuncture (AC) for Autism Spectrum Disorder (ASD). V. C. N. Wong*, *The University of Hong Kong,*

Background:

Parents of children with ASD sought for CAM treatment. (1) The approach in TCM is "holistic" with a philosophical background of

balancing "Yin-and-Yang". The patho-physiological basis aimed to improve "energy" or "body-flow" or "de-Qi". Depending on the symptoms of ASD, clinical manifestations could be categorized into different TCM syndromes: "Delay in Development; Speech and Language problems; Hearing problems; or Emotion problems". The sites of the pathological changes had been postulated to be in the 'brain, heart, spleen, liver and kidney meridian". In our experience, TCM approach for autism is postulated to be related to lower intelligence due to "Heart-meridian and Kidney-meridian imbalance" resulting in communication problem and "Liver-meridian imbalance" leading to behavioral problem. (2, 10)

Objectives:

We adopted a different approach to assess the efficacy of AC in improving the functional status with organ and meridian concept of TCM model as a fundamental basis to improve behavior, cognition or communicative ability.
Methods: During 1998-2008, we had conducted case study (2) and Randomized control trials (RCT) of using of short 80-12 weeks courses of AC. (3-9).

Results:

Our pilot case studies had demonstrated efficacy of acupuncture for ASD. (2). Our RCT Trials had demonstrated improvement in various modalities including behavior, language, functional status and cortical cerebral metabolism using Positron Emission Tomography. (3-9).

RCT 1- A pilot study with 30 ASD using Tongue Acupuncture had demonstrated improvement in core (language, social communication, cognition) and secondary features (hyperactivity, attention, aggression, temper tantrum, sleep, functional independence).

RCT 2- A single-blind RCT conducted on 50 children using acupuncture versus sham acupuncture in ASD had demonstrated statistically significant improvement in the Treatment as compared to the Control group in self care and cognition domains of the WeeFIM ®.

RCT 3 - RCT using Tongue Acupuncture in ASD with PET scan for clinical correlation was performed on 21 ASD and 9 Controls. The Treatment group had significant improvement on behavior (p=0.0211); language (p=0.0211); functional status (p=0.0011); Clinical Global Impression Scale (p=0.0003); and cortical cerebral metabolism using PET (p=0.0451).

RCT 4- This RCT studied short-term electro-acupuncture for ASD (n=30) versus Sham Electro-acupuncture (SEA) (n=25). There were significant improvement in language comprehension domain of WeeFIM® (p=0.02), self-care caregiver assistant domain of PEDI (p=0.028), and CGI-I (p=0.003) for the EA group.

RCT 5- A RCT was performed to study the sustainability of the acupuncture effect in Treatment (n=18) and Control groups (n=18 and showed that acupuncture could be useful in improving language, social skills, irritability and stereotypy in ASD. The effects could be sustained for at least two months after acupuncture.

Conclusions:

Short courses of AC can improve functional aspects in ASD. Acupuncture could be used as an adjunct therapy for early intervention program. Given the minimal side effects and potential usefulness, acupuncture could be recommended as an adjunctive treatment if available for children with ASD. We had submitted a protocol for Cochrane Review on Acupuncture in ASD. (9) Further research is needed to evaluate the optimal acupuncture protocol for different subtypes of ASD and the mechanism of acupuncture.

130.097 118 SENSE Theatre: a Promising Intervention for Children with Autism Spectrum Disorders. B. Corbett*[1], J. Gunther[1], D. Comins[2], J. Price[3], N. Ryan[1], D. Simon[1] and T. Rios[2], (1)*M.I.N.D. Institute, University of California at Davis*, (2)*M.I.N.D. Institute*, (3)*Davis Musical Theatre*

Background: Social behavior is complex; therefore, interventions developed to address the challenging needs of children with autism

must target a broad array of behaviors. Almost by definition, the theatre involves the teaching and performance of many aspects of social and emotional functioning to include verbal and nonverbal communication, emotional expression, movement, pretend play, and reciprocal social interaction. Therefore, theatrical techniques in combination with established behavioral approaches may provide a rich and promising platform to treat children with autism.

Objectives: The pilot investigation evaluated a community-based theatrical intervention program, SENSE Theatre, designed to improve socioemotional functioning and reduce stress in children with autism spectrum disorder (ASD). The intervention included peer and video modeling, behavior therapy techniques, social reinforcement and theatrical techniques, which were embedded in a full musical theatrical production. The primary aim was to assess SENSE Theatre in the context of an enjoyable, ecologically valid social experience. We hypothesized that children with autism would demonstrate significant improvement in the identification of faces, the expression of emotions, and theory of mind (TOM) skills. In was also hypothesized that biological changes would occur to include a reduction in salivary cortisol level and a rise in the level of plasma oxytocin following intervention.

Methods: Eight children with ASD were paired with typically developing peers that served as expert models. Neuropsychological (face perception, theory of mind (TOM), and emotion identification), biological (cortisol and oxytocin) and behavioral measures were assessed in a pretest-posttest design using paired sample t-tests. To evaluate stress responsivity, the SENSE participants provided salivary samples at the beginning and end of practice for the First, Middle, and Last Rehearsal, which were analyzed using a repeated measures approach.

Results: The results of neuropsychological measures indicate statistically significant differences between the pre- and post-treatment measures for the identification of faces (t(7)-2.32, P=0.05, and TOM skills (t(7)-2.35, P=0.05). Regarding cortisol, there was a significant interaction between Intervention Time (First, Middle, and Last rehearsals) and Rehearsal Time (Pre and Post Rehearsal) $F(1,6)=19.302$, $P=0.001$. There were also main effects for Time $F(1,6)=16.81$ $P<0.0001$ and for Pre-Post Rehearsal, $F(1,6)=127.36$, $P<0.0001$.

Conclusions: Taken together the findings suggest that the children with ASD exhibited improvement in social perception skills and reduced stress responsivity ostensibly in response to the intervention. The pilot intervention of SENSE Theatre shows promise in improving the socioemotional functioning of children with ASD through the utilization of peers, video and behavioral modeling, and theatrical techniques in a community-based theatrical setting.

130.098 119 Social Skills Groups for College Students On the Autism Spectrum. C. D. Jones*, M. Manzella and C. Oldewage, *University of Puget Sound*

Background: Social skill deficits are frequently described as the key to understanding the true nature of autism and educators/therapists are becoming more skilled at teaching to these deficits for younger children. In contrast, research on and education of social skills for *college* students on the spectrum has seen very little attention.

Objectives: The purpose of this study is to examine the effectiveness of social skills groups for teaching social communication skills to college students on the autism spectrum.

Methods: Four college students on the autism spectrum experienced 16 weekly one and a half hour groups where they learned about a new social skill, observed the skill being used, practiced using the skill themselves and, through homeworks, reflected on their personal use of the skill in their lives outside of the group. The effectiveness of the groups was evaluated through three college adaptation/attachment measures and two measures of social understanding. Additionally, observational data were collected to subjectively evaluate the

understanding of weekly skills by each participant.

Results: While there was considerable variability across each student for the outcome measures, all students increased their normed percentile scores on standardized assessments by at least 1 standard deviation. Additionally, for assessments without norm references, all students demonstrated increases in college adaptation, indicating more comfort in the college environment. Most important, after 2 years, all of the students are still attending the university compared with an 80% drop out rate the previous year.

Conclusions: With early childhood interventions now reliably being used with children on the spectrum for more than 20 years, we are seeing a greater increase of students with autism attending colleges and universities. This study demonstrates the effectiveness of teaching these students skills that they need to succeed in college and, ultimately, prevent drop outs in a potentially socially fragile population.

130.099 120 Stress in Parents of 6-Month-Old Infants with Older Siblings with Autism Spectrum Disorders. A. M. Estes*[1], S. L. Alvarez[1], E. Dupont[1], K. M. Burner[1], J. Kelly[1], G. Dawson[2], J. Munson[1], B. King[3] and S. J. Webb[1], (1)*University of Washington*, (2)*UNC Chapel Hill*, (3)*University of Washington and Children's Hospital and Regional Medical Center*

Background: There is growing awareness among scientists and the general public of increased risk for ASD in infants with older siblings with ASD. However, ASD is not currently able to be reliably diagnosed until 24 months of age or later. Thus, parents with an older child with ASD and an infant who is too young to be diagnosed may be aware that their infant is at-risk. This means that they may be unable to obtain definitive clinical information about their infant's prognosis for two or more years after birth. This parental awareness may confer additional risk for stress in parents as they attempt to juggle the demands of monitoring the development of an at-risk infant and providing therapy for an older sibling with ASD. Objectives: To document levels of parental stress among parents of infants at risk for ASD. Specifically, this study will explore the levels of psychological distress and parenting-related stress, and family factors such as marital relations, social support and disruptive life events in parents of 6-month old infant siblings and make comparisons with parents of low-risk infants. Methods: In the context of a randomized trial of an intervention to support parent-infant interaction, parents of infants with older siblings with ASD (ASD-risk; n=27) and older siblings with typical development (TYP; n=24) were assessed when their infant was 6-months of age, before the intervention was provided. Domains of psychological distress, parenting-related stress and family factors (marital relations, social support, and disruptive life events) were assessed. Results: We predict that parents of an infant at risk for ASD will experience increased psychological distress and parenting-related stress as compared to parents of low-risk infants. It is further predicted that, although increased parental stress will be present among parents of at-risk infants, other family factors, including marital relations and social support, will not differ between parent groups. Conclusions: Previous research has shown that parents of children with ASD are at increased risk for psychological distress and parenting-related stress. This study investigates parental distress, parenting-related stress and family factors in families with a very young infant who is at-risk for ASD, prior to the onset of ASD symptoms. If parents of at-risk infants report increased distress, parenting-related stress or other family stress factors, evidence-based interventions providing support to parents of infants at-risk for ASD should be developed to support family functioning during this developmental period.

130.100 121 The Double ABCX Model of Adaptation in Racially Diverse Families with a School-Age Child with Autism. M. Manning*[1] and L. Wainwright[2], (1)*University of Massachusetts Medical School*, (2)*University of Massachusetts Boston*

Background:

Compared to families of typically developing children and families of children with other developmental disabilities, autism spectrum

disorders create unique stressors for families (Randall and Parker, 1999). Some studies suggest that family functioning is negatively impacted by having a child with autism and that families show reduced family adaptation compared to families of children with other disabilities or typically developing children (Higgins, Bailey and Pearce, 2005). Other studies suggest that adaptation in families with autism is often within a healthy, normative range, and that families report positive effects as a result of having such a child (e.g. Hastings & Taunt, 2002). Given the substantial impact on family life as well as the knowledge that its challenges are different from other child disabilities, additional research focusing on family adaptation is important to help practitioners to better assist the families with whom they work by delivering interventions tailored to this disorder.

Objectives:

The objective of this study was to investigate the relationship between family adaptation, severity of autism and behavior problems, social support, religious coping, and reframing in a racially diverse sample of families with a school-age child with autism. It was predicted that (a) the Double ABCX model would predict parental distress and family functioning and (b) families in this study would report higher parental distress and lower family functioning compared to normative data.

Methods:

The sample included 195 school-age children with autism spectrum disorders (161 boys and 34 girls; 51% white). Average age of the children was 8.8 years (SD = 2.1), with a range from 6 to 12 years of age. Primary caregivers of children with ASD were recruited through autism parent support groups, medical clinics, conferences, and schools. Families were mailed questionnaire packets, consisting of standardized measures assessing the constructs of the ABCX model. 195 participants completed and returned the questionnaire packet, a return rate of 79%.

Results:

Hierarchical regression results revealed that the Double ABCX model of family adaptation accounted for a substantial amount of the variance in family functioning (28%) and parental distress (46%). Findings suggest that child behavior problems and reframing are most strongly associated with family outcomes. In addition, results suggested that families in this study experienced higher levels of stress, but that their overall family functioning was within a healthy range.

Conclusions:

This study is an important step in continuing to understand how to best help families who are coping with autism. The increased level of stress experienced by these families underscores the need for researchers and clinicians to provide appropriate family-based interventions. On the positive side, families with autism appear to be adapting in healthy ways even in the face of their increased stress. The findings suggest implications for clinical interventions for families with autism including the use of strength-based approaches, highlighting parents' ability to cope with their challenging circumstances.

130.101 122 The Dyadic Psychoanalytic Treatment of Young Children with Autism Spectrum Disorder. S. P. Sherkow*[1] and W. Singletary[2], (1)*New York Psychoanalytic Institute*, (2)*Margaret S. Mahler Psychiatric Research Foundation*

Background:

For many years, children with Autism Spectrum Disorder were thought to be suffering from a psychological disorder--the product of a failed bond between mother and infant. However, recent developments in autism research have led to models of ASD in which neurobiological factors are seen as interfering with the development of the social brain system and thus, with social engagement and emotional connections including the child's relationship with the mother. Unfortunately, the current multidisciplinary approach to the treatment of ASD usually excludes psychotherapy which, in fact, can help to preserve and nurture the bond between mother and child. Thus, psychotherapy can play an indispensable role in facilitating the child's development and ability to engage in and benefit from other

treatments.

Objectives:

The poster will aim to educate about ways in which a multidisciplinary approach that includes psychotherapy for both the child and mother can be used in a clinical setting for the treatment of young children with ASD. It will also highlight recent evidence of neuroplastic changes taking place in children undergoing psychoanalytic and other treatments for ASD.

Methods:

This poster will describe a dyadic approach to treatment for children with autism that both engages the child on a psychodynamic level and works toward addressing the mother's need to repair the rupture she perceives as having occurred between her and her child as a result of the child's condition. Accordingly, this allows successful, continued progress of both the psychoanalytic treatment and other ongoing management of the child's disorder.

Results:

To illustrate use of this approach in a clinical setting, the poster will include excerpts from the treatment of "Johnny," a two-and-a-half-year-old boy on the autistic spectrum, and will also detail the methodology used in this approach and illustrate developmental themes as they unfold in the course of treatment.

Conclusions:

As a result of this treatment, "Johnny's" relationships with his family and others around him improved dramatically and initiated further developmental and social-behavioral improvement. The poster will reflect on these changes both anecdotally as well as through clinical reevaluation toward the end of treatment.

130.102 123 The Effectiveness of Medication Combined with Intensive Behavioral Intervention for Reducing Aggression in Youth with Autism Spectrum Disorder. T. W. Frazier*[1], E. Youngstrom[2], T. Haycook[1], A. Sinoff[1], F. Dimitriou[1], J. Knapp[1] and L. Sinclair[1], (1)*Cleveland Clinic*, (2)*University of North Carolina at Chapel Hill*

Background: Aggression is a frequent and impairing symptom in individuals with autism spectrum disorder. Growing evidence supports the use of intensive behavioral intervention (IBI; Howlin, et al. 2009; Matson, et al. 1996) or medications (Chez, et al. 2004; Malone, et al. 2005; McDougle 2002) to treat aggressive behavior in children with ASD. To the author's knowledge, no studies have evaluated the simultaneous application of medication and IBI treatments toward reducing aggression in youth with autism.

Objectives: The purpose of the present study was to examine the effectiveness of adding IBI to medication in the treatment of aggressive behavior in youth with ASD.

Methods: Youth with a DSM-IV diagnosis of Autistic Disorder or Pervasive Developmental Disorder NOS were eligible for inclusion if they received an IBI plan targeting aggressive behavior. Each participant received IBI for >/=30 hours/week, comprised of at least six hours per day, five days per week year round. Any participant with at least four aggressive behaviors per day and at least one day per week of multiple aggressive behaviors was eligible to be placed on an aggression behavior reduction plan. Aggressive behavior was defined as any behavior that either harms or attempts to harm another person or causes destruction of property. Inclusion criteria were intentionally broad to enhance the generalizabilty of this effectiveness study (Ernst and Pittler 2006; Gartlehner, et al. 2006). Youth were prescribed medication by their treating physician. Medication usage was recorded for all participants. Three medication classes were coded based upon the pattern of specific medication usage observed in this sample: 1) antipsychotics, 2) mood stabilizers, and 3) non-stimulant medications treating ADHD and/or sleep symptoms. To determine the effectiveness of medication classes, a Cox regression analysis was computed with medication classes as predictors, the number of behavior plan sessions as the time variable, and success of the behavior plan as the endpoint/status variable.

Results: Thirty-two youth with ASD (Mean Age = 11.16, SD=3.31; range=4-16, 75% male) received a behavior reduction plan targeting aggression. Of these, 18, 10, and 12 were taking antipsychotic, mood stabilizing, and non-stimulant medications. The presence of antipsychotic medication significantly decreased the number of sessions required to achieve behavior plan success (_2(1)=5.67, p=.017; no antipsychotic - Mean=228.1, SE=52.9, Median=149.0, SE=60.8, 95% CI=29.8-268.2; antipsychotic - Mean=83.2, SE=29.6, Median=30, SE=4.2, 95% CI=21.7-38.3). No other medication classes significantly influenced aggressive behavior.

Conclusions: IBI alone, while showing substantial decreases in aggressive behavior, was more effective when paired with antipsychotic medication. These findings extend previous efficacy data for antipsychotics (Kratochvil, et al. 2005; McCracken, et al. 2002; McDougle, et al. 2005) by demonstrating effectiveness in augmenting behavior therapy in the treatment of aggression. Furthermore, results of the present study suggest that a combined antipsychotic-IBI treatment approach warrants further exploration in larger-scale efficacy and effectiveness studies. Mood stabilizing medications and non-stimulant medications used to treat ADHD symptoms and/or sleep difficulties (primarily clonidine) were not effective in reducing aggressive behavior.

130.103 124 Training in Evidence-Based Pivotal Response Treatments: Exploring Different Models of Parent-Training and Direct Implementation. S. A. Northington* and R. E. Daniels, *Chicago Children's Clinic*

Background: There is substantial evidence that early, intensive behavioral interventions (EIBI) for children with autism are effective. Historically, providing effective treatment to children with autism required substantial time and resources. Traditional, direct service models of treatment require at least 25 hours a week of treatment, 12 months a year, for several years to produce published outcomes. Pivotal Response Treatment (PRT), with its emphasis on family and school involvement, targeting "Pivotal" areas for treatment in natural environments, has demonstrated outcomes that are unmatched in the autism literature (Koegel, Koegel, Shoshan & McNerney, 1999; Koegel, 2000; Koegel, Koegel & Brookman, 2003). Because parents spend more time with their children during the days, evenings, and weekends, they can provide more consistent and time intensive intervention for their children (R.L. Koegel, Koegel, Frea & Smith, 1995). Thus, it seems natural to incorporate parents into the treatment team for their child. Research shows that parents of children with autism can be trained as effective implementers of programs for their children (R.L. Koegel et al., 1996; R.L. Keogel et al., 1991; Laski et al., 1988; McClannahan et al., 1982; Sanders & Glynn, 1981; Stiebel, 1999; Vaughn, Clarke & Dunlap, 1997). By providing parents with training in PRT implementation, children demonstrated improved functional communication skills, mean length of utterance, reciprocal play skills, and a decrease in disruptive behaviors.
Objectives: To determine the efficacy of parent training in PRT in bringing about improvement in their child's functioning. Three families were followed, utilizing the models described below; one model per family.
Methods: Three different models of parent-training were provided: 1) a three-day intensive (4-hour per day; 12 hours in total) parent training, with minimal direct implementation with the child; 2) a 25-hour (approximately 5 hours per week) parent-training model over a 5-week period, with minimal direct implementation with the child; or 3) a 25-hour parent-training model over a 5-week period, followed by direct implementation with the child for approximately 10 hours per week, and parent training sessions weekly, as needed. Three different families were trained in PRT. Data were collected for the following treatment goals: 1) increase functional verbal utterances (decrease scripting) of the child, 2) increase mean length of verbal utterances of the child, 3) increase the number of spontaneous verbal utterances and initiations of the child, and 4) parents demonstrate fidelity of implementation of the PRT procedures 80% of the time within a 10-minute video sample.

Results: Regardless of parent training method employed, all parents eventually demonstrated fidelity of implementation. All children demonstrated marked improvements in their goal areas.
Conclusions: Different models of parent-training were found to be effective at improving child outcomes with substantially less than 25 hours a week of direct intervention from clinicians. Future research is needed to determine child and parent factors that influence the amount of parent training and direct intervention with PRT needed to achieve treatment goals. Training parents in PRT is an efficient, economical, and effective method to bring about significant improvement in the functioning of children with autism.

130.104 125 Treatment of Children and Adolescents with Autism Spectrum Disorders with Omega-3 Polyunsaturated Fatty Acids. Description of the Methodology of a Multicenter Randomized Double-Blind Crossover Placebo-Controlled Trial. C. Moreno*[1], R. Calvo Escalona[2], M. Graell Berna[3], P. M. ruiz Lazaro[4], C. Llorente[1] and M. Parellada[1], (1)*Hospital General Universitario Gregorio Marañón.*, (2)*Hospital Clinic i Provincial*, (3)*Hospital Infantil Universitario Niño Jesús*, (4)*Hospital Clínico Lozano Blesa*

Background: Ethiological and fisiopathological basis of Autism Spectrum Disorders (ASD) remain uncertain. Recent developments suggest that oxidative stress disturbances may affect lipid composition of neuronal membranes in patients with ASD. Lipids present in the brain are mostly structural phospholipids rich on polyunsaturated fatty acids (PUFAS) that can be synthesized only in a low proportion and need to be incorporated from the diet. Most studies have found low levels of PUFAS in autism. Some other evidence suggests that oral administration of PUFAS may improve clinical features of ASD, although their mechanism of action remains unknown.

Objectives: This is a pilot study that has been designed to evaluate the effect of treatment with PUFAS omega-3, DHA and EPA, on oxidative stress and symptoms among children and adolescents with ASD. We hypothesize that 8-week treatment with PUFAS will lead to greater improvement on oxidative stress parameters and ASD clinical features compared to placebo. The study of minors is justified because, if treatment with PUFAS is proven safe and effective, early treatment could help to prevent damage caused by chronic exposure to oxidative stress.

Methods: Crossover multicenter randomized clinical trial controlled with placebo in children (5-11 years) and adolescents (12-17 years). Patients are eligible for inclusion if they meet DSM-IV criteria for Pervasive Developmental Disorders, confirmed if deemed necessary by the Autism Diagnostic Observation Schedule (ADOS). Power sample size calculations are based on previous studies with PUFAS omega3 on children and suggest a sample size of 80 patients.
Study treatment: Participants will be randomized to receive treatment with fish oil with a high concentration of PUFAS omega3 (experimental treatment) or paraffin oil (placebo) during 8 weeks. PUFAS omega-3 daily doses will be EPA 577.5 mg/day + DHA 385 mg/day for patients 5-11 years old and EPA 693 mg /d + DHA 462 mg /d for 12-17 (divided doses, tid). After this, patients will undergo a 2-week wash out phase. During the second 8-week treatment phase, patients receiving placebo will switch to PUFAS omega-3 and vice-versa. Before and after every treatment phase blood draws and clinical evaluations will be performed. Both treatment phases will be double blind. Experimental treatment and placebo will consist on identical soft gelatin capsules. Patients taking other psychoactive medications were permitted to continue doing so at stable doses, except antipsychotics and omega3 supplements. During the trial, subjects were not allowed to start new psychopharmacological adjunctive medication or changing doses of adjunctive treatments.
Outcome measures: Efficacy assessments will be performed on weeks 8, 10, and 18. Safety and tolerability will be assessed weekly. The primary efficacy measure is oxidative stress level measured as level of PUFAS on erythrocyte membrane, total antioxidant oxidative stress, and plasma level of glutathione. Secondary efficacy measures include changes on clinical symptoms.

Results: study is currently in the recruitment phase. Results will be available shortly after recruitment is completed (June 2010).

Conclusions: Ongoing study.

130.105 126 Using the Revised ADOS Algorithm to Evaluate a Behavioral Intervention in a Large Public School District. C. M. Harker*[1], E. M. Reisinger[2], A. D. Sherman[1], S. Shin[2] and D. S. Mandell[1], (1)*University of Pennsylvania School of Medicine*, (2)*University of Pennsylvania*

Background: Though intended as a diagnostic tool, there is an increasing trend in autism research to use the Autism Diagnostic Observation Schedule (ADOS) as a severity and outcome measure. In response to the growing need for a measure that would allow for longitudinal comparisons of symptom severity, Gotham et al. (2009) developed a revised ADOS algorithm, allowing for across-module comparisons, and can be a useful tool when evaluating severity over time. To date, however, this algorithm has been used only for long-term comparisons, not for periods of time generally used to test interventions. Due to the relatively short time span between baseline and outcome assessments in intervention studies, students who move from one algorithm age group to another during the study may receive a more severe symptom severity score once their raw score is calibrated in an older age bracket.

Objectives: To examine the utility of the ADOS symptom severity algorithm as an outcome measure in a 9-month behavioral intervention study.

Methods: The sample included 153 students from 39 K-2nd grade autism support classrooms in a large, urban school district that were participating in a randomized trial of two classroom-based autism interventions. Students were assessed at the beginning (W-1) and end (W-2) of the academic year using the ADOS Modules 1-3. Trajectories of the group were calculated using both the original and revised ADOS algorithms.

Results: 21.6% of the sample changed ADOS modules from W 1-2. 14% of the sample aged into a different algorithm age bracket over the course of the academic year. There was no statistically significant difference in symptom severity score from W-1 (Mean=6.91, SD=1.74) to W-2 (Mean= 6.41, SD= 1.79) for the 22 students who changed age brackets. There was a significant improvement ($p<.01$) in symptom severity score between W-1 (Mean=6.77, SD= 2.01) and W- 2 (Mean= 5.98, SD= 2.21) for the remaining131 students.

Conclusions: Analysis is ongoing; preliminary results suggest the utility of the ADOS severity algorithm for assessing change in students over a relatively brief period of time.

130.106 127 You Lead, I'll Follow: Parent-Child Interactions with Infants at Risk for Autism Spectrum Disorder. A. J. Smith*[1], A. M. Steiner[2], G. W. Gengoux[3] and K. Chawarska[1], (1)*Yale University School of Medicine*, (2)*Yale University*, (3)*Stanford School of Medicine*

Background: The literature suggests an important relationship between synchronous parent behavior and developmental outcomes for preschoolers with autism (Siller & Sigman, 2002; 2008). Preliminary work from prospective studies reveals differences in levels of parent synchrony beginning in infancy in parent-child dyads of infants who have an older sibling with autism (High-Risk, HR-ASD) compared to those who do not (Low-Risk, LR). Such differences were most evident in child-led interactions (Yirmiya, et al., 2006), suggesting that HR-ASD infants may exhibit behaviors which hamper synchronous parent-child interactions.

Objectives: In the current study, we hypothesize that differences in the quality of parent-child interactions in HR-ASD infants relate not to overall differences in parenting style, but rather to specific infant behaviors which trigger compensatory parenting strategies.

Methods: Participants included HR-ASD and LR parent-infant dyads at 12-months (N = 14). Parents were videotaped interacting with their children and a standardized set of toys for five minutes. Videotapes were coded using a scheme adapted from Siller & Sigman (2002) for both child (appropriate, inappropriate, no directed behavior) and parent behavior (undemanding, demanding,

directive). Directive parent behavior was defined as parental attempts to direct the infant's attention when the infant was either not engaging with a toy or engaging in an inappropriate fashion.

Results: Preliminary data indicate no overall differences in parent-child interactions based purely on the infant's risk status. However, parents of a subset of HR-ASD infants who exhibited higher levels of autism symptomatology engaged in less synchronous and more directive behavior compared to other HR-ASD and LR dyads (p = .004*).* Likewise, this subset of HR-ASD infants also demonstrated lower levels of appropriate child behavior than other infants (p = .009). Furthermore, parents of infants who had more abnormal scores on an autism diagnostic instrument (ADOS-T) and lower expressive language skills were more likely to use directive behavior (r = .78, p = .001; r = -.60, p = .02, respectively).

Conclusions: Results suggest that while there may be differences in the quality of parent-child interactions in HR-ASD dyads, these differences could be directly related to specific atypical child behaviors. In fact, these behaviors may make synchronous engagement challenging for parents, as many parents seemed to naturally "intervene" with directive behaviors to facilitate appropriate child behavior. These results will be discussed in terms of implications for early identification, intervention, and parent education.

130.107 128 Parent-Mediated Intervention for Infants at-Risk for ASD. L. Watson*, G. T. Baranek, L. T. Brown, E. R. Crais, J. S. Reznick, L. Wakeford, L. M. Little, L. Boyd and C. Tashjian, *University of North Carolina at Chapel Hill*

Background: Based on current theories and empirical evidence regarding the transactional effects of biology and environment on neurodevelopment, Dawson (2008) proposed that intervening with infants at risk for autism prior to the emergence of all the diagnostic symptoms could be more efficacious than interventions initiated after diagnosis. To date, however, there is a notable lack of empirical data demonstrating the efficacy of interventions with infants at-risk for autism.
Objectives: To evaluate the potential of a parent-mediated intervention designed for one-year-olds at-risk for autism to (a) improve developmental functioning and (b) ameliorate the severity of symptoms of autism.
Methods: The First Year Inventory, a parent questionnaire designed to identify 12-month-olds who are at risk for an eventual diagnosis of autism, was mailed to families in our catchment area. Parents of infants with scores above the 95th percentile were invited to bring their infants for an extensive developmental assessment. If autism risk indicators were confirmed in the Time 1 assessment, families were invited to enroll in the intervention study. Eligible families who consented to participate were randomly assigned to an experimental intervention called Adapted Responsive Teaching (ART; adapted from Mahoney & MacDonald, 2007) or to a Community Services (CS) group, using a 2:1 randomization ratio. Sixteen families have been enrolled, with 11 assigned to ART and 5 to CS. ART families participated in a 6-month home-based intervention designed to enhance parent responsiveness and promote "pivotal" behaviors in infants in social-communication and sensory-regulatory domains. Children participated in Time 2 assessments after the completion of the ART intervention (at 22-24 months of age).
Results: To date, 7 children have been assessed at Time 2: 5 in the ART group and 2 in the CS group. Children assigned to ART improved on 3 different measures of communication/language functioning: (1) mean standard scores on the Communication and Symbolic Behavior Scales [CSBS] improved from 91 to 102; (2) mean standard scores on the Vineland Communication Scales [VineComm] improved from 93 to 98; and (3) mean scores for spoken words on the MacArthur-Bates Communicative Development Inventories [MCDI] improved from the 27th %ile to the 57th %ile. One child in the CS group showed decreases on all 3 measures (78 to 65 on CSBS; 73 to 64 on VineComm; 10th %ile to 5th %ile on MCDI), whereas the other child in the CS group showed negligible changes (92 to 94 on CSBS; 100 to 94 on VineComm; and 5th %ile

to 5th %ile on MCDI). The remaining 9 children will complete Time 2 assessments by March, 2010. Also, planned analyses will examine symptom severity on the Autism Observation Schedule for Infants (Time 1) and the Autism Diagnostic Observation Schedule-Toddler Module (Time 2). Conclusions: Preliminary findings support the promise of parent-mediated early intervention with infants at-risk for autism in improving communication/language functioning. A larger RCT is required to evaluate the efficacy of the treatment and test parent responsiveness as a hypothesized mediator of outcomes.

130.108 129 Puberty and Relationships 101: Evaluation of a Group Psycho-Education and Skill Building Curriculum for High Functioning Adolescent Males with Autism Spectrum Disorders. S. Nichols*[1], M. Roth[2] and G. Reilly[1], (1)*Advantage Care Diagnostic and Treatment Center*, (2)*Contemporary Guidance Services*

Background: Sexuality education for adolescents with high functioning autism spectrum disorders (ASDs) is critical, yet has received only limited attention in the literature. Teens with ASDs face unique issues regarding sexuality due to the nature of the disorder (e.g., understanding the social underpinnings of sexuality). To date, no research has examined how to address these issues.

Objectives: To develop and evaluate a group-based psycho-education and skill building curriculum created specifically for youth with ASDs that will enable families, professionals and educators to best understand how to teach this population about their developing sexuality.

Methods: Curriculum development was based on current literature on sexuality and ASDs and the authors' clinical outcome data. Two primary underlying themes for the group were the social foundations of sexuality and safety of self and others. Group sessions addressed six topics: (1) the body and growing up (2) personal and other people's boundaries, and public and private behavior (3) establishing friendships (4) romantic interests, (5) introduction to dating (including risky situations and legal issues), and (6) safety. Thirteen adolescent males (ages 15-18, M = 16.12, SD = 1.02) with an average verbal IQ and their parents were recruited for the current study. Adolescents attended 1of 2 eight-week groups that met weekly for 1.5 hours. Measures included adolescent and parent report during pre-group and post-group phases (see results). Parents and adolescents each selected two goals for the adolescent to achieve by the end of the group sessions.

Results: A wide-range of goals was set by participants (e.g., to better understand attraction, to master his grooming routine). A Wilcoxon matched pairs signed-ranks test indicated that parents and teens demonstrated significant progress towards their goals throughout the course of the group (parents session 2: M = 1.00, SD = .92, post-group: M = 2.85, SD = 1.28, Z (N = 13) = -3.10, p = .002; teens session 2: M = 2.08, SD = 1.12, post-group: M = 4.54, SD = .63, Z (N = 13) = -3.07, p = .002). Comfort level with the topic of sexuality also increased (parents pre-group: M = 40.71, SD = 4.87, post-group: M = 44.77, SD = 5.02, Z (N = 13) = -2.45, p = .01; teens pre group: M = 25.71, SD = 13.47, post-group: M = 35.85, SD = 12.20, Z (N = 13) = -2.20, p = .028). Additional analyses will compare pre-post changes in adolescents' understanding of their developing sexuality, feelings of stress associated with growing up, parental concerns and acceptance of their adolescent's emerging sexuality, and parents' feelings of competence in being able to address issues related to sexuality.

Conclusions: Findings from the current study are promising for addressing the concerns of both adolescent males with ASDs and their parents regarding emerging sexuality and adolescent development. Next steps and recommended changes will be discussed.

130.109 130 Recommended Practices for Toddler Autism Intervention: Current Research and Future Needs. H. Schertz*[1], C. Baker[2], S. Hurwitz[3] and L. Benner[1], (1)*Indiana University*, (2)*University of Northern Colorado*, (3)*University of North Carolina at Chapel Hill*

Background:

The 2001 recommendations of the National Research Council (NRC), based largely on

research with children over age 3, may need revision if applied to toddlers. Part C of the Individuals with Disabilities Education Improvement Act, the Division for Early Childhood (DEC) of the Council for Exceptional Children, and the National Association for Education of Young Children (NAEYC) provide guidance for toddler intervention. Currently, intensive and structured intervention approaches are widely represented in autism research with older children and the prevalence and appropriateness of these methods for toddlers is worthy of examination. Other considerations for toddler interventions are the focus of intervention efforts, the environments in which intervention occurs, and the role of parents in intervention delivery.

Objectives:

This study explored the extent to which emerging early intervention autism research "pushed down" approaches commonly used with older children, if and how recommended practices for early intervention influenced intervention research approaches, and how specific developmental needs of toddlers with ASD were addressed in researched intervention. This study did not aim to describe the effectiveness of reported interventions.

Methods:

A survey of online databases for intervention research conducted with toddler-aged participants with autism risk or diagnosis yielded 23 reports of intervention. Inclusion was limited to studies with a majority of participants aged 36 months or less, intervention descriptions, and participant risk or diagnosis of ASD. Two authors independently coded for the presence or absence of indicators of recommended practice for toddler-aged children.

Results:

Ten of the studies referenced one or more sets of recommended practices including Part C or DEC (4), NAEYC (6), and/or the NRC report (7). A large majority of studies used structured behavioral intervention approaches (19), applied the intervention in settings that were neither the child's natural environment nor fully inclusive (15), and used professional, clinical, or paraprofessional personnel as the primary agent of child-focused intervention (15). Of the 22 studies that reported intensity in hours per week, eight provided over 15 hours weekly of professionally delivered intervention. These results suggest that research methods were heavily influenced by earlier research conducted with older children with ASD. Recommended practices for toddlers such as those promoted by DEC or NAEYC were under-represented in these studies. The preverbal pivotal competency of joint attention, a critical foundation for social communication that presents special difficulty for toddlers with autism, was explicitly reported in only half of the intervention studies.

Conclusions:

These results call for discussion on the need for early intervention autism research to model recommended practices for early intervention for the field. Additionally, the field should consider whether autism is a special case; that is, whether intensive, highly structured, and clinically-oriented intervention practices are appropriate for widespread application before less intensive, developmentally appropriate, and family-centered intervention methods have been systematically researched. Finally, comprehensive interventions for toddlers with autism targeted for replication in the field should consider developmental foundations that are critical for development of verbal and social communication (e.g., joint attention).

130.110 131 Systematic Review and Multi-Metric Meta-Analysis of Social Stories™ Research. C. R. Peterson[1], D. B. McAdam[2], D. A. Napolitano[2] and J. Breidbord*[3], (1)*University of Wisconsin–Stout*, (2)*University of Rochester School of Medicine*, (3)*University of Cambridge*

Background: Used to provide information about social situations to people with a clinical autism diagnosis, Social Stories™ may be a convenient strategy for improving specific functional skills and reducing specific problem behaviors. As story-based materials have become common in classroom

treatment programs, intervention procedures have been subject to continual revision leading to a large corpus of highly varied research. Meta-analyses give some evidence of questionable intervention efficacy but provide limited information about the quality of intervention studies and the suitability of research reports for determination of Social Stories™ empirical support.

Objectives: This review of current Social Stories™ research aims to synthesize results from studies with any experimental design and to summarize characteristics of research reporting.

Methods: Reports of Social Stories™ interventions published between 1993 and 2009 were identified via comprehensive pearl growing. Characteristics of intervention procedures (e.g., assessment of comprehension), experimental methods (e.g., study design), and research reporting (e.g., description of participants) were coded. Intervention efficacy was summarized using common graphical-data overlap metrics (i.e., PND and PEM) and those that were developed recently for comparison with standard effect sizes (i.e., PAND and NAP).

Results: Empirical investigations included 6 controlled trials and 39 studies that used a single-case experimental design. Among all single-case evaluations, 13 studies reported detailed characteristics of each participant (e.g., standardized assessment information) and 20 studies included three or more demonstrations of experimental effect (e.g., across participants, across behaviors). Although 29 investigations used other techniques (e.g., differential reinforcement) as part of a Social Stories™ strategy, recent reports describe specific evaluation of Social Stories™ or evaluation of specific intervention components. For each metric, relatively high efficacy was found for interventions used to reduce problem behaviors and those used in combination with other treatment techniques; however, overall efficacy differed significantly among several metrics (41.2 PAND, 47.2 NAP, 65.6 PND, 72.5 PEM). The PND results are consistent with prior findings of questionable intervention efficacy.

Conclusions: Methods-oriented review of Social Stories™ research shows increasing interest in specific intervention studies. The divergence of efficacy metrics supports ongoing efforts to improve methods of single-case meta-analysis. Other targets for scientific research include the format and text of intervention materials.

130.111 132 Systematic Review of Single Subject Design Research On Parent and Teacher Training in ASD. P. Mirenda*[1], V. Smith[2], S. Patterson[2], L. Mark[1] and S. Verheyden[1], (1)*University of British Columbia*, (2)*University of Alberta*

Background: Most autism treatments in home and school settings are implemented by parents or teachers, respectively; yet, most treatment-oriented research is conducted in clinical or laboratory settings by highly trained researchers or clinicians. It is especially important to examine the extent to which parents and teachers can be taught to implement social and communication-related interventions in natural contexts, since these skills are required in all aspects of daily life.

Objectives: The goal was to conduct a systematic review to identify, appraise, and synthesize the single subject research design (SSRD) studies that contribute to our empirical understanding of the effectiveness of parent and teacher training interventions designed to teach social and communication skills to individuals with autism spectrum disorders (ASDs).

Methods: A systematic search was conducted in 20 electronic databases (e.g., MEDLINE, PsycINFO, ERIC, etc.) covering educational and psychosocial articles that were published in English between 1994-2008. Relevant articles were identified according to a set of selection criteria. The level of evidence and quality of conduct of the studies was assessed using the rating scales developed by the AACPDM work group (Logan, Hickman, Harris, & Heriza, 2008) and by Smith et al. (2007). The AACPDM scale consists of 14 questions that address the selection and description of participants, description of intervention, and accuracy of measurement. The Smith et al. scale consists of 7 questions that address criteria in similar areas.

Information regarding the study design, participants, intervention, outcomes, and conclusions were extracted into a common database.

Results: Fifteen parent training and six teacher training SSRD studies met the selection criteria and were included. A total of 75 individuals with ASD ranging from toddlers to adolescents and their parents/teachers were represented across these studies. Parents (almost all mothers) included those with low to high education and low to high socio-economic status. One study was rated as having high quality, 20 were of moderate quality, and one was weak in quality. Overall, the studies reported mastery of the target procedures by parents and teachers and concomitant increases in child social-communicative behaviors. Parents were trained to implement discrete trial teaching (DTT), pivotal response training, various forms of natural environment and incidental teaching, time delay, other systematic instructional techniques. Teachers were taught to use DTT and various types of prompts and contingent reinforcement.

Conclusions: A small number of studies of moderately-high quality have been conducted to examine approaches for training parents and teachers to implement social-communication interventions with individuals with ASD across the range of age and ability. Although these studies provide some guidance with regard to effective training strategies for real-world settings, future work is needed to develop additional training procedures that are both effective and efficient and that can be implemented in home and school settings.

130.112 133 Teaching Parents of Children with Autism to Empirically Evaluate Their Child's Interventions. K. L. Berquist*[1] and M. H. Charlop[2], (1)*Stanford University School of Medicine*, (2)*Claremont McKenna College*

Background: Currently there are various intervention options for children with autism that proponents claim are effective. However, efficacy of these interventions, with the exception of Applied Behavior Analysis and some psychotropic medication, is based on non-scientific evidence. Studies report that 74% to 92% of children with autism are enrolled in programs that are not empirically validated. To decrease children's enrollment in ineffective and non-empirically interventions, research suggest that parents should be taught to empirically evaluate the efficacy of their child's interventions.
Objectives: The purpose of the current study was to investigate the effectiveness of a parent education program to teach parents 1) how to distinguish between treatment options for their children with autism and 2) scientifically design and evaluate their child's interventions.
Methods: A multiple baseline design across parent participants was used to assess the effectiveness of a parent education program to teach parents evaluative behaviors (e.g., operationally defining a variable of interest, data collection, taking baseline data, accurately analyzing data) necessary to determine the efficacy of their child's interventions. Pre- and post-test comparisons with a non-experimental control group were used to assess variables related to parent reported behavior, psychosocial indicators, and knowledge of evaluative information.
Results: Six parents have participated so far in this project. Preliminary analyses indicate that all participants increased in their evaluative behaviors from baseline to after implementation of the parent education program. Additionally, evidence of generalization and maintenance of parents' evaluative behaviors was demonstrated. Results also revealed that, in comparison to controls, parents with training increased their ability to distinguish between interventions that are empirically validated and those that are not.
Conclusions: This study is the first of its kind to address the need of educating parents on how to evaluate the effectiveness of their child's interventions. To date, no study has attempted to empirically investigate reducing the adoption of non-empirically supported interventions through the implementation of a parent education program. This study provides preliminary results on how to successfully increase parents' abilities to scientifically evaluate their child's interventions.

130.113 134 Teaching Social Skills to Preschool Children with Autism Spectrum Disorders: Examining Treatment Efficacy

and Benefit of Continued Participation in the UCLA PALS Program. J. Sanderson*, Y. C. Chang, S. Mallam, R. W. Ellingsen, C. Ferber and E. Laugeson, *UCLA Semel Institute for Neuroscience & Human Behavior*

Background: Children with Autism Spectrum Disorders (ASDs) are receiving behavior and language focused intervention at an earlier age, due to research on the importance of early intervention. Comparatively few interventions for young children specifically target social skills, and even fewer evaluate treatment efficacy using multiple raters and valid and reliable standardized assessment measures.

Objectives: This study examines the efficacy of improving overall social functioning among preschool children with ASDs using the UCLA Preschool Applied Learning of Social Skills (PALS) Program, a 15-week manualized social skills intervention.

Methods: 29 children participated in the PALS intervention as part of their enrollment in an intensive therapeutic social recreational program for children ages 3 to 6 with an ASD. Many participated in PALS multiple times due to continued enrollment in the broader social recreational program. Prior to treatment and after each round of the PALS intervention, parents and teachers rated 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). PALS includes 20-minute treatment sessions administered 2-3 times per week using puppet-facilitated scripted didactic lessons with role-playing exercises by group leaders and peer models, structured and unstructured behavioral rehearsal of skills with peers, and weekly handouts for parents with strategies for reinforcing skills in other settings. Children learn concrete rules and steps of social etiquette for social communication, turn-taking, sharing, peer entry, good sportsmanship, teamwork, helping behavior, and body boundaries.

Results: Within-subjects ANOVAs were conducted for approximately 18 participants to examine treatment efficacy and improvement in social skills over time. Children who received PALS only once and/or who had missing data were excluded from the analyses. Tukey-Kramer pairwise comparisons were completed post-hoc to investigate potential continued improvement after participating in PALS a second time, followed by Bonferroni correction for conservative reporting of results. Parent-reported overall Social Responsiveness ($p < .05$) and Social Cognition ($p < .01$) on the SRS improved significantly after receiving PALS once. Teacher-reported overall Social Skills ($p < .01$) , Cooperation ($p < .05$), and Assertiveness ($p < .01$) on the SSRS, and parent-reported Social Communication ($p < .01$) on the SRS also improved significantly after receiving PALS once, and continued to improve after receiving PALS a second time. Teacher-reported overall Social Responsiveness ($p < .05$) and Social Awareness ($p < .01$) on the SRS, and Self-Control ($p < .01$) on the SSRS improved significantly after receiving PALS twice. Trends were found for improved teacher-reported Problem Behaviors ($p = 0.0585$) and Hyperactivity ($p = 0.069$) on the SSRS, and Social Motivation on the SRS ($p = 0.054$) after participating in PALS twice. Preliminary analysis of predictors of treatment success demonstrated that parent-reported Social Motivation at baseline significantly predicted parent-reported overall Social Responsiveness following PALS ($p < .01$); parent-reported Autistic Mannerisms was tested but not found significant.

Conclusions: These findings suggest that PALS may be efficacious in improving the social functioning of preschool-aged children with ASDs, with additional improvements expected after continued participation in PALS.

130.114 135 The Importance of Early Intensive Behavioral Intervention in Very Young Children with ASDs for Core Symptoms and Cognitive Development. M. Foscoliano*[1], P. M. Peruzzi[1], F. Casano[1], L. Ferretti[1], R. Fadda[2] and G. Doneddu[3], (1)*A.O. Brotzu*, (2)*University of Sheffield*, (3)*Azienda Ospedaliera Brotzu*

Background: Most studies on the outcomes of behavioural techniques have investigated the gains on standardized tests of children with Autism after 4 years (McEachin et al.,

1993; Sheinkopf & Siegel, 1998; Eikeset et al., 2002). However, due to advances in diagnosing Autism Spectrum Disorders (ASDs) in children as young as 1 – 2 years old, there has now been an increased diagnosis rate of ASDs followed by early intensive intervention in very young children with ASDs (Cox et al., 1999; Itzachak et al., 2009; Lord et al., 1995). It has been assumed that very early intervention would yield improved outcomes because plasticity of neural systems in young children permits significant changes in the central nervous system (Dawson et al., 2000). However, evidence about the effect of interventions in very young children has been limited due to the scarcity of follow-up outcome studies in this population.

Objectives: The current study investigated the effect of early intensive Applied Behavioural Analysis intervention (ABA-int) in very young children with ASDs on standardized tests of cognitive performance (Leiter-R) and adaptive behavior (Vineland Adaptive Behavior Scale – VABS). We also analysed changes in severity of ASDs core symptoms as defined in the ADOS.

Methods: 27 children with ASDs (20M: 7F), age range 23 - 65 mths (mean age = 37 mths; SD = 12), received ABA-int (10 hrs of ABA in DTT form and 5 hrs of speech therapy at week), were compared with 16 children with ASDs, age range 23-73 mths (mean age = 43 mths; SD = 13) that received Eclectic interventions (play group, psicomotricity, music therapy, for an average of 4 hours - week). All the children were tested twice (T1-T2 = 12 months) with the Leiter-R scale, with the VABS and with the ADOS.

Results: The groups were equivalent at T1 for Leiter-R scale and VABS scores. After 6 months, there was a 23 point IQ gain in the ABA-int group ($t = -3,85$;$df = 26$; $p<0,05$) while the Eclectic group did not show any significant change in standardized test scores ($t = -1,05$; $df = 15$; $p>0,05$). VABS scores increased significantly both in the ABA-int (+ 7 mths; $t = -3,31$;$df = 26$; $p<0,05$) and in the Ecletic group (+ 6 mths; $t = -3,86$; $df = 15$; $p<0,05$). The children in the ABA-int group scored significantly lower on the ADOS ($t = 5,34$; $df = 26$; $p<0,05$) while the severity of ASDs symptoms in the Ecletic group remained stable.

Conclusions: Our results point to the effectiveness of early intensive behavioural intervention in very young children with ASDs for cognitive development and in reducing symptoms severity. At same time, as ABA early intervention seems to does not appear to influence adaptive abilities, these findings highlight the importance of generalization in intervention programs in order for children to be successful in daily routines.

130.115 136 The Picture Exchange Communication System: More Than a Menu?. J. Koudys*, A. Perry and K. McFee, *York University*

Background:

The acquisition of functional communication skills largely dictates the extent to which individuals with autism participate in daily activities at home and school and develop social relationships. Further, the attainment of a communication system has been directly linked to the prevention and reduction of problem behaviour. Numerous studies link the Picture Exchange Communication System (PECS) to enhanced communication and speech development, as well as decreases in inappropriate behaviour. However, few explore the quality of children's communication skills following PECS use in detail. As such, there exists little information about vocabulary diversity (i.e., breadth/type of word use), sophistication of communication (i.e., mean length of utterance, use of attributes/proper syntax) or the range of functions the system serves (i.e., requests, social interactions). Further, little is known about the environments and activities in which PECS is used. Most significantly, little is known about specific areas of difficulty (i.e., spontaneity, distance, discrimination).

Objectives:

The purpose of this research is to describe children's use of PECS in real world settings. Generalization factors such as the different types of reinforcers requested, vocabulary breadth, the activities and settings within which PECS is used will be described, as well

as more quantitative outcomes, such as PECS phase achieved and frequency of requesting. Finally, the impact of PECS training on overall communicative behavior, in both home and community environments will be described.

Methods:

Data was collected from 22 children using PECS in a community-based summer program. Pre- and post-camp assessments included measures of children's requesting behavior and PECS phase. Two graduate level doctoral students conducted live and video review of children's pre-post communicative behavior. Interobserver agreement was above 90%. Parent communication questionnaires were also completed pre- and post-camp to assess general communicative behavior across settings. Finally, daily data logs recording types of reinforcers requested, frequency of requests and environments in which PECS was used were completed by camp staff.

Results:

Results indicate that children gained at least one PECS phase during the 7-week summer camp and were reported to use a variety of different pictures (mean = 40, range 15-68) to request reinforcers from several different categories (mean = 4.5 categories, range = 3-5). PECS use was observed in many different activities and environments (mean= = 8.35 environments, range = 6-13). Reductions in problem behavior were also observed. Parent reports indicate overall communicative benefits following PECS training.

Conclusions:

PECS was used by children with autism spectrum disorders and significant cognitive impairments to access numerous different reinforcers across a variety of environments. Overall improvements in communicative behavior were observed across settings.

130.116 137 Therapeutic Horseback Riding in Children with Autism Spectrum Disorders. J. A. Agnew*[1], R. Gabriels[1], Z. Pan[1], K. Holt[1], S. Martin[1], G. H. Clayton[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: 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 few studies have evaluated such interventions scientifically. 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 10 one-hour weekly lessons of standardized THR treatment in three core areas: 1) Self-regulation behaviors, 2) adaptive daily living skills, and 3) motor coordination, organization and planning. Compare changes made following THR intervention with changes made during a ten-week waitlist control period, occurring immediately before THR.

Methods: Forty-one subjects (35 male, 6 female) between the ages of 6 – 16 years (mean age: 8.7 years) with an ASD received pre- and post-intervention 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 completed ratings (ABC-C) of the child's behaviors on a weekly basis. Sixteen subjects also participated in a wait-list control group before THR.

Results: Subjects from the THR group demonstrated significant improvements on the Irritability, Lethargy, Stereotypic Behavior, Hyperactivity and Inappropriate Speech subscales of the ABC-C; Short Form of the BOT-2; SIPT Verbal Praxis and Communication raw score and Adaptive Total score of the VABS-II. For the Irritability, Lethargy, Stereotypic Behavior and Hypersensitivity subscales of the ABC-C, significant improvement was noticed as early as the third week of THR. The expressive and receptive language subdomain raw scores of

the VABS-II Communication domain were examined and subjects displayed significant improvement on the measure of expressive language, but there was a trend towards improvement on receptive language.

The waitlist control group enabled further analysis of the data to determine if the improvements were due to THR or if they might be due to a different, unidentified factor. ANCOVA analyses were performed to compare the change from pre-test to post-test. Significant improvements were found in subjects who participated in THR vs. waitlist period on the Irritability, Lethargy, Stereotypic Behavior and Hyperactivity subscales of the ABC-C.

Conclusions: The presence of a significant difference on the ANCOVA analysis suggests that the degree of change from the pre-test to the post-test differs significantly between the waitlist and the THR conditions and, therefore, may be due to the treatment itself. Lack of significant results on this ANCOVA analysis could mean that any differences observed on the t-tests described above may be due to developmental changes, lack of statistical power to identify a significant difference using the ANCOVA analysis or other factors that cause fluctuations between testing sessions.

130.117 138 Treatment Needs of Adolescents with High-Functioning Autism: An Interpretative Phenomenological Analysis Incorporating Multiple Perspectives. T. D. Perry*, B. M. Rupp, L. M. Turner Brown and D. L. Penn, *University of North Carolina*

Background: Interest in the development of interventions addressing the unique needs of adolescents with high-functioning autism (HFA) has grown steadily in recent years. Despite this interest, however, the treatment needs of this population continue to be poorly understood.

Objectives: To inform the development of a group intervention to improve social cognitive skills among teens with autism, four focus groups were conducted. Feedback was obtained from different groups with vested interests in treatments for this group.

Methods: One focus group was composed of professionals (i.e., therapists, direct care providers) working with teens with HFA (N=4); another included parents or other close relatives of adolescents with autism (N=7); a third was comprised of the teens with HFA themselves (N=6); and the final focus group was made up of individuals from all three of the aforementioned groups (N=14). Each group responded to a series of identical questions during focus group sessions lasting approximately one hour and thirty minutes. Data was analyzed using interpretive phenomenological analysis (IPA) which focuses on the primacy of subjective human experience and the ways in which individuals make sense of their experiences.

Results: Reported findings include emergent themes including areas of agreement between these groups (i.e. central role of motivation, unique challenges of this age group) as well as areas of disagreement (i.e., role of parents in the intervention process, appropriate focal points of treatment).

Conclusions: Implications and possible uses for this information in the development of targeted, tolerable, and effective interventions for adolescents with high-functioning autism are discussed. Suggestions for future research aimed at identifying salient themes in this group are also presented.

130.118 139 Use of Complementary and Alternative Medicine in Children with Autism and Controls: Associations with Ethnicity, Child Co-Morbid Symptoms and Parental Stress. M. D. Valicenti-McDermott*, B. Burrows, L. Bernstein, K. Hottinger, K. Lawson, R. M. Seijo, M. Schechtman, L. Shulman and S. Shinnar, *Albert Einstein College of Medicine*

Background: Families of children with Autism Spectrum Disorder(ASD) frequently engage in the use of complementary and alternative Medicine(CAM). Little information is available about frequency/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

ASD and to assess the relationship of CAM with feeding, gastrointestinal, sleeping and behavioral problems and parent stress. Methods: Cross sectional study with structured interview in 50 children with ASD and 50 children with other developmental disabilities(DD), matched by age and gender. Interview included: CAM questionnaire, Gastrointestinal (GI) Questionnaire, Child's Sleep Habits Questionnaire, Aberrant Behavior Checklist and Parenting Stress Index. Statistical analysis included chi-square, t test, and Logistic Regression. Results: To date we have recruited 50 children with ASD and 30 children with other DD, 15% White, 44% Hispanic and 24% African American, mean age 8+/-3 yr. CAM use was reported in 67% of the ASD group including supplements (44%) and gluten-casein free diet (29%). The number of CAM therapies used ranged from 0 to 8. CAM usage was more prevalent in families of children with ASD (67% vs.28% p=0.001) and these families used more types of CAM (2+/-2 vs. 0.3+/-0.6 p<0.001) than families of children with other DD. Children with ASD presented more co-morbid symptoms such as GI (66% vs.40% p=0.04), sleeping (78% vs.33% p<0.001)and behavioral problems (78% vs.33% p<0.001) and their parents reported greater stress (45% vs.20% p=0.03).CAM use was associated with child irritability (73% vs.44% p=0.01), and parental stress (70% vs.40% p=0.04). The association between CAM use and ASD diagnosis persisted after adjusting for child-comorbidities, parental stress and level of maternal education (OR 4.7 95%CI 1.7-13.6). Compared to White mothers, Hispanic mothers used fewer types of CAM therapies (0.7+/-1 vs. 2.9+/-3 p=0.01). No association was observed between CAM use and feeding, GI or sleeping problems.
Conclusions: Families of children with ASD were more likely to utilize CAM than families of children with other DD. Hispanic families used fewer types of CAM therapies. CAM use seems to be related to child irritability and parental stress.

130.119 140 Using Commercially Produced Videos to Teach Receptive Body Part Identification to Young Children with Autism: Pilot Data. K. A. Kroeger*[1], A. W. Duncan[1], L. S. Srivorakiat[2], S. Breving[2] and K. C. Currans[1], (1)*Cincinnati Children's Hospital Medical Center*, (2)*Xavier University*

Background: The average preschooler watches two hours of screen media (e.g., television, video) per day. While research has demonstrated that children over the age of three are able to learn information from screen media programs such as Sesame Street (see Fisch, Truglio, & Cole, 1999), studies have not been conducted that investigate the ability of toddler and preschool aged children with autism spectrum disorders (ASD) to learn concepts from screen media. While it has been clearly shown that young children with autism learn new concepts through discrete trial training (DTT; see Smith, 2001), and alternatively through created video modeling stimuli utilizing DTT methodology (see Kroeger, Schultz, & Newsom, 2007), it is also important to determine if commercial screen media provides a supportive learning environment that is conducive to skill acquisition in this population of children.

Objectives: This pilot study aimed to investigate the effectiveness of using commercially produced videos to teach receptive identification of body parts to a group of young children with autism. Furthermore, the study investigated if the use of screen media was more or less effective in teaching the target goals than empirically validated DTT strategies.

Methods: Study participants included three boys (ages 2-, 3-, and 4-years-old) diagnosed with autistic disorder enrolled in an early intensive behavioral intervention classroom affiliated with a children's hospital. The target behavior was receptive identification of body parts using Baby Einstein's *Baby Da Vinci from Head to Toe* video. Six targets of receptively identifying body parts were chosen for the pilot and divided equally between video modeling teaching and DTT. Multiple baseline probes were conducted to ascertain that the children were not able to already identify the target body parts, that they did not learn them by multiple presentations of baseline probes and that they did not learn them simply by viewing the commercially produced video.

Video segments were played for students in a group setting where the children were systematically oriented to the specific body part during the viewing segment. The discrete trial teaching comparison was conducted in a structured, individual setting within the classroom. Pre- and post-teaching probes were conducted on all targets each session to determine acquisition, maintenance and generalization.

Results: Preliminary results indicate that targets were not learned in baseline probes where the children were simply viewing the video and then asked to identify the target. Acquisition rates for targets varied per child from equal learning times using video modeling and DTT to demonstrated quicker acquisition time for targets using DTT methodology.

Conclusions: Commensurate with the established literature regarding typically developing toddlers, preliminary results suggest that merely viewing commercially produced videos is not likely to lead to skill acquisition in young children with autism. Applying structured teaching strategies to video viewing leads to skill acquisition, however, this teaching using video modeling does not appear to be any more effective or efficient than traditional discrete trial teaching.

130.120 141 Pilot Testing of a Sleep Training Program for Children with Autism Spectrum Disorders. C. Johnson*[1] and B. Handen[2], (1)*University of Pittsburgh*, (2)*Univ of Pittsburgh School of Medicine*

Background: Core features of autism include deficits in social interaction and communication as well as repetitive and restrictive patterns of behavior. In addition to these core diagnostic features, children with autism frequently present with a host of associated behavioral issues. Sleep problems are estimated to occur in 30-86% of this group of children disruptive sleep patterns and habits appear to occur at a higher rate among children with autism than typically developing children based on both parental reports and other objective measures of sleep. Sleep problems further seem to occur at high rates in children with high functioning autism and Asperger Disorder suggesting that sleep disruption may not be fully attributed to intellectual disability. Hence, there is an immediate need to develop and test efficacious interventions to address sleep disturbances in this population.

Objectives: This is a pilot study to evaluate the efficacy of a manualized behavioral parent training program for the amelioration of sleep disturbances in young children with autism. This work will be used to examine the feasibility, acceptability and efficacy of five, individually delivered sessions targeting a number if sleep problems. Outcome measures include parental report measures as well as actigraphy.

Methods: A sample of young children with autism between the ages of 24 months and 60 months are being recruited for this pilot study. The children must have at least one significant sleep problem (bedtime resistance, delayed sleep onset, sleep association problems, night wakings, morning wakings). Parent(s) / primary caregiver will participate in five parent training sessions. A home visit is also made in the beginning of the program. Parent training topics include: 1) Basic behavioral principles; 2) Addressing prevention techniques and bedtime routines; 3) Addressing reinforcement and extinction procedures; 4) Addressing delayed sleep onset and sleep association procedures; 5) Booster and maintenance. The sessions include didactic training, completion of parent activities and the use of video vignettes. While the parent training is manualized, it also allows for individualization, for example based on the types of sleep disturbances, functioning level of the child, and parent preferences of procedures.

Results: Participants thus far presented with bedtime resistance, delayed sleep latency, sleep association problems and frequent night wakings. Treatment integrity and parent adherence has been 100% as has been parent attendance and parent satisfaction. Parents rated improvements in sleep as measured on the composite sleep index of the Modified Simond & Parraga Sleep Questionnaire. Improvements in

parental stress have also been reported. Actigraphy data supporting improvements have been variable.

Conclusions: This manualized parent training program to address an array of sleep problems can be delivered successfully. Further study is warranted to determine the efficacy of the program as well as to determine any predictors of success.

Keynote Address Program

131 Infants' Grasp of Others' Intentions

Speaker: A. Woodward *University of Maryland*

This talk will consider the early development of social perception in typically developing infants. The perception of others as intentional agents is fundamental to human experience and foundational to development. Recent research reveals that this cornerstone of social perception has its roots early in infancy, and that it draws structure from the universal, early emerging human experience of engaging in goal-directed action. Infants' own action capabilities correlate with their emerging tendency to view others' actions as organized by goals. Moreover, interventions that facilitate new goal-directed actions alter infants' perception of those same actions in others. These effects seem to depend on the first-person aspects of infants' experience. These findings open new questions about how doing leads to knowing in the social domain.

Invited Educational Symposium Program

132 Medical Care of Children and Adolescents with Autism Spectrum Disorders: Findings From the Autism Treatment Network

Moderator: C. Lajonchere *Autism Genetic Resource Exchange/Cure Autism Now*

Knowledge of medical conditions that accompany ASD is limited. Recommendations for evaluation and management are often based on small case series and reports, and supporting data have not been consistent. Common medical problems include gastrointestinal symptoms, sleep problems, and seizures. The Autism Treatment Network (ATN) was formed to advance understanding of medical comorbidities of ASD and to use this knowledge to shape best practices. This session will (1) describe common medical co-morbidities seen in children and adolescents with ASD using data from the ATN patient registry of over 1200 individuals, and (2) discuss approaches to treatment. Panelists will discuss methods of screening, evaluation, and treatment of gastrointestinal, sleep and EEG abnormalities; development of evidence-based guidelines for managing medical co-morbidities; and newly initiated research studies regarding the physical health of children and adolescents with ASD.

132.001 Introductory Remarks.

132.002 ASD and GI Co-morbidities: What do we know?. G. J. Fuchs*, *University of Arkansas for Medical Sciences*

GI symptoms are one of the most common concerns of parents, but controversy continues: Are they more frequent than in other developmental disorders, how much evaluation should be undertaken, what treatments are effective? Dr. Fuchs will present a review of the literature and data from the ATN patient registry. Directions for future research will be discussed.

132.003 Sleep disorders in ASD - Diagnosis and Treatment. B. A. Malow*, *Vanderbilt University*

Symptoms of insomnia, disrupted sleep and early awakening are frequently seen in ASD. The cause of sleep problems in ASD is uncertain and several theories suggest a variety of potential treatments. Dr. Malow will review the literature and discuss research methods used in documenting sleep disorders in ASD as well as the effectiveness of non-pharmacologic treatments.

132.004 EEG Abnormalities: Identification and significance. S. E. Swedo*, *National Institute of Mental Health, National Institutes of Health*

Approximately 30% of individuals with ASD are diagnosed with epilepsy, but prognostic factors are not clear. EEG abnormalities, whether epileptogenic or not, are of questionable significance. There are reports of varying frequencies of these abnormalities, and the possible benefit of treating these abnormal results pharmacologically. The most recent findings will be presented along with suggestions for further research in this area.

132.005 Next Steps: Clinical Guidelines and Research in Progress. D. L. Coury*, *Nationwide Children's Hospital*

At present, published practice guidelines for children and adolescents with ASD are based on expert clinical consensus with limited evidence to support them. The development of evidence-based clinical guidelines requires implementation of consensus guidelines, careful measurement of outcomes, and

revision of these guidelines based on the derived data. Progress in the development of clinical guidelines and the status of other research in progress in the ATN will be presented.

Brain Imaging Program
133 Brain Imaging 2

133.001 Growth Curves for Longitudinal Regional Brain Volumes in Autism Vs. Typical Development. J. E. Lainhart*[1], C. Ravichandran[2], A. Froehlich[1], M. B. DuBray[1], T. Abildskov[3], E. Bigler[1], A. L. Alexander[4] and N. Lange[5], (1)*University of Utah*, (2)*McLean Hospital/Harvard Medical School*, (3)*Brigham Young University*, (4)*University of Wisconsin*, (5)*Harvard University*

Background: Although cross-sectional samples of regional brain volumes in autism are widely available, longitudinal samples are few and of smaller sample size covering shorter age spans. The necessary caveats on reported associations between age and brain structure sizes in autism derived from these samples remain. Clinically useful growth curves for regional volumetric brain development in autism are severely lacking and highly needed.

Objectives: Our goal is to derive valid and reliable volumetric growth curves for total and regional brain development in autism and to compare them to corresponding growth curves in typical development.

Methods: The subset of our larger longitudinal sample studied thus far contained N = 102 high-functioning males on the autism spectrum aged 3-40 years, matched with N = 53 typically-developing controls. We extracted volumes of all oft-used brain structures by FreeSurfer. The number of scans/subject was 1 (20 autism, 17 control), 2 (55 autism, 27 control) and 3 (26 autism, 26, 11 control). We conducted a longitudinal growth-curve analysis of each structural volume separately to determine its possible dependence on group, age, and group by age interaction.

Results: (1) In autism, while controlling for volume-age associations, we found that all regional volumes depended on total brain size, except for ventricular volume. Relationships between total and regional brain volumes were similar in autism and controls except in the putamen and mid-posterior corpus callosum (CC); volumes of these regions were found to depend more strongly on total brain size in autism (both $p < 0.00005$). (2) No group mean volume differences were observed for any structure when we accounted for age and total brain size associations. (3) All volumetric growth-curves in both groups were found to be linear in age; no quadratic or other curvilinear relationships were detected. The following regions showed significant volumetric changes with age in autism but not in typical development: intracranial cavity (increasing), cerebrum (decreasing), gray matter (decreasing), white matter (increasing) (all $p<0.00005$) and ventricles (increasing) ($p=0.0391$). The total and regional mean volumes and coefficients of variation of our control sample were consistent with those observed in the recent large nationwide study of representative healthy brain development (N = 152 males). Linear volumetric changes with age found in the subset of our control sample 4.8-18.3 years of age matching the age range of the nationwide sample.

Conclusions: As indicated by our wide 3-40 year age range, volumetric growth-curves suggest that total and regional brain growth may be more protracted in autism than in typical development. Total and regional brain structure sizes in autism appear, thus far, to conform to typical values with the 4.8–18.3 range derived from the nationwide longitudinal study of typical peers. More detailed and comprehensive studies of our longitudinal sample are underway, specifically of a possible disturbance in associations between total brain and putamen and mid-posterior CC sizes Acknowledgements and Disclaimer: 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.

133.002 An Examination of Brain Size in Infants at High Risk for Autism: Preliminary Findings From the Infant Brain Imaging Study. H. C. Hazlett*[1], K. Botteron[2], H. Gu[3], R. McKinstry[4], S. Paterson[5], M. Styner[6] and J. Piven[3], (1)*University of NC*, (2)*Washington University*, (3)*University of North Carolina*, (4)*Washington University in St. Louis*, (5)*University of*

Pennsylvania and Children's Hosptial of Philadelphia, (6)*UNC*

Background:

The Infant Brain Imaging Study (IBIS) Network is an NIH funded Autism Center of Excellence and consists of a consortium of 7 universities in the U.S. and Canada. The IBIS study involves the national recruitment of infants at high-risk for autism (based on having an older sibling diagnosed with autism) and a control group of typically-developing infants. Infants are assessed longitudinally at ages 6, 12 and 24 months. Measures include MRI and DTI scans in addition to a battery of behavioral and developmental tests. This longitudinal study is currently ongoing, but we are reporting on preliminary findings from the cross-sectional data obtained on 100 high-risk infants at age 6 months.

Objectives:

Brain enlargement has been observed in individuals with autism as early as age 2. Studies of head size using head circumference measurements suggest that the period of brain enlargement is a postnatal event and may occur between 6-12 months of age. In this report, we examined the cross-sectional data from 6 month olds at high risk for autism and typically-developing controls participating in the longitudinal study.

Methods:

Four clinical sites participated in the data collection: University of North Carolina, Washington University, Children's Hospital of Philadelphia, and the University of Washington. All the brain MRI scans were completed on a 3T Siemens scanner during natural sleep. Measures of brain volumes were obtained using an automated atlas-based pipeline for the tissue segmentation (ITK-EMS, AutoSeg) and/or semi-automated image processing tools (ITK-SNAP, HeadCirc).

Results:

Group based comparisons for the high-risk infants compared to controls were completed for the selected brain volumes. Brain volumes examined include intracranial volume (ICV), total brain volume (TBV), cerebrum, cerebellum, cortical lobe volumes, lateral ventricles, and head circumference. Statistical analyses included important covariates such as gender, site, body size, and age at scan. We are currently completing the planned statistical analyses for the 6 month dataset, and are unable to include our findings in this abstract. However, these analyses will be completed well before the conference.

Conclusions:

The results from this preliminary cross-sectional analysis will provide new information regarding early brain size in infants at high-risk for autism. This study represents the largest known examination of brain volume in an at-risk population.

*__IBIS Network__: The IBIS (Infant Brain Imaging Study) Network is an NIH funded Autism Center of Excellence (HDO55741) and consists of a consortium of 7 Universities in the U.S. and Canada. ***Clinical Sites*****:** University of North Carolina: J. Piven (IBIS Network PI), H.C. Hazlett, C. Chappell; University of Washington: S. Dager, A. Estes; Washington University: K. Botteron, R. McKinstry, J. Contstantino, L. Flake ; Children's Hospital of Philadelphia: R. Schultz, S. Paterson; University of Alberta: L. Zwaigenbaum. ***Data Coordinating Center*****:** Montreal Neurological Institute: A. Evans, L. Collins, B. Pike, R. Aleong, S. Das. Image Processing Core: University of Utah: G. Gerig; University of North Carolina: M. Styner. ***Statistical Analysis Core*****:** University of North Carolina: H. Gu. ***Genetics Analysis Core*****:** University of North Carolina: P. Sullivan, F. Wright.

133.003 Subgroups of Abnormal Growth Trajectories: A Longitudinal Analysis of Amygdala Growth in Young Children with Autism. C. W. Nordahl*, R. C. Scholz, T. J. Simon, S. J. Rogers and D. G. Amaral, *M.I.N.D. Institute, University of California at Davis*

Background:

Several studies have demonstrated amygdala enlargement in young children with autism (Sparks 2002, Schumann 2004, Mosconi 2008, Schumann 2009). However, longitudinal data on rate of growth has not yet been extensively evaluated.

Objectives:

We report findings in a large sample of 2-3 year old males (n = 101; 72 ASD 29 Typical development). A subset of children in this sample received a longitudinal one year follow up scan (n = 38; 24 ASD, 14 Typical development). Rate of amygdala growth relative to total cerebral volume was examined.

Methods:

All MRI scans were acquired during natural nocturnal sleep, without the use of sedation or anesthesia. A high-resolution 3D MPRAGE sequence was acquired using a 3T Siemens Trio system. Total cerebral volume and amygdala volume were manually traced using Analyze 9.0 software. For longitudinal analyses, amygdala volume was normalized to total cerebral volume and percent change was calculated, taking into account ages at baseline and follow-up MRI scans.

Results:

Cross-sectional results of the entire sample indicate a larger right amygdala (p = .04) and a trend towards a larger left amygdala (p = .07) in the ASD group after covarying for age and total cerebral volume. Longitudinal analyses revealed substantial heterogeneity within the autism group. For typically developing children, the mean percent change was 4.3%. Twelve out of 24 (50%) children with autism demonstrated a similar rate of growth (4.2% increase). However, there were two distinct subgroups within the ASD group, one with rapid growth (n = 7 (29%), 17.6% increase), and one with slow growth (n = 5 (21%), -5.6% growth [negative number signifies that TCV was growing more rapidly than amygdala]).

Children in this study are part of a larger multi-disciplinary study, the Autism Phenome Project, through which various measures, including extensive behavioral indices, immunological and genetic profiles, and auditory event related potentials are being collected in the same population of children. Efforts will be made to characterize the three different subgroups based on these other measures. Preliminary findings suggest autism severity is positively correlated with increased rate of amygdala growth.

Conclusions:

While overall enlargement of the amygdala is present in 2-3 year old children with autism spectrum disorders, there is substantial heterogeneity in the rate of growth. Specifically, while the typical group showed considerable homogeneity in their growth pattern, more than a quarter of children with ASD showed accelerated amygdala growth of four times the typical rate. One in 5 showed dramatically slower than typical growth. Overall, increased rates of amygdala growth are correlated with more severe symptoms of autism. The identification and further characterization of subgroups such as these will be fundamental to understanding the heterogeneity within autism spectrum disorders.

133.004 Multimodal MRI Analysis of White Matter in Young Children with Autism: A Diffusion Tensor Imaging, Tractography, and Structural MRI Study. M. Shen*[1], C. W. Nordahl[1], R. C. Scholz[1], L. M. Perry[2], R. F. Dougherty[2], T. J. Simon[1], S. J. Rogers[1], B. A. Wandell[2] and D. G. Amaral[1], (1)*M.I.N.D. Institute, University of California at Davis*, (2)*Stanford University*

Background:

Abnormalities in white matter microstructure and connectivity have been reported in autism, but no studies have included a large sample in early childhood. It is also unclear how measures of microstructure, connectivity, and cortical shape interact and are associated with autism symptomatology.

Objectives:

To evaluate multiple aspects of white matter integrity in a large sample of young children with autism. Analyses include an examination of the microstructure of white matter tracts, the connectivity between tracts

and cortical regions, and patterns of cortical folding and sulcal organization. This study was conducted as part of a larger multidisciplinary study at the M.I.N.D. Institute, the Autism Phenome Project.

Methods:

Diffusion-weighted images were acquired on 100 children (64 ASD, 36 TD; mean age ASD 3.2 years, TD 3.4 years). The total sample included 75 boys and 25 girls; the subset of girls will be analyzed separately. Tract-based spatial statistics (TBSS) were applied to determine whether specific white matter tracts show between-group differences in measures of white matter integrity. Tractography analyses were performed to examine the connectivity between white matter tracts, particularly fibers that project through the corpus callosum. Manual segmentation of callosal fibers allowed for the identification of fibers that projected to each cortical area (e.g. occipital, parietal, temporal, and frontal fibers). Diffusion-weighted variables such as fractional anisotropy (FA), mean diffusivity (MD), and radial diffusivity (RD) were analyzed as measures of white matter integrity.

Results:

Preliminary results of the tract-based analysis show reductions in FA for the autism group, in several regions including: the corpus callosum, left medial parietal lobe adjacent to the splenium of the corpus callosum, left superior temporal lobe, and right middle frontal gyrus. Tractography results suggest that children with autism have compromised white matter integrity in corpus callosum fibers that project to the frontal lobe, particularly oribitofrontal cortex. Moreover, greater white matter irregularity in these fibers correlated with more severe autism symptoms.

Conclusions:

These findings provide evidence in early autism for white matter abnormalities in specific tracts and in fibers that project between cortical areas, including the frontal lobe. This is a reflection of impaired anatomical connectivity that may underlie cortical networks important for social cognition, which may relate to autism symptoms. Surface-based analyses of structural MRIs will be conducted to examine whether cortical folding abnormalities are related to regions of abnormal white matter microstructure and connectivity. Finally, this multimodal MRI analysis will be correlated with other behavioral, diagnostic, genetic, and immunological measures to further understand how possible subtypes of autism are associated with differential development of white matter.

133.005 Brain Anatomy in Adult Autism: a Multi-Centre Neuroimaging Study. C. Ecker*[1] and M. R. C. AIMS Consortium[2], (1)*Institute of Psychiatry, King's College London*, (2)*University of Cambridge; Institute of Psychiatry, King's College London; University of Oxford*

Background:

Autism spectrum disorder (ASD) is a highly heterogeneous neurodevelopmental condition with multiple causes, co-morbid conditions, and a wide range of symptoms and symptom severity. This makes the neuroanatomy of ASD inherently difficult to describe. Although several autistic 'core' structures have repeatedly been highlighted in the literature, reports of region-specific differences in ASD are highly variable. Such variable findings may simply be explained by confounds such as clinical heterogeneity between studies, or analytical techniques. Alternatively, variability in findings may indicate that differences in brain anatomy in ASD are relatively subtle and spatially distributed. Hence, very large sample sizes of well-characterized individuals are required to yield to reliable results. So far, however, most neuroimaging studies on ASD are limited by small sample sizes.
Objectives:

The aim of this study was therefore to investigate (1) the feasibility of multi-centre structural MRI acquisition, and (2) to examine brain anatomy in ASD in a very large sample of well characterised male adults with ASD and matched controls.
Methods:

Overall, 178 participants were recruited and scanned at three participating centres - (1)

Institute of Psychiatry, London, (2) Autism Research Centre, Cambridge, (3) Autism Research Group, Oxford. The total sample included 89 adults diagnosed with ASD, and 89 healthy controls (matched for age and FSIQ), with approximately equal numbers of people with ASD and controls recruited at each site. All participants with ASD were diagnosed using the Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observation Schedule (ADOS). Quantitative imaging (relaxometry) was used to acquire multi-centre compatible structural Magnetic Resonance Images (MRI). A conventional non-parametric voxel-based approach employing the GLM was used to examine differences in grey and white matter volume between groups.
Results:

There were no significant group differences in total brain volume, total grey and white matter, and total CSF. However, significant grey matter volume differences were observed in three large clusters including temporal, frontal and occipital regions. Differences in white matter were observed throughout the brain and were dominated by regional deficits in the ASD group relative to controls. There were significant relationships between differences in brain anatomy and behaviour.
Conclusions:

This study is one of the first to demonstrate the feasibility of multi-centre MRI acquisition of brain anatomy in ASD, and to investigate neuroanatomical differences in a large and well-characterized sample of adults. Our results confirm the hypothesis that adult ASD is accompanied by localized anatomical abnormalities that are related to variation in specific behaviours, rather than global differences.

133.006 Atypical Asymmetry of Superior Temporal Gyrus and Temporal Stem White Matter Microstructure in Autism. N. Lange*[1], M. B. DuBray[2], J. E. Lee[3], M. P. Froimowitz[4], A. Froehlich[2], N. Adluru[5], B. Wright[2], C. Ravichandran[6], P. T. Fletcher[2], E. Bigler[2], A. L. Alexander[3] and J. E. Lainhart[2], (1)*Harvard University*, (2)*University of Utah*, (3)*University of Wisconsin*, (4)*McLean Hospital*, (5)*University of Wisconsin-Madison*, (6)*McLean Hospital/Harvard Medical School*

Background: Previous studies find that developmental deviations of functional hemispheric asymmetry in autism are associated with language functioning and cognitive ability impairments in the absence of volumetric differences. The pathogenesis of autism could thus involve atypical inter-hemispheric organization of white matter microstructure.

Objectives: We sought to determine if such atypicality is present in the superior temporal gyrus and temporal stem in autism and to quantify its effects on language functioning, if any.

Methods: Thirty high-functioning males with idiopathic autism aged 8-26 years and 30 matched controls participated in a case-control diffusion tensor magnetic resonance imaging study. All autism subjects met full criteria for autism. Convention tensor measures were recorded. A novel tensor asymmetry index, language functioning and psychotropic medication usage were also measured. We also studied an independent replication sample of 12 males with idiopathic autism and 7 matched controls.

Results: In our sample, we observed atypical losses and reversal of leftward asymmetry, atypical reductions in spatial organization and atypical age-related decreases of white matter microstructure in the superior temporal gyrus and temporal stem. Six of these measurements, including the novel tensor asymmetry index, discriminated between control and autism subjects with 91.6% accuracy, 93.6% sensitivity and 89.6% specificity. The classification ability of our method remained equally high with our second sample. Without the novel tensor asymmetry index, results dropped to unacceptably low levels between 66.7 and 71.4%.

Conclusions: Our results suggest that the hemispheric asymmetry, fiber organization and age-related changes in white matter microstructure in the superior temporal gyrus and temporal stem are atypical in autism. These brain circuitry abnormalities could be due to genetic and/or epigenetic dysregulation in brain development and are consistent with a hypothesis of increased

proximal connectivity and underdeveloped distal connectivity in the disorder. We also find that six of these atypicalities, including our novel tensor asymmetry index, could serve as useful biological indicators of autism in populations of individuals similar to our own.

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133.007 Altered Functional Connectivity During Rest is Related to 5-HTTLPR Genotype in Autism Spectrum Disorders. J. L. Wiggins*, S. J. Peltier, J. K. Bedoyan, S. Ashinoff, S. J. Weng, M. Carrasco, R. C. Welsh, C. Lord, D. M. Martin and C. S. Monk, *University of Michigan*

Background: Altered connectivity among brain structures has been found in individuals with Autism Spectrum Disorders (ASD) and is thought to underlie symptoms in these disorders. Whereas most ASD studies on connectivity used specific tasks, few examined the strong activation patterns during rest. Studies comparing individuals with ASD to healthy controls found altered posterior-anterior connectivity of the default network (a group of structures, including prefrontal regions, medial posterior regions, and the angular gyrus that are highly activated and connected when individuals are not doing a particular task). In addition, genetic research suggests that the serotonin transporter-linked promoter region (5-HTTLPR) gene may play a role in brain dysfunction and ASD symptoms. Studies with typical participants demonstrated that altered connectivity of brain regions is associated with variations in the 5-HTTLPR genotype. Furthermore, the low-expressing variant was associated with more severe social symptoms in individuals with ASD. However, the relationship between 5-HTTLPR variants and resting connectivity in individuals with ASD has not been examined.

Objectives: This study examines posterior-anterior connectivity in the default network during rest in relation to ASD symptoms and 5-HTTLPR genotype. We hypothesized that (1) posterior-anterior default network connectivity would be altered in individuals with ASD compared to controls; (2) individuals with ASD with the low-expressing variant of 5-HTTLPR would show altered connectivity in regions that differed between individuals with ASD and controls; and (3) altered connectivity would be related to social symptom severity in individuals with ASD.

Methods: Forty-one individuals with ASD and 32 controls were instructed to "let your mind wander" while being presented with a fixation cross for 10 minutes during fMRI acquisition. To calculate connectivity, a self-organizing map algorithm was used to identify the cluster containing the posterior hubs (posterior cingulate and angular gyrus) of the default network for each subject. Then, this cluster's average timecourse was correlated with all other voxels in the brain. PCR and DNA sequencing were performed on saliva samples to ascertain genotype.

Results: Individuals with ASD evidenced altered posterior-anterior connectivity compared to controls. Specifically, the right inferior frontal gyrus (rIFG) showed stronger connectivity with the posterior portion of the default network in individuals with ASD (xyz=46, 16, 6, t_{70}=4.18, p=0.048 small volume corrected for right prefrontal cortex, controlling for age and IQ). With the 31 individuals with ASD genotyped to date, a preliminary analysis revealed that those with the low-expressing variant of 5-HTTLPR had stronger connectivity in the rIFG, compared to individuals with ASD without the low-expressing variant (xyz=50, 18, 22, t_{30}=3.76, p<0.001 uncorrected). Genotyping is underway on the remaining 25 control and 10 ASD participants to address this hypothesis with the full set of participants. Lastly, connectivity in the rIFG was positively related to social impairment in individuals with ASD (xyz=50, 28, -6, t_{38}=4.20, p=0.026, small volume corrected for rIFG, controlling for IQ).

Conclusions: Compared to controls, individuals with ASD exhibit stronger posterior-anterior connectivity in the default network during rest. Within the ASD group,

stronger connectivity in the default network is related to both 5-HTTLPR genotype and social symptoms.

133.008 A Preliminary Investigation of GAD65 and Cortical Morphometry in ASD. P. Johnston*, C. Ecker, E. Daly, C. M. Murphy, J. Powell and D. G. Murphy, *Institute of Psychiatry, King's College London*

Background: Prior neuroimaging studies, which compared people with ASD to controls, have reported significant (regional) differences in cortical volume. However, by definition, cortical volume (CV) is a product of cortical thickness (CT) and surface area (SA). This is important because CT and SA have different neurodevelopmental and genetic determinants. (Panizzon et al., 2009). Hence it is unknown whether differences in CV are driven by CT or SA; and in turn what the genetic basis of those differences are. As a first step we previously reported a significant genetic association of Glutamic Acid Decarboxylase (GAD) 65 and ASD; and that genetic variation in GAD65 modulated CV of the entorhinal cortex (Johnston et al., 2008). However it is unlikely that the effect of GAD65 is restricted simply to the entorhinal cortex.

Objectives: Hence we extended our prior work and examined the influence of genetic variation in the GAD65 gene throughout the whole brain of individuals with and without ASD. We investigated all three measures of cortical anatomy (i.e. CV, CT, and SA).

Methods: Structural MRI data was acquired from 70 young adult males with autism (all above ADI-R cut offs) and 70 age and IQ matched healthy controls. FreeSurfer software was used to determine CV, CT and SA. All individuals were genotyped for the GAD65 SNP rs4994426 using iPLEXMassARRAY standard procedures. A general linear model was established using both diagnostic group and genotype as fixed factors. An interaction term of diagnostic group by genotype was also included.

Results: Significant differences ($p < 0.003$) in cortical morphometry were noted between ASD individuals and controls in discrete, localised regions of the cortex. Additionally ASD individuals expressing the AG genotype of the GAD65 SNP displayed significant reductions (in all three cortical morphometric measures) in both the frontal and parietal cortex, compared to both ASD individuals with the GG genotype and controls.

Conclusions: These results suggest that difference in cortical morphometry between individuals with and without ASD are partially modulated by common genetic variation of the GAD65 gene.

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134.001 A Genetic Epidemiological Approach to the Sensory Over-Responsivity Phenotype. H. H. Goldsmith*, C. Van Hulle and N. L. Schmidt, *The University of Wisconsin-Madison*

Background: Strong responses to seemingly mild sensory stimulation are frequently reported as a non-diagnostic feature of the autism spectrum. A thorough understanding of this phenomenon requires investigation of sensory symptoms per se. We previously evaluated 1394 toddler-aged twin pairs using parental report of auditory and tactile over-responsivity (Goldsmith et al., 2006). We observed fairly strong genetic effects for tactile over-responsiveness (83% of MZ--genetically identical--pairs, compared with 32% of DZ pairs were concordant for tactile symptoms).

Objectives: We investigated the phenotypic and genetic distinctiveness of sensory symptoms and common features of childhood behavioral problems in middle childhood.

Methods: Twins were identified from statewide birth records, and 2095 children (all twins) were screened at age 6-7 years on the Health and Behavior Questionnaire (HBQ), a survey of DSM symptoms in the internalizing and externalizing domains and Miller's sensory screener. Follow-up data on a subsample enriched for behavioral problems were available on 765 participants, mostly aged 7-8 yrs. Probable diagnoses were obtained using the DISC, which is a structured psychiatric interview (of parents) that yields DSM-IV diagnoses and symptom counts.

Results: Almost half (44%) of children who screened positive for SPD did not qualify for any DISC diagnoses. When we examined symptoms rather than diagnoses, we found overlap between behavior problem symptoms and sensory symptoms. This indicates that sensory issues are problematic for children with other recognized behavioral problems. We also examined mother reports of physical health for children who screened positive for SPD and qualified for a DISC diagnosis, children who only screened positive for SPD, children who only qualified for a DISC diagnosis, and non-diagnosed children. In general, children who screened positive for SPD only did not have more major health problems than other groups.

We examined the relationship between *symptoms* of SPD and *symptoms* of DISC diagnoses and explored possible genetic and environmental factors that contribute to both. We collapsed the psychiatric symptoms into two broad factors: anxiety and externalizing (impulsivity, conduct problems). Then, we conducted quantitative genetic analyses to answer a series of questions: Are there genetic influences on sensory symptoms? Yes. Are there genetic influences on anxiety symptoms? Yes. Are there genetic influences on externalizing symptoms? Yes. Then, we asked whether the more critical question: do the genetic influences on sensory symptoms overlap with genetic influences on anxiety and externalizing symptoms. Briefly, bivariate genetic modeling indicated that sensory symptoms were only weakly correlated with anxiety and externalizing, but the correlation that did exist could be accounted for by genetic factors.

Conclusions: Our analyses generally supported the phenotypic distinctiveness of the high standing on sensory symptoms. Given that the genetic factors for sensory symptoms and other common (anxiety, externalizing) symptoms largely did *not* overlap, we also have evidence for the genetic distinctiveness of sensory symptoms. We discuss various qualifications to these analyses.

We are currently expanding this line of research to examine sensory symptoms in a sample of twins, one or both of whom have an autism spectrum diagnosis. Preliminary results will be presented.

134.002 Association Between Inherited and Congenital Diseases and Autism Spectrum Disorders: A Nation-Wide Register-Based Study. M. B. Lauritsen*[1] and E. Parner[2], (1)*Regional Centre for Child and Adolescent Psychiatry, Aarhus University Hospital*, (2)*University of Aarhus*

Background: Some studies have been performed that studied the medical disorders seen in individuals with autism spectrum disorders (ASD). Several diseases have been found to be associated with ASD based on case reports and clinical samples reporting associated medical disorders in patients with ASD, and association of some of these medical disorders have been confirmed in the few epidemiological studies performed. Some of the most common medical disorders include tuberous sclerosis, fragile X syndrome, Down syndrome, neurofibromatosis, and epilepsy.

Objectives: To study the association of ASD with inherited medical disorders including congenital disorders in terms of contributing to the common knowledge of associated medical disorders. This study may have implications for studying etiological factors of autism spectrum disorders.

Methods: A population-based cohort including a total of approximately 1.5 mio individuals born in Denmark 1980-2003 was identified. The cohort members were checked for medical disorders registered in the Danish National Patient Registry that were previously hypothesized to be associated with autism. Information on autism was obtained from the Danish Psychiatric Central Register which included analyses of both childhood autism and ASD. We considered both the medical disorder as the exposure and ASD as the outcome and vice versa ASD in the child as the exposure and the medical disorder as the outcome. Follow-up time began for all children from birth and continued until the diagnosis of ASD, death, or the end of follow-up, on December 31, 2008.

This study does not include infectious disorders seen in individuals with ASD.

Results: The preliminary findings in our study show association between ASD and congenital hypothyroidism, epilepsy, chromosomal abnormalities, and congenital anomalies.

Conclusions: Our study confirms previous findings of association of ASD with medical disorders like epilepsy and congenital hypothyroidism. We also contribute to the discussion about a possible association between autism and some inherited medical disorders and congenital malformations including certain chromosome abnormalities.

134.003 Co-Occurring Epilepsy Among Children with Autistic Spectrum Disorder: Results From the Missouri ADDM Epilepsy Surveillance System. R. Fitzgerald*[1], E. Trevathan[2], C. Soke[1], A. Hoog[1] and J. N. Constantino[1], (1)*Washington University School of Medicine*, (2)*Centers for Disease Control and Prevention*

Background: Epilepsy is a common co-occurring condition among children with autism spectrum disorders (ASDs). Some previous studies, based on clinical populations, have reported epilepsy in as many as 30% of children with ASDs. The Missouri ADDM site (Washington University in St. Louis) developed an electroencephalogram (EEG) laboratory-based surveillance system to monitor the occurrence of epilepsy among its ASD cases.

Objectives: Monitor the frequency of epilepsy among children with ASD ascertained from the general population over time and compare two methods for determining co-occurring epilepsy among ASD cases.

Methods: Confirmed cases of ASD identified as part of the Missouri ADDM 2006 study year (children born 1998 and who were 8 years of age in 2006 and ascertained in the 5-county region in and around St. Louis, Missouri) were evaluated for epilepsy via the EEG lab-based surveillance system. The epilepsy surveillance system collected data from all EEG laboratories in the study area that performed EEGs on children, as well as records of clinicians who ordered the EEGs and/or who made clinical diagnostic decisions related to epilepsy. A pediatric neurologist with expertise in clinical neurophysiology and epilepsy reviewed all clinical and EEG data for each child identified through the epilepsy surveillance system. Epilepsy case status was assigned using standardized criteria for epilepsy diagnosis and classification. Alternatively, during routine data collection for ASD, abstractors (with no medical training) recorded co-occurrence of epilepsy (Yes, No, Suspected) based on information contained in the records. No additional expert review was conducted.

Results: 321 children with ASD were ascertained via the ADDM surveillance system in Missouri (estimated ASD prevalence of 12.1 per 1000; 95% CI =10.8, 13.5). 28 (8.7%) ASD cases had co-occurring epilepsy based on the EEG lab-based surveillance method. 30 (9.3%) ASD cases were determined to have epilepsy based solely on the presence of information obtained during routine data collection for ASD surveillance. The routine data collection method identified 3 epilepsy cases and 22 suspected cases that were not identified through the EEG lab-based surveillance method whereas the EEG lab-based surveillance method identified 3 epilepsy cases that were not identied as such by the routine data collection method.

Conclusions: The two methods used to ascertain co-occurring epilepsy among ASD cases yielded similar results. Furthermore, the prevalence of co-occurring epilepsy (based on the EEG lab surveillance) among 8 year-old children in 2006 with ASD is similar to the 8.9% found among 8 year-old ASD cases in 2002 using the same EEG lab-based methodology.

134.004 Decreased Levels of Total Immunoglobulin in Children with Autism Is Not a Result of B-Cell Dysfunction. L. S. Heuer*[1], M. Rose[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 are a heterogeneous group of behaviorally defined disorders of unknown etiology. Current research has implicated immunological, neurological, genetic, and environmental factors as possible contributors to this complex disorder. Recently, we have reported a correlation between decreased levels of immunoglobulin (Ig) and behavioral outcome in children with

autism. Immunoglobulin production is the end result of B-cell activation generated during an immune response and decreased levels are indicative of an immune defect. Evidence of an immune deficiency coupled with severity of behavioral measures would suggest a common defect in both neuro- and immunodevelopment. Thus, identification of the immune defect responsible for reduced Ig production may provide insight into common affected pathways in neurodevelopment. Objectives: To determine if reduced plasma levels of Ig in children with autism are the result of defective B-cell development, activation, or function. Methods: Subject selection was determined based upon Ig status. B-cell development was evaluated by phenotypic analysis of population densities in peripheral blood through flow cytometry. B-cell activation was assessed in-vitro using pokeweed mitogen, Staphylococcus aureus, T-cell conditioned medium, and the TLR-9 ligand, CpG. Activation was measured by flow cytometry for proliferation and intracellular production of Ig. Cell function was assessed through measurement of total Ig production in the supernatants of stimulated cells. Results: Phenotypic analysis of B-cell populations in the peripheral blood of autism patients and typically developing controls showed no difference between groups in the absolute number of naïve or memory B-cells. The ability of these B-cells to receive and respond to activation signals is the same across groups based on both proliferation and initiation of Ig production. Likewise, we were unable to detect any difference between the autism and typically developing groups with respect to the production of soluble Ig in the supernatants of stimulated cell cultures. Conclusions: We observed no difference in B-cell number, response to activation, or functional production of immunoglobulin between autism children and typically developing controls. Thus, the previously observed decrease in Ig levels within autism children does not appear to be the result of B-cell dysfunction. This suggests that the reduced production of Ig may be the result of a defect in the T cell and/or monocyte/macrophage populations, both of which play a role in B-cell differentiation and Ig production.

134.005 GI Symptoms in Autism Spectrum Disorders(ASD): An Autism Treatment Network Study. K. C. Williams*[1], G. J. Fuchs[2], G. T. Furuta[3], M. Marcon[4], D. L. Coury[5] and A. T. N. GI Subcomittee[6], (1)*Vanderbilt University Medical Center*, (2)*University of Arkansas for Medical Sciences*, (3)*University of Colorado at Denver*, (4)*Hospital for Sick Children*, (5)*Nationwide Children's Hospital*, (6)*N/A*

Background: The prevalence of GI symptoms in children and adolescents with ASD is uncertain, with studies reporting conflicting results.

Objectives: To determine the frequency of GI symptoms as reported by parents in a large ASD registry, and to identify factors associated with GI symptoms in children with ASD.

Methods: Autism Treatment Network Registry enrolled 1420 children, age 2-18 years, with an ADOS-confirmed ASD diagnosis (autism, Asperger disorder, or PDD-NOS) at 15 sites in the US and Canada. Parents completed a GI symptom inventory tailored to the needs of nonverbal children, as well as Child Behavior Checklist (CBCL), Child Sleep Health Questionnaire (CSHQ) and Pediatric Quality of Life (PedsQL) at time of enrollment.

Results: GI symptom data were available for 1185 children. Overall 45% of children were reported to have GI symptoms at time of enrollment. Of GI complaints that occurred within the 3 months prior to enrollment, abdominal pain was most common (59%) followed by constipation (51%), diarrhea (43%), other (40%), nausea (31%) and bloating (26%). Reports of GI symptoms increased with age, ranging from 39% in those under 5 years to 51% in those 7 years and older ($p<0.0001$). Children ages 1 to 5 years with GI symptoms had higher CBCL t-scores for total problems and for the emotionally reactive, anxious/depressed, somatic complaints, sleep problems, internalizing problems, affective problems, and anxiety problems subscales, all $p<0.05$. Children ages 6 to 18 years with GI symptoms had higher CBCL t-scores for total problems and for all subscales ($p<0.01$). Sleep problems occurred more frequently in children with than those without GI symptoms (70% versus 30%, $p<0.0001$). Children with GI symptoms had lower PedsQL scores

(overall score and all five subscales, $p<0.01$) compared to children without GI problems. Presence of GI problems did not differ by gender, ASD subtype, race, or IQ.

Conclusions: Parents of children with ASD report a high prevalence of GI symptoms in their children. This prevalence increases with age. GI complaints are significantly associated with behavioral abnormalities in all age groups. GI symptoms are also significantly associated with sleep disturbances and decreased health-related quality of life. Further definition is needed on the role and potential impact of treatment of GI disorders on behavior, sleep disturbance, and quality of life in children with ASD.

134.006 Genetic and Environmental Influences On the Overlap Between Autistic-Like Traits and ADHD Behaviors in Early Childhood. A. Ronald*[1], L. R. Edelson[2], P. Asherson[3] and K. J. Saudino[2], (1)*Birkbeck College, University of London*, (2)*Boston University*, (3)*Institute of Psychiatry*

Background: ASD and ADHD are both neurodevelopmental disorders that begin in early childhood. Although their core diagnostic symptoms do not explicitly overlap, high levels of comorbidity between ASD and ADHD have been reported. Previous family and twin studies have explored the degree of shared familial and genetic influences across these two disorders in middle and late childhood.

Objectives: The present study aimed to investigate for the first time the association between autistic-like traits and ADHD behaviors in early childhood, in a community sample of 2-year-olds. By employing a classic twin design, the study aimed to determine the degree to which autistic-like traits and ADHD behaviors covary due to genetic and environmental influences.

Methods: Twins from the Boston University Twin Project (N = 312 pairs) were assessed on their second birthday by their parents on autistic-like traits and ADHD behaviors using the Childhood Behavior Checklist. Structural equation model-fitting was carried out.

Results: Phenotypic analyses showed that after controlling for general cognitive ability and socioeconomic status, autistic-like traits (total scale as well as social and nonsocial subscales) correlated positively with ADHD behaviors (r = .23-.26). Structural equation model-fitting revealed that both ADHD- and autistic traits were moderately heritable in early childhood and that there were modest shared genetic influences between them (genetic correlation = .27). Common environmental influences also explained part of the covariation between these behaviors.

Conclusions: These findings show that there is a significant positive association between autistic-like traits and ADHD behaviors in 2-year-olds, which concurs with findings from clinical studies. This association is caused by both shared genetic and shared environmental influences. Compared to studies of older children and young adults, the relationship between autistic-like traits and ADHD behaviors appears to be weaker, both phenotypically and genetically, suggesting that the covariance of these behaviors, and the degree of shared genetic influences, may increase with age. This evidence for overlap between ASD and ADHD behaviors both clinically and when assessed as quantitative traits should be used as a springboard for evaluating diagnostic rules concerning dual diagnoses of ASD and ADHD, as well as for developing hypotheses for molecular genetic research.

134.007 Screening for Autism Spectrum Disorders in Children with Down Syndrome in New York State. E. S. Kuschner*[1], S. Hyman[2], E. van Wijngaarden[2], C. I. Magyar[1], S. B. Sulkes[1], A. Diehl[2], N. J. Roizen[3] and C. M. Druschel[4], (1)*University of Rochester Medical Center*, (2)*University of Rochester*, (3)*Case Western Reserve*, (4)*New York State Department of Health Congenital Malformations Registry*

Background: People with Down syndrome (DS) are often described as social and friendly. However, families and professionals have long recognized that some individuals with DS have diminished social reciprocity, atypical communication development and unusual routines and habits, i.e., symptoms that are characteristic of an autism spectrum disorder (ASD). Objectives: To determine the prevalence of ASD in children with DS in a large, diverse population and to examine best practices for screening and diagnosing ASDs in individuals with DS and co-morbid

intellectual disability. Methods: A tiered approach was employed to screen and diagnose ASD in children with DS. First, children ages 3-13 years with DS born in New York State (outside the 5 boroughs of New York City) were recruited through the New York Congenital Malformation Registry, parent groups and clinics and screened for ASD using the Modified Checklist for Autism in Toddlers (MCHAT), the Social Communication Questionnaire (SCQ), and the Pervasive Developmental Disorder in Mental Retardation Scale (PDD-MRS). Subsequently, a subgroup of screen positive (on any screening measure) and screen negative (on all screening measures) children were evaluated with the Autism Diagnostic Interview–Revised via telephone interview. Of those, geographically available children who were ADI-R positive and an equal number who were ADI-R negative were administered an Autism Diagnostic Observation Schedule (ADOS) and an assessment of their intellectual and language ability. Sensitivity and specificity of the three screening tests were examined relative to the ADI-R diagnostic and current algorithms, the ADOS, and expert clinical consensus using the DSM-IV checklist. Results: The families of 457 children completed the screening, 221 went on for an ADI-R, and 76 completed the ADOS and psychological evaluations. Expert clinical consensus was applied to all children that completed both ADI-R and ADOS. Findings indicated that as many as 29-44% of children with DS screened positive for symptoms compatible with an ASD. Compared to the ADI-R diagnostic algorithm, sensitivity and specificity, respectively, of the screening tests were: MCHAT (0.727 and 0.719), SCQ (0.568 and 0.930) and PDD MRS (0.580 and 0.867). Comparison to the clinical consensus diagnosis yielded similar results. Sensitivity was increased when using the ADI-R current algorithm but specificity was reduced. Conclusions: Many of the participants with DS demonstrated symptoms of an ASD as indicated by elevated scores on the screening and diagnostic assessments, supporting previous reports that some individuals with DS exhibit symptoms consistent with an ASD diagnosis. This finding suggests that primary care practitioners should screen for ASD as part of their routine monitoring of health and development. Positive screens in primary care settings warrant referral for comprehensive evaluations because of the complexity of differential diagnosis of ASD comorbidity with intellectual and language disabilities. However, future research should evaluate the validity of these screening measures to inform best clinical practice for sufficiently sensitive and specific screening and diagnosis for children with DS. Findings have implications for timely and effective treatment of children with DS and co-morbid ASD.

134.008 Testing Epilepsy Candidate Genes in Autism. M. L. Cuccaro*[1], R. Tuchman[1], D. Ma[2], E. R. Martin[2], R. K. Abramson[3], H. H. Wright[3], J. Gilbert[4], J. P. Hussman[5] and M. A. Pericak-Vance[2], (1)*University of Miami*, (2)*Hussman Institute for Human Genomics*, (3)*University of South Carolina School of Medicine*, (4)*University of Miami Miller School of Medicine*, (5)*Hussman Foundation*

Background: Autism and epilepsy are common complex disorders which independently result in significant behavioral and developmental problems. Their co-occurrence, which often results in a more severe phenotype and extremely poor prognosis, is conservatively estimated at 25% to 30%.The biologic mechanisms that account for this co-occurrence have eluded discovery. Several conceptual models have proposed a common brain pathology in which autism and epilepsy are independent consequences of the same underlying disorder. Given the overlap in these two disorders we proposed that epilepsy risk genes could be etiologically relevant to autism. Objectives: To test the hypothesis that epilepsy related candidate genes may confer risk to autism.
Methods: Using existing genome wide association study (GWAS) data, we examined 20 candidate genes, selected on the basis of previous reports of association or biological relevance to epilepsy or epilepsy and co-occurring autism. The discovery dataset consisted of 438 autism families from the Hussman Institute for Human Genomics (HIHG) autism program genotyped on the Illumina 1M chip. The validation dataset consisted of 457 autism families from the Autism Genetics Resource Exchange (AGRE) genotyped on the Illumina 550K. The 1M Beadchip is redundant to the 550K Beadchip

with the addition of approximately 500,000 more SNPs Results: We examined markers in our autism GWAS dataset for each of the 20 candidate genes All SNPs were tested for association to autism using the Pedigree Disequilibrium Test (PDT), a family based test for association. A finding was declared significant if a marker was nominally significant in the HIHG and AGRE datasets and showed greater significance in the joint analysis. Examination of PDT results showed two SNPs in CACNA1G (rs11079919 and rs9898731) that were significant in the HIHG, AGRE, and joint analyses. Both are in CACNA1G but are in intronic regions and are in high linkage disequilibrium (LD). A third SNP, (rs2240119), while not significant in the HIHG dataset, is significant in the AGRE dataset (p=0.002) and highly significant (9.55E-04) in the joint analysis.
Conclusions: Testing genes with biological relevance to epilepsy yielded a significant association to SNPs in CACNA1G. CACNA1G is a calcium channel gene which has recently been implicated in autism as well as idiopathic generalized epilepsy. The role of ion channel genes in autism risk is supported by evidence showing that calcium channel dysfunction is tied to both syndromic and non-syndromic autism. For example, Timothy Syndrome, a multisystem disorder characterized by cardiac, immune, and cognitive abnormalities along with a clearly defined autism phenotype results from a CACNA1C mutation. Calcium dependent defects that perturb neural development lead to changes common to those found in autism (e.g., cell-packing density, decreases in neuron size and arborization, and alterations in connectivity. Further, calcium channel variants in autism (e.g.CACNA1G) are tied to increased calcium signaling suggesting a role for calcium dependent activation in this disorder.

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135.001 Altered Cyctoarchitecture, Decreased GABA and Serotonin Receptor Subtypes, but Normal Density of Neurons and Interneurons in the Posterior Cingulate Cortex and Fusiform Gyrus in Autism. A. Oblak*[1], T. Gibbs[1], T. Kemper[1], M. L. Bauman[2] and G. Blatt[1], (1)*Boston University School of Medicine*, (2)*MassGeneral Hosptial for Children/Harvard Medical School; Boston University School of Medicine*

Background: Striking characteristics of individuals with autism is a pervasive impairment in social interaction with others and difficulties in identifying facial expressions and emotions. Processing the human face is at the focal point of most social interactions. Atypical social behaviors have been observed in early development of children with autism and have led to the contention that autism is a condition where the processing of social information, particularly faces and emotions, is impaired. Two areas involved in emotion and memory processing and face processing are the posterior cingulate cortex (PCC) and fusiform gyrus (FFG).

Objectives: To determine whether there are alterations in cytoarchitecture, neuron and interneuron density, and GABA and serotonin receptor subtypes in the PCC and FFG in adult post-mortem autism and control brains.

Methods: Thionin stained sections were used to analyze the cytoarchitecture of the PCC and FFG and immunohistochemistry to identify parvalbumin and calbindin positive GABAergic interneurons. Unbiased, design-based stereological principles were implemented to quantitatively assess the density of thionin, parvalbumin, and calbindin neurons. Receptor binding autoradiography was used to determine the density of GABAergic ($GABA_A$, $GABA_B$, benzodiazepine) and serotonergic ($5HT_{1A}$, $5HT_{2A}$) receptors and transporters (uptake sites; $5HT_U$).

Results: Cytoarchitectonic abnormalities were observed in the PCC but not in the FFG in the autism cases. The PCC had a poorly defined layer IV, displaced layer V neurons, and increased neurons in the white matter. There was no significant difference in the density of thionin-positive neurons or calbindin- and parvalbumin-positive interneurons in either region. Significant reductions in the density of $GABA_A$ and $GABA_B$ receptors, benzodiazepine binding sites, $5HT_{1A}$ and $5HT_{2A}$ receptors, and $5HT_U$ were observed throughout the PCC and FFG.

Conclusions: The presence of cytoarchitectonic abnormalities in the PCC provides further support for the occurrence of developmental abnormalities within the limbic lobe in the brain in autism. The reduced density of GABAergic and serotonergic receptors does not appear to be the result of a reduced density of neurons within the PCC or FFG, but could be the result of reduced receptors on dendrites or cell bodies or alterations in genes encoding GABA and serotonin receptors. These receptor changes could result in altered synaptic transmission contributing to altered intrinsic and/or extrinsic circuitry with resultant altered processing of emotions and faces, and abnormal social behaviors.

135.002 Association of Autism with Polyomavirus Infection in Postmortem Brains. C. Lintas, L. Altieri, F. Lombardi, R. Sacco and A. M. Persico*, *Univ. Campus Bio-Medico*

Background: Autism is a highly heritable behavioural disorder. Yet, very few cases can be solely explained on the basis of *de novo* genetic mutations or cytogenetic abnormalities. Environmental factors interacting with the genetic background of each individual can contribute to explain familiality in the presence of genomic instability and low rates of disease-specific genetic mutations.
Objectives: To assess the presence of neurotropic viruses in *post-mortem* brains of autistic patients and matched controls.
Methods: We assessed by nested-PCR and DNA sequence analysis the presence of CMV, EBV, HSV1, HSV2, HHV6, BKV, JCV, and SV40 in genomic DNA extracted from *post-mortem* temporocortical tissue (Brodmann Areas 41/42) belonging to 15 autistic patients and 13 controls.
Results: BKV, JCV, and SV40 combined are significantly more frequent among autistic patients compared to controls (67% vs 23%, respectively; $P<0.05$). No difference is recorded for all other viruses, which are found in relatively few individuals ($N\leq3$). Also poly-viral infections tend to occur more frequently in the brains of autistic patients compared to controls (40% vs 7.7%, respectively; $P=0.08$).

Conclusions: Polyomaviruses are over-represented in our sample of autistic *post-mortem* brains compared to controls; autistic brains also display higher frequencies of positivity to more than one virus. Hence polyomaviruses represent attractive candidates for follow-up studies exploring gene x environment interactions as possible contributors to autism pathogenesis.

135.003 Cathepsin D and Apoptosis Related Proteins Are Altered in the Brain of Autistic Subjects. A. Sheikh*, X. Li, G. Wen, Z. Tauqeer, W. T. Brown and M. Malik, *NYS Institute for Basic Research in Developmental Disabilities*

Background:

Autism is a severe neurodevelopmental disorder characterized by problems in communication, social skills, and repetitive behavior. Many areas of the brain in autism show abnormalities including decreased Purkinje cell counts in cerebellar hemispheres and vermis, loss of granule cells and Purkinje cell atrophy. Recent studies suggest that apoptotic mechanisms may contribute to the pathogenesis of this disorder. Cathepsin D is the predominant lysosomal protease and is abundantly expressed in the brain. It plays an important role in regulation of cellular apoptosis and has been shown to mediate apoptosis induced by inflammatory cytokines TNF-_ and IFN-_.

Objectives:

The aim of this study is to determine whether cathepsin D activities are altered in the brain of autistic subjects and whether the alterations are associated with the pathogenic apoptotic processes in autistic brain.

Methods:

Frozen human brain tissue (frontal cerebral cortex and cerebellum) of 7 autistic subjects (mean age 8.1±2.1 years) and 7 age-matched control subjects (mean age 7.7±1.9 years) 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 cathepsin D, Bcl2 and caspase-3 in the brain homogenates. Immunohistochemistry studies were used to examine the expression of cathepsin D in the brain sections.

Results:

We found that cathepsin D protein expression was significantly increased in the frontal cortex, in pyramidal and granule cells of the hippocampus, and in cerebellar neurons in autistic subjects as compared to controls. In addition, we found that the expression of the anti-apoptotic protein Bcl2 was significantly decreased, while caspase-3, a critical executioner of apoptosis, was increased in the cerebellum of autistic subjects. Previously our studies have shown that Bcl2 expression is decreased and the BDNF-Akt-Bcl2 pathway is compromised in the frontal cortex of autistic subjects, which suggested that increased apoptosis may be involved in the pathogenesis of autism. Our current finding of decreased Bcl2 and increased capase-3 in the cerebellum of autistic subjects further supports this suggestion.

Conclusions: Our findings suggest that cathepsin D may play an important role in the pathogenesis of autism through its regulation of apoptosis.

135.004 Decreased GABAergic Biomarkers in Cerebellar, Limbic and Cortical Areas in Autism: Neuropathological and Developmental Implications. G. Blatt*, A. Oblak, T. Gibbs and J. J. Soghomonian, *Boston University School of Medicine*

Background: Intrinsic and extrinsic GABAergic activity act as a dual inhibitory control to inhibit or disinhibit glutamatergic neurons thereby modulating the normal local and global balance of inhibitory:excitatory synaptic interactions. In autism, this balance is hypothesized to be disturbed suggesting a developmental origin with disruption of local and/or long cerebellar and cortical circuits. This balance is essential during neural tissue genesis including proliferation, migration and differentiation of neuronal precursors as well as synapse formation and refinement of cortical circuits. GAD65/67 are key synthesizing enzymes for GABA and reduced protein levels are associated with decreased GABA levels. Ionotropic GABA-A receptors and metabotropic GABA-B receptors play critical roles in early neuronal development and are distributed both synaptically and extrasynaptically. The levels/densites of these key GABA biomarkers are consistently reduced in cerebellar, limbic and cortical areas in postmortem examination in individuals with autism compared to age- and post-mortem interval-matched controls.

Objectives: To provide an overview of current studies from our laboratory and others demonstrating remarkably consistent findings of decreased GAD mRNA levels, and decreased GABA-A receptors, benzodiazepine binding sites and GABA-B receptors throughout many brain areas in adult autism cases.

Methods: *In situ* hybridization histochemistry for GAD65/67 mRNA levels was used in the Crus II and dentate regions of the cerebellum in adult autism cases and matched controls. *In vitro* ligand binding techniques for GABA-A and GABA-B receptors and benzodiazepine binding sites were used in cerebellum, hippocampal formation, cingulate cortices and fusiform gyrus.

Results: Significant reductions in GAD65 mRNA levels were found in the dentate nucleus and decreases in GAD67 mRNA levels were found in Purkinje cells. Significant decreases in the density of GABA receptors and benzodiazepine binding sites were found in parts of the cerebellum, hippocampal formation, anterior and posterior cingulate cortex and in the fusiform gyrus.

Conclusions: Results from these investigations combined with reported findings from the literature suggest that in autism, specific types of GABAergic biomarkers are downregulated in brain areas that participate in many of the core neural

features of the disorder. Overall, findings suggest a dysregulation of GABAergic modulatory control of glutamatergic neurons potentially impacting neural development and in the balance of inhibitory:excitatory synaptic circuitry in the mature autism brain.

Acknowledgements: Human tissue was obtained from the NICHD Brain and Tissue Bank for Developmental Disorders at the University of Maryland, Baltimore (Dr. R. Zielke, Director), and the Autism Tissue Program (Dr. J. Pickett, Director) and The Autism Research Foundation (Dr. M.L. Bauman, Director) via the Harvard Brain Tissue Resource Center (Dr. F. Benes, Director). The authors are very grateful to the brain banks and to HBTRC for their generosity and professionalism in obtaining tissue for these studies.

135.005 Defects of Neurogenesis, Neuronal Migration and Dysplastic Changes in the Brains of Autistic Subjects. J. Wegiel*[1], I. Kuchna[1], K. Nowicki[1], H. Imaki[1], J. Wegiel[1], E. Marchi[1], S. Y. Ma[1], A. Chauhan[2], V. Chauhan[2], I. Cohen[2], E. London[2], W. T. Brown[2] and T. Wisniewski[1], (1)*New York State Institute for Basic Research in Developmental Disabilities*, (2)*NYS Institute for Basic Research in Developmental Disabilities*

Background: An emerging theory of autism-related encephalopathy integrates evidence of (a) abnormal acceleration of brain growth in early childhood (Redcay and Courchesne 2005), (b) minicolumn pathology (Casanova et al 2002, 2006), (c) curtailed neuronal development (Bauman and Kemper 1985), brain-structure-specific delays of neuronal growth in early childhood, and desynchronization of neuronal development.

Objectives: The aims of this study were to detect the patterns of focal qualitative developmental brain defects, including the type, topography and severity of changes, and to identify the structures and brain regions that are prone to developmental alterations in autism.

Methods: Formalin-fixed brain hemispheres of 13 autistic (4–60 years of age) and 14 age-matched control subjects were embedded in celloidin and cut into 200-_m-thick coronal sections, which were stained with cresyl violet and used for neuropathological evaluation.

Results: Thickening of the subependymal germinal matrix and subependymal nodular dysplasias in two autistic children were indicative of active neurogenesis. Subcortical, periventricular, hippocampal and cerebellar heterotopias were detected in the brains of four autistic subjects (31%) reflecting abnormal neuronal migration. Multifocal cerebral dysplasias seen in the neocortex (31%), in the entorhinal cortex (15%), in the cornu Ammonis (31%) and in the dentate gyrus (15%) reflect frequent developmental distortions of brain cytoarchitecture. Cerebellar floculonodular dysplasia detected in six subjects (46%) and hypoplasia in one case indicate local failure of cerebellar development in 54% of the autistic subjects. Dystrophy with calcification and focal damage within meninges, cortex and white matter was present in all examined brains of autistic and control subjects.

Conclusions: Detection of focal dysplasia in one control subject and of a broad spectrum of focal qualitative neuropathological developmental changes in 12 of 13 (92%) examined brains of autistic subjects indicates a multi-regional dysregulation of neurogenesis, neuronal migration and maturation in autism. This may contribute to the heterogeneity of the observed clinical phenotype.

135.006 Increased Protein Oxidation in Cerebellum, Frontal and Temporal Cortex in Autism. A. Chauhan*[1], M. M. Essa[2], B. Muthaiyah[1], W. T. Brown[1], J. Wegiel[3] and V. Chauhan[1], (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*Sultan Qaboos University, College of Agricultural and Marine Sciences*, (3)*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 risk factors in the pathophysiology of autism. Brain tissue is highly heterogeneous with different functions localized in specific areas, and it is highly vulnerable to oxidative stress due to its limited antioxidant capacity and higher energy requirement. Protein oxidation is defined as the covalent modification of a

protein induced either directly by reactive oxygen species (ROS) or indirectly by reaction with secondary by-products of oxidative stress. Protein carbonyl derivatives of amino acids (pro, arg, lys, thr) are the most common products of protein oxidation.

Objectives: In this study, the status of protein oxidation 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: Frozen human brain tissue (cerebellum, frontal cerebral cortex, temporal cortex, parietal cortex and occipital cortex) of autistic and age-matched control subjects were obtained from the NICHD Brain and Tissue Bank for Developmental Disorders at the University of Maryland. Protein oxidation was assessed in the brain homogenates by quantitation of protein carbonyls using ELISA kit (Cell Biolab). The method is based on the derivitization of the carbonyl group with dinitrophenylhydrazine (DNPH) to DNP hydrazone, which is probed with anti-DNP antibody.

Results: Protein oxidation, assessed by quantitation of protein carbonyls, was significantly increased in autism by a mean of 123 % in frontal cortex ($p<0.001$), by 108 % in temporal cortex ($p<0.01$), and by 100 % in cerebellum ($p<0.01$) as compared with controls. On the other hand, its levels in parietal and occipital cortex were similar between autism and control groups. There was no or minimal overlap of protein carbonyl levels in the frontal and temporal cortex between autism and control groups. In cerebellum, 57 % of autism subjects had protein carbonyl levels above the upper cutoff value of range for control group.

Conclusions: These results suggest that oxidative stress differentially affects selective regions of the brain, i.e. cerebellum, frontal and temporal cortex, in autism.

135.007 Quantification of the Gray/White Matter Boundary in ASD.
T. A. Avino* and J. J. Hutsler, *University of Nevada, Reno*

Background:

Magnetic resonance imaging (MRI) measures of cortical thickness in autism spectrum disorders (ASD) have revealed conflicting findings, reporting both increased cortical thickness and no differences in cortical thickness between ASD subjects and typical subjects. Because cortical thickness measurements in MRI often depend on thresholding to establish a boundary between the cortex and underlying white matter, any differences between ASD subjects and typicals may be attributable to neuroanatomical differences at this boundary. Previous neuroanatomical studies have suggested this boundary may be less distinct in ASD (Hutsler et al, 2007).

Objectives:

The aim of the present study was to objectively quantify the gray/white matter boundary in ASD and age-matched control subjects. If the ASD brain shows a more indistinct boundary, this could contribute to findings of cortical thickening using MRI techniques.

Methods:

Postmortem tissue was acquired from 16 male subjects (8 ASD and 8 age-matched controls) ranging in age from 10-51 years old. Tissue blocks were taken from the superior temporal gyrus (BA 21), dorsolateral frontal lobes (BA 9), and dorsal parietal lobes (BA 7). The tissue samples were sectioned perpendicular to the gyral axis and cell bodies were labeled with a Nissl stain. Approximately 300 digital photomicrographs of the gray/white matter boundary were acquired from these tissue samples. The images were then converted to grayscale and subjected to a noise removal filter. A sigmoid curve was fitted to the transition zone between layer VI and white matter. The slope of this curve indicated the spatial extent of the transition zone. A 'shallow' sigmoid curve represents an indistinct boundary, while a 'steeper' sigmoid curve represents a distinct boundary.

Results:

The results from the sigmoid curve analyses indicate that ASD subjects showed an indistinct boundary between cortical layer VI and white matter. For all three cortical regions examined, ASD subjects showed 'shallower' sigmoid curves compared to typicals, (F[1,14] = 6.45, p = .02).

Conclusions:

These results support previously documented neuroanatomical abnormalities in the lower boundary of cortical layer VI. An indistinct boundary suggests that during neuronal migration a portion of neuroblasts are not reaching their proper position within the developing cortical plate. Furthermore, these results raise question about the use of cortical thickness measurement techniques that rely on gray/white matter thresholding; an indistinct transition zone could lead to a misplaced cortical boundary resulting in an overestimation of cortical thickness. We would like to thank the Autism Tissue Program for their assistance in acquiring the brain tissue used in this study.

135.008 The Relationship Between Foetal Testosterone Exposure, Head Circumference, and Repetitive Behaviours in Typically Developing Preschool and Older Children. J. C. Sullivan*, B. Auyeung, T. Tavassoli, V. Pütz, S. Suessenbachers, A. Humphrey and S. Baron-Cohen, *University of Cambridge*

Background: While suggestions of a relationship between foetal testosterone (fT) levels and autistic-like traits in the typically developing population (e.g. Auyeung et al., 2009) have catalysed a great deal of research and attention, surprisingly little work has been conducted on fT's effect on postnatal growth patterns. Abnormal growth trajectories have been noted in autism, namely a period of neural overgrowth (Redcay and Courchesne, 2006) as well as possibly faster corporeal growth (Dissanayake et al., 2006). Animal studies suggest fT exposure has gender-specific effects on postnatal growth patterns (Von Engelhardt, 2006). For instance, fT has been implicated in the development of behaviours such as persistent and repetitive actions (Schwabl, 1996) and faster perceptual learning and discrimination (Bertin et al., 2009), all features noted in autism (Singer, 2009; Jones et al., 2009). Indeed Schwabl (1996) suggests the increased growth associated with increased fT exposure in birds is the result of these persistent and fixated behaviours, as these translate to effective food begging actions.

Objectives: This study aimed to look at the effects of fT on one aspect of physical growth, head circumference (HC), in a typically developing population of children and if there were any interactions or relationships between HC and the presence of repetitive behaviours. HC is thought to be a robust indicator of brain volume in children (Hazlett et al., 2005), and as such is an easily obtainable proxy of both individual differences in brain growth in typically developing children and of early atypical neural growth trajectories in autism (Redcay & Courchesne, 2005). Only two studies have analyzed the effects of fT on brain size in humans, both using indirect measures of fT. Ronalds et al., (2002) found weak effects of 2d:4d on birth HC to birth length ratios in males with larger than average placentas. Peper et al., (2009) found that 9 year old children with a twin brother, thus exposed to higher intrauterine levels of fT, had larger brain volumes than those children with a female co-twin, although this was not replicated in adults.

Methods: Two groups of typically developing children, one 3-5 years (25 male, 25 female) and one 9-13 years (25 female and 25 male) for whom amniotic fT levels were assayed at 14-22 weeks of gestation were followed up in a large longitudinal study. Head circumference, height, and a questionnaire measure of repetitive behaviours (RBQ-2; Leekam et al., 2007) were analysed.

Results: Multiple regression and correlation analyses were performed on the data, results indicate that fT influences both absolute and relative head size. Preliminary analysis suggests a role of fT on head size in females and a relationship between head circumference and repetitive behaviors. Gender differences and age-related changes were also analysed.

Conclusions: These results will be discussed, as well as a consideration of how these

findings advance our current state of knowledge of hormonal and allometric differences in autism.

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136.001 1 Executive Functioning Profiles in Children with Autism Spectrum Disorders. K. D. Tsatsanis*, J. Tirrell, M. Levine and P. Ventola, *Yale University*

Background: Executive functioning (EF) impairments are reported in children with autism spectrum disorders (ASD) (Bennetto et al., 1996; Goldstein et al., 2001; Minshew et al., 2002; Ozonoff et al., 1991, 2004; Szatmari et al., 1990; Verte, et al., 2006). Most studies on EF skills have used laboratory-based measures, but parent-report data also has merits, as it offers greater breadth and ecological validity than traditional laboratory-based measures. There are just a few studies to date using parent-report data, and they have also found children with ASD to have EF impairments (Gilotty et al., 2002; Goia et al. 2002; Kenworthy et al. 2005).

Objectives: The purpose of the current study is to expand on the existing research and further investigate the EF profiles in children with ASD using a parent-report measure, the Behavior Rating Inventory of Executive Function (BRIEF) in a large sample of school-aged children with ASD.

Methods: The sample included 99 children: 38 from a clinic-referred sample and 61 from a longitudinal study of ASD. Mean age was 9.1 years (s.d. 2.8; range 5-17). Level of cognitive functioning was assessed using the Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV) or the Differential Abilities Scale, Second Edition (DAS-II). For the children who received the WISC-IV, mean IQ score was 96.6 (s.d. 19.4; range 54-149). For the children who received the DAS-II, mean IQ score was 94.3 (s.d. 18.2; range 53-134). All children received the ADOS and were characterized by a team of experienced clinicians.

Results: Mean scores on the BRIEF indices were at or just below the clinically significant range overall; however, the group averages obscure the wide variability in the sample. For each of the 8 clinical scales on the BRIEF, 33 to 51% of the sample scored within the clinically significant range. Sixteen percent of the sample had no elevated scores, 13% had clinically significant elevations in only one domain, and 14% had clinically significant elevations on 7 or 8 domains. Hierarchical cluster analysis revealed two clusters, which were distinguished based on severity of EF impairment. There were no differences between the two cluster groups on cognitive ability or symptom severity, as measured using ADOS calibrated severity scores. However, there were significant differences in adaptive functioning, as measured using the Vineland Adaptive Behavior Scales, Second Edition (VABS-II), with the group with greater EF impairments having lower adaptive skills.

Conclusions: Behavioral impairments in regulatory and metacognitive functioning characterize many but not all children with ASD. There appears to be a subset of children for whom these challenges are present to a significant degree, independent of IQ and ASD symptom severity. This raises the question whether EF behaviors represent another dimension by which to characterize subgroups of ASD and whether there are implications for neurobiological mechanisms and the genetics of the disorder. From a clinical standpoint, the level of impairment in this group and the significant relationship to adaptive functioning suggest a need to focus on this domain of behaviors when assessing and treating children with ASD.

136.002 2 Gesture as a Methodological Tool? Adolescents with ASD Use Their Hands to Explain Balance. C. V. Dombrowski*, A. B. de Marchena and I. M. Eigsti, *University of Connecticut*

Background: Deficits in gesture, an expression of non-verbal communication, are included in the diagnostic criteria for autism spectrum disorders (ASD). Although all forms of gesture are thought to be reduced in ASD, gesture has received scant empirical attention in this population. As studied in typically developing (TD) individuals, information expressed through gesture often complements speech and adds complexity to interpersonal exchanges. In addition to its

communicative function, gesture has also been shown to benefit speakers during problem solving by allowing them to entertain multiple representations simultaneously (i.e., one in speech and one in gesture). Given the clinical assumption that gesture use is impaired in ASD, it might be expected that individuals with ASD benefit less from gestures in cognitive problem solving; this hypothesis has not been tested.

Objectives: This study explores the role of gesture as a conceptual aid for speakers with ASD during problem solving. We compared strategies encoded in both speech and gesture by adolescents with TD and ASD on a task that requires participants to balance wooden beams and verbalize their strategies for doing so. Explanations of balance are naturally conducive to gesture, and allowed an assessment of whether adolescents with ASD also use gesture to facilitate conceptual representations. If they do, clinical formulations of gesture impairments in ASD may benefit from more detailed or precisely defined descriptions.

Methods: Participants included 15 high-functioning adolescents with ASD and 13 TD adolescents matched for age, gender, IQ, and receptive vocabulary (all F's < 2, p's > .18). Participants were asked to balance eight wooden beams on a fulcrum, and to explain this process. Videos of task performance were analyzed separately for strategies expressed in speech and gesture. Strategies involving concepts of weight, centeredness, and distance were coded separately (as in Pine, Lufkin, and Messer, 2004).

Results: All participants performed at ceiling, demonstrating that they were successfully able to balance all beams. Although adolescents with ASD used significantly fewer speech strategies (p = .01), there was no group difference in the number of gesture strategies expressed (p = .75). Overall, the ASD and TD groups represented each balance strategy within the same modality (main effect: speech or gesture, p < .001; group X modality interaction: ns); for example, most participants tended to express weight through speech and distance through gesture.

Conclusions: When asked to provide a verbal explanation for balancing, adolescents with ASD spontaneously produced gestures at the same rate as adolescents with TD, despite reduced reliance on speech to express the same strategies. Moreover, adolescents with ASD appear to choose the same communicative modality in which to express specific concepts as TD adolescents do. These findings suggest that adolescents with ASD may use gesture during problem solving similarly to TD adolescents. Gesture may in fact be an important methodological tool for the study of implicit cognition in ASD, and cited gesture impairments in ASD may reflect a quality other than rate (e.g., timing, integration with speech, etc.). Research pursuing this possibility is currently being conducted in our laboratory.

136.003 3 High/Low Autism Spectrum Behaviors and Executive Function. R. Pytlik*, F. R. Ferraro, R. Brindley and K. Schroeder, *University of North Dakota*

Background: Last year, we demonstrated the usefulness of the Executive Function Index (EFI, Spinella, 2004) with regard to a non-clinical sample by examining the relationship between high functioning Autism Spectrum disorder (HFA), as measured by the Autism Spectrum Quotient (ASQ) questionnaire, and underlying neuropsychological performance (frontal lobe, executive function). The EFI is a quick, reliable, and valid indicator of various domains of executive function and appears useful for those investigating the impact of frontal lobe deficit on HFA individuals. The ASQ can also rapidly quantity where an individual falls on the autism-normality continuum by distinguishing clinically significant levels of autistic traits.
Objectives: We used the High/Low ASQ score dichotomy (Lindell et al, 2009, *Laterality;* High ASQ scores of 16-30), Low ASQ scores of 5-15). They found reduced hemispheric asymmetry for language processing, which has been highlighted in autistic populations, can be observed in a normal, non-clinical sample using theHigh/Low ASQ dichotomy. We applied this High/Low dichotomy to provide converging evidence.
Methods: One-hundred undergraduates took the ASQ (50 questions, 10 each in 5 domains including social skill, attention switching,

attention to detail, communication, and imagination) and the EFI. (27 self-report items that measures areas associated with frontal lobe function including motivational drive, strategic planning, organization, impulse control, empathy, plus a total score). In 2009, we showed that increases in ASQ score (suggesting more HFA behaviors), resulted in decreases in EFI scores (suggesting more executive function deficit, especially for Motivational Drive, Organization, and EFI Total Score). We used the Lindell et al (2009) dichotomy to further test this relationship.

Results: A total of 67 subjects scored in the Low ASQ range (5-15, mean ASQ = 10.99, SD = 2.52); 33 scored in the High ASQ range (16-30, mean = 20.27, SD = 3.52). None scored above 32, a cut-off established by Baron-Cohen et al. (2001). The correlations of ASQ and EFI across subjects remained the same as in 2009: Motivation/ Drive ($r = -.22$, $p < .02$), Impulse Control ($r = -.04$, $p = .36$), Empathy ($r = -.16$, $p = .056$), Organization ($r = -.26$, $p < .01$), Strategic Planning ($r = -.11$, $p = .15$), EFI Total ($r = -.26$, $p < .01$). A one-way ANOVA, with High ASQ/Low ASQ as the between-subjects factor, resulted in a similar pattern: Motivation/Drive $F = 2.69$, $p = .10$; Impulse Control $F = .96$, $p = .33$; Empathy $F = 1.33$, $p = .25$; Organization $F = 3.67$, $p = .058$; Strategic Planning $F = 2.05$, $p = .14$; EFI Total $F = 5.86$, $p < .02$.

Conclusions: The significant associations observed in 2009 persisted (as ASQ increases, EFI decreases) using the High/Low ASQ dichotomy. EFI Total score results suggest that the various EFI components all show decrement with ASQ increases. We are refining these results by examining these relationships using the RBANS (Randolph, 1998) neuropsychological test battery.

136.004 4 Impaired Detection of Temporal Synchrony for Social and Nonsocial Events in Children with Autism Spectrum Disorders. L. E. Bahrick, J. T. Todd, M. Vaillant-Molina, B. M. Sorondo* and C. H. Ronacher, *Florida International University*

Background: Intersensory processing develops across the first year of life and is a fundamental building block for typical social and communicative functioning (Bahrick & Lickliter, 2002). However, children with autism spectrum disorders (ASD) appear to show altered intersensory processing with impaired temporal synchrony perception (Bebko et al., 2006), impaired use of visual speech in noise (Smith & Bennetto, 2007), and a wider temporal window for audiovisual integration (Foss-Feig et al., under review). Furthermore, they show social attention deficits, including impaired disengagement and decreased attention to social as compared with nonsocial events (Bahrick et al., 2009; Newell et al., 2007). Given that social events provide an extraordinary amount of intersensory redundancy (synchrony, rhythm, tempo, and intensity changes invariant across face, voice, and gesture), a general intersensory processing disturbance could lead to impairments in social orienting in ASD.

Objectives: The objective of the current research was to assess intersensory processing of audiovisual temporal synchrony for social and nonsocial events in young children with ASD, typical development (TD), and developmental delay (DD) using the intersensory measure from our Behavioral Attention Assessment Protocol (BAAP; Newell et al., 2007). We predicted that compared to TD and DD children, children with ASD would show intersensory processing impairments, particularly for social events.

Methods: Children with ASD (N = 7; 3.98 yrs), DD (N = 7, 4.18 yrs), and TD (N = 10, 3.18 yrs) (matched on Mullen composite scores) were presented with trials consisting of a 3 s central stimulus followed by two side by side peripheral events (10 s). One peripheral event was synchronous with the soundtrack and the other was out of synchrony. Three event types were presented in blocks of 20 trials depicting social neutral (woman speaking with neutral affect), social positive (woman using infant directed speech with positive affect, exaggerating intersensory redundancy), and nonsocial events (objects impacting a surface in an erratic temporal pattern). The proportion of total looking time (PTLT) spent fixating the sound synchronous event was calculated for each event type.

Results: An ANOVA revealed a significant main effect of group, with TD children showing greater PTLTs than children with ASD

(p = .01). In addition, TD and DD children showed significant matching of films and soundtracks (PTLTs greater than chance, .50) for both types of social events (ps < .05) and TD children also matched nonsocial events (p = .04). In contrast, children with ASD showed no evidence of audiovisual matching for any events (ps > .50).

Conclusions: Consistent with predictions, our findings indicate that children with ASD show impaired intersensory processing skills. They showed no evidence of detecting face-voice synchrony in social events or object-sound synchrony in nonsocial events. In contrast, typically developing children detected audiovisual synchrony in all event types, and children with other developmental delays detected face-voice synchrony in social events. These findings are consistent with prior findings of impaired audiovisual temporal synchrony detection in children with ASD and are compatible with a general intersensory processing disturbance underlying the development of social orienting impairments in ASD.

136.005 5 No Autistic Advantage in Inspection Time When Groups Are Matched Using the Raven's Progressive Matrices. E. B. Barbeau*[1], I. Soulières[1], T. A. Zeffiro[2] 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: The Inspection Time (IT) Task measures visual processing speed and has good face validity as a method to estimate neural information processing time. It is strongly correlated with the Wechsler IQ, particularly performance IQ, in typical populations. However, conflicting results have been reported concerning IT in autism when using standard IQ estimation procedures to match group properties (Scheuffgen et al., 2000; Wallace et al., 2009). An alternative matching procedure utilizes a test of matrix reasoning ability, the Raven's Progressive Matrices (RPM), a test for estimating general intelligence that is expected to be less affected by differences in verbal abilities than the Wechsler IQ. Autistics are known to achieve higher RPM scores than their Wechsler IQ predicts.

Objectives: Investigate the relationships among IT, RPM scores and Wechsler IQ measures in autistic and typically developing individuals.

Methods: We measured IT, matrix reasoning, and Wechsler IQ in 21 autistic and 28 typically developing participants (Wechsler FSIQ range: 78-126; age range: 14-34). In the inspection time task, two vertical lines of different length were presented on a monitor for durations of 10-200 ms and then immediately masked by two irregular lines. Participants indicated the longer of the two lines by pressing one of two keys on a response box and no instructions as to speed of response were given. The stimulus duration was adaptively varied in a staircase psychophysical procedure. Between-group IT comparisons were made in subsamples matched for either FSIQ or RPM percentile. We used a mixed effects model with group as a between-subjects factor and subject as a random factor.

Results: Using the FSIQ as a group matching variable, autistics had shorter inspection times (autistic mean IT = 88.4 ms and typical mean IT = 113.4 ms; p = .042). In contrast, using RPM percentile as the group matching variable yielded different results, with autistic and typical samples showing no IT differences. Examination of the correlations among the measures provided an explanation for the different results obtained with the different group matching strategies. For autistics, there was a strong correlation between RPM and IT (r=-.79, p<.001) but not between FSIQ and IT (r=-.36, p=.114). In the typical sample RPM percentile and IT (r=-.57, p=.002) were correlated more strongly than FSIQ and IT (r=-.21, p=.281).

Conclusions: Because of the observed shared variance between IT and matrix reasoning, it is clear that some care should be taken in selecting matching variables for studies of cognitive abilities in autism. The apparent advantage observed in autistics for IT task may actually result from using matching variables that share processing mechanisms with target task.

136.006 6 Non-Spatial Auditory Information Does Not Improve Complex Visual Search for Persons with Autism and Asperger Syndrome : « Pip » but No « Pop ». O. Collignon*[1], G. Charbonneau[1], M. Nassim[2], F. Peters[3], M. Lassonde[1], L. Mottron[2], F. Lepore[1] and A. Bertone[2], (1)*Centre de Recherche en Neuropsychologie et Cognition (CERNEC), Université de Montréal, Canada*, (2)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (3)*Centre de Recherche, Institut Universitaire de Gériatrie de Montréal (CRIUGM), Canada*

Background: Searching for a visual target from among a spatially complex environment is facilitated when an auditory tone or « pip » is presented in synchrony with a visual change in the target's attribute (i.e., color change). This « pip and pop » effect (van de Burg et al., 2008) is argued to result from the integration between temporally synchronized changes in auditory (non-spatial auditory « pip ») and visual (target color change) events, resulting in a salient multi-modal feature that typically draws attention to the target. This paradigm is well-suited to test the hypothesis that persons with autism integrate input from multiple sensory modalities less efficiently (Iarocci & McDonald, 2006). Such hypotheses are congruent with findings of atypical pattern of neural connectivity between specific brain areas that are sensitive to information from different sensory modalities in autism.

Objectives: To assess audio-visual integration abilities for non-social information in person with autism and Asperger syndrome by assessing whether they benefit from the synchronous presentation of auditory and visual events (manifest a « pip and pop » effect) during a demanding visual search task.

Methods: Twelve high-functioning autistic, 10 non-autistic, and 11 participants with Asperger syndrome matched for chronological age, full-scale IQ, gender and handedness were asked to complete a difficult visual search task. Participants searched for a horizontally- or vertically-oriented line segment (target) from among 24, 36 or 48 obliquely-oriented distracters (van de Burg et al., 2008; Exp.1). At random intervals, a random number of distracters changed color, between red and green. The target's color also changed, never coinciding with the distracter color change - it was the only changing item. In the tone-absent condition, participants were instructed to search for either the vertical or the horizontal target and to respond as quickly and accurately as possible to its orientation. In the tone-present condition, the task was the same except that the visual (color) target change was simultaneously accompanied by a short auditory « pip ».

Results: ANOVAs revealed that visual search times for the control group decreased significantly for the tone-present compared to the tone-absent condition ($p < 0.05$), reflecting the beneficial result of audio-visual integration. However, the performance of participants in both the autism and Asperger groups was unaffected by the presence of the auditory tone ($p > 0.05$), suggesting that target saliency was not increased by integrative audio-visual processes. Between-group differences were not evidenced for the tone-absent visual search conditions ($p > 0.05$).

Conclusions: The present findings suggest than persons with autism or Asperger syndrome do not necessarily benefit from typically facilitatory multimodal integration during a demanding visual search task. The absence of the « pip and pop » effect in these groups is suggestive of atypical/impaired integration of low-level perceptual cues originating from different sensory modalities. The lack of superior autistic performance on the tone-absent conditions may be related to the complexity (dynamic and spatial changes) of attributes defining the target and distracter search items. The results are discussed within the context of perceptual and cognitive theories in ASD.

136.007 7 Perception in Autism, 2006 - 2009: Updating the Enhanced Perceptual Functioning Model. L. Mottron*[1], I. Soulières[1], F. Samson[1], A. C. Bonnel[1], J. A. Burack[1], A. Bertone[1], T. A. Zeffiro[2] and M. Dawson[1], (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*Neural Systems Group, Massachussetts General Hospital*

Background: According to the enhanced perceptual functioning (EPF) model, advantages in perceptual processing are central to the autistic cognitive and behavioral phenotype. Autistic perception appears to be characterized by local orientation as a default setting; enhanced low-level perceptual operations; greater activity in perceptual areas during a range of visuospatial, language, working memory, and reasoning tasks; autonomy with respect to top-down influences; and strong involvement of perceptual expertise in savant syndrome.

Objectives: To provide an updated review of the literature relevant to perceptual functioning in autism.

Methods: We conducted a review of the behavioral, cognitive, psychophysical and brain imaging literature on autistic perception spanning 2006 - 2009. New empirical and theoretical content was considered as to its consistency, or lack thereof, with the eight principles composing the 2006 EPF model.

Results: Superior pitch processing is now the second most replicated example of an autistic perceptual peak. The autistic visual system appears to be more sensitive to high spatial frequencies. Reduced crowding effects, absence of critical distances in crowding, and greater thickness in perceptual cortices, all indicate atypical neural organization. Altered lateral neural interactions are a possible elementary mechanism accounting for superior extraction of perceptual features in both visual and auditory modalities. More sensitive and rapid detection of patterns may underlie superiorities in multiple perceptual domains and be especially developed in autistics with exceptional skills. Low level perceptual abilities in autism contribute to superior visuo-constructive ability and are positively related to performance in matrix reasoning. The role of visual perception in fluid reasoning is also demonstrated by enhanced extrastriate activity during performance on Raven's Progressive Matrices. A meta-analysis of functional imaging studies indicates that autistics' primary and associative visual areas are consistently more active on tasks involving face, object, and written language processing, while frontal areas are less engaged. Performance on a wide range of tasks, from perception of regularities within social information, to detection of anomalies in an ecological change blindness task, to a test of logical consistency, suggests an overall more independent and versatile functioning of cognitive processes in autism.

Conclusions: Most propositions of the EPF model have been supported by results reported in recent years. In addition, there are indications for a greater role of associative perceptual areas in autistic performance peaks involving visual perceptual tasks and fluid intelligence.

136.008 8 Relationship Between Executive Functioning, Autistic Symptomatology, and Adaptive Behavior. P. Ventola*, M. Levine, J. Tirrell and K. D. Tsatsanis, *Yale University*

Background: Deficits in adaptive behavior have been widely reported in individuals with ASD. Executive functioning (EF) deficits are also common in these individuals. The research on the relationship between adaptive behavior and EF is more limited. There is also little research on the relationship between EF and autistic symptomatology. Gilotty et al. (2002) found that deficits in metacognitive skills as measured by the Behavior Rating Inventory of Executive Function (BRIEF) were important contributors to adaptive functioning impairments, and Liss et al. (2001) found significant correlations between adaptive skills and perseverative errors on the WCST and performance on the WISC-R Mazes, but the relationships were mediated by Verbal IQ. South et al. (2007) examined the relationship between repetitive behaviors and flexibility and found significant correlations between WCST perseverations and repetitive behaviors scores on the ADOS and ADI-R.

Objectives: The purpose of the current study is to further evaluate the relationship between executive functioning skills, as measured by parent-report data from the Behavior Rating Inventory of Executive Function (BRIEF) and adaptive behavior, as measured by the Vineland Adaptive Behavior Scales, Second Edition (VABS-II), using a large sample of school-aged children with

ASD. A secondary purpose of the study is to investigate the relationship between autistic symptomatology, based on ADOS calibrated severity scores, and EF skills.

Methods: The sample included 73 children: 31 from a clinical sample and 42 from a longitudinal study of ASD. Mean age was 8.9 years (s.d. 2.1; range 6-16). Level of cognitive functioning was assessed using the Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV) or the Differential Abilities Scale, Second Edition (DAS-II). For the children who received the WISC-IV, the mean IQ score was 96.0 (s.d. 18.9; range 68-149). For the children who received the DAS-II, mean IQ score was 92.2 (s.d. 17.3; range 53-134). All children received the ADOS and were characterized by a team of experienced clinicians.

Results: Overall cognitive ability was not correlated with EF, but the Working Memory and Processing Speed domains from the WISC-IV were negatively correlated with EF impairment. There were no significant relationships between EF behaviors and autistic symptom severity, as measured by the ADOS calibrated severity score. EF behaviors were significantly positively correlated with adaptive functioning, particularly adaptive socialization, daily living, and expressive language skills.

Conclusions: The severity of autistic symptoms is not associated with severity of EF behavioral impairments. However, level of adaptive functioning is associated with EF behaviors. Thus, whereas EF impairments are not related to the social disability in ASD, they are significantly related to level of social ability. The direction of the relationship cannot be determined from this study, but it is reasonable to hypothesize that EF behaviors impact adaptive functioning but also that areas of adaptive functioning (e.g., expressive language skills) may impact EF behaviors, such as regulatory control and problem solving. The clinical implications of these findings include the need to address EF behaviors when treating children with ASD.

136.009 9 Remembering and Knowing Old-New Word Effects in Autism Spectrum Disorder. E. Massand* and D. M. Bowler, *City University, London*

Background:

Recognition memory in non intellectually disabled individuals with ASD tends to be undiminished compared to TD individuals (Bowler et al., 2000), however the question remains of whether the processes underlying recognition in ASD result from similar or different mechanisms than in TD. Behavioural studies have used the Remember/Know paradigm to assess the contributions of the episodic and semantic memory systems to recognition. Compared to TD individuals, people with ASD show diminished episodic Remember experiences but undiminished semantic Know responses (Bowler et al., 2000a; 2000b and Bowler and Gaigg, 2007).

Event-related potentials (ERPs) were used to record the brain activity during item recognition and Remember/Know judgements in a sample of ASD and age and IQ-matched TD adults. ERP studies in TD individuals have shown that that correctly recognised words show enhanced positive potentials relative to new words - the 'Old-New ERP effect' (Rugg and Curran, 2007). The effect is thought to reflect the contribution of both the episodic Remember responses and semantic Know responses (parietal positivity 400-800ms for remember responses and earlier frontal positivity 300-500ms for know responses, Curran et al., 2006).

Objectives:

The early Old-New effect (300-800ms), the late Old-New effect (800-950ms) for Remember and Know judgements were compared across groups to assess the qualitative similarity of Remember responses in the ASD group to those of the TD group.

Methods:

Fourteen ASD (mean age and VIQ; 36.2years, 113) and 19 TD (36.5 years, 111) individuals participated in a Remember/Know recognition memory task. ERPs were recorded from 32 scalp sites and averaged according to correctly recognised words judged as Remember or Know versus correctly rejected new words.

Results:

Behavioural data revealed no significant difference in overall recognition between the two groups, $F(1,31)=1.67$, *n.s.* There was a trend towards less Remembering and more Knowing in the ASD group compared to the TD group (in line with existing findings).

Early Old-New effects (300-800ms) did not differ between groups, $F(1,31)=0.95$, *n.s.,* however the late Old-New effect for overall recognition was significantly attenuated from 800-950ms in the ASD group, $F(1,31)= 9.29$, $p<.01$. Remember-New differences in this time window were significantly diminished in the ASD group compared to the TD group ($F(1,31)=6.89$, $p<.05$). There were no differences in the Know-New ERPs from 800-950ms across groups ($F(1,31)=1.61$ *n.s.*). Both ASD and TD individuals' Remember responses were characterised by a positive Remember-New effect from 400-800ms ($F(1,31)=0.01$, *n.s.*). The results demonstrated that TD individuals had a residual Remember positivity from 800-950ms, which was absent in the ASD group.

Conclusions:

The findings suggest that the Remember component of overall recognition in ASD is in large-part qualitatively similar to that of TD individuals, reflecting existing behavioural work. However the late (800-950ms) group difference for Remember responses may reflect processes that contribute to a quantitative diminution in overall rates of remembering in the ASD group. This has implications for our understanding of the operation of the episodic memory system of individuals with ASD.

136.010 10 Social and Non-Social Memory in Children and Adolescents with ASD. R. S. Brezis*[1], O. L. T. Wong[2] and J. Piggot[2], (1)*University of Chicago*, (2)*University of California, Los Angeles*

Background: Studies of memory abilities in ASD have consistently shown a discrepancy between difficulties in episodic memory for personally experienced events, relative to a preserved semantic memory for facts (Boucher and Bowler, 2008). How may we explain these findings? Are autobiographical memory deficits simply the extreme of a graded scale of information-processing deficits, or do they present a qualitatively independent impairment? This question relates more broadly to the search for a core deficit in autism, split between those arguing for a specific impairment in self and social abilities (Baron-Cohen et al., 2000, Hobson et al., 2006) and those arguing for a broader cognitive information-processing impairment (Happe and Frith, 2006; Minshew and Williams, 2007). Previous studies of memory in autism have generally compared simple semantic recall (such as word-generation, narrative memory) with complex episodic recall (Crane and Goddard, 2008; Losh and Capps, 2003; Klein et al., 1999), thus precluding the possibility of directly testing each alternative hypothesis. The present study aims to disentangle the underlying components of episodic and semantic memory, extending previous studies through carefully controlled behavioral measures, and through detailed phenotyping of social and cognitive skills.

Objectives: (1) To disentangle the relative importance of information-processing deficits from self- and social-processing deficits in ASD using episodic and semantic memory tasks matched for level of complexity. (2) To determine the neuropsychological co-variates of memory patterns in ASD, using in-depth clinical tests of social and cognitive processing.

Methods: Participants included 40 8-18 year-old subjects with ASD and 40 age, sex and IQ-matched controls. Autism diagnoses were confirmed using ADOS (Lord et al., 1999) and ADI-R assessments (Lord et al., 2003), and all subjects completed the Social Responsivity Scale (SRS) (Constantino, 2000) and Social Communication Questionnaire (SCQ) (Berument et al., 1999). Sub-tests from the NEPSY-II (Korkman et al., 2007) were used to obtain standardized measures of social and non-social semantic memory and organizational ability. The experimental tasks included a Levels-of-Processing task (based on Toichi et al., 2002) and a narrative recall task (based on Crane and Goddard, 2008) comparing memory for self, mother and favorite fictional character.

Results: Preliminary results, based on 15 ASD participants, support a self-reference effect ($p = 0.018$), with memory for self greater than memory for mother ($p=0.056$) and favorite fictional character ($p=0.012$) (contrary to Toichi et al., 2002 but in line with Lombardo et al., 2009; Henderson et al., 2009), thus providing support for the social-impairment hypothesis of autism. Further data collection, between-group and regressional analyses are underway to provide a more detailed picture of the underlying social and cognitive skills shaping the discrepant memory patterns in ASD.

Conclusions: By determining whether deficits in episodic memory in ASD arise from a particular impairment in organizing events in the world around their sense of self, or whether they are driven by broader information-processing deficits, our study aims to advance our understanding of the social communication deficit seen in autism as it unfolds over time, and to further specify targeted interventions.

136.011 11 Social Versus Memory Demands On Cognitive Set Shifting. O. Johnston*, S. E. White, A. Clawson, E. Krauskopf, M. J. Larson and M. South, *Brigham Young University*

Background: Ozonoff (1995) reported that children and adolescents diagnosed with high-functioning autism performed better on the Wisconsin Card Sort Test (WCST), a test of set shifting and perseveration, when it was administered by computer than by a human. Ozonoff suggested that social demands may interfere with cognitive tasks although executive functions may be largely intact in autism; and that variables related to task administration play an important role in understanding cognitive dysfunction in autism. Despite inconsistency in the results across executive function studies in autism, task administration variables are rarely discussed.

Objectives: We aimed to replicate and extend the Ozonoff study by comparing person-administered (Person Only, PO), and computer-administered (Computer Only, CO) versions of the WCST and by adding a third condition: we videotaped a person administering the task and showed the administration on computer (Person-Computer, PC). In accordance with Ozonoff's hypothesis, we expected that performance on the PC version would fall between the CO condition (best) and the PO condition (worst) for autism relative to controls.

Methods: We tested 45 children and adolescents diagnosed with autism spectrum disorders (ASD), 15 in each test condition. ASD was diagnosed by an expert rater based on information from the standardized ADOS-G clinician observation and SCQ parent checklist; Verbal and Full Scale IQ were above 80 for all participants. An age-, sex-, and IQ-matched comparison group (n = 45) also completed the task. The PO version was administered using standard instructions (Heaton, 1993). The CO and PC conditions were presented using our own E-Prime-based software program. The card stimuli on the CO version were identical to those used in the actual card set, and the young adult male shown in the PC version used the actual cards. We made one modification to the CO task compared to standard commercially-available versions: in order to simulate the lag time that accompanies the human administrator reaching for the card deck and raising it to show the participant, we added a short (2 second) video of a point-light display of a rotating circle or square in-between each trial. Total time from the end of one trial to the possibility of making the next choice was about 4 seconds in all three conditions.

Results: There was no significant main effect of diagnostic group for the person-only condition. However, both computer-based versions were significantly more difficult for the ASD group: repeated measures ANOVA demonstrated significant group x condition interactions showing increased perseverative errors and fewer completed categories for the autism group.

Conclusions: We suggest that perhaps the improved performance on the computer version in the Ozonoff (1995) study arose because there was less lag time between choices, so that the ASD participants had less chance to lose the context of their previous choices in informing their next choice. In the present study, participants may have been distracted by the short videos that played in-

between choices, thereby losing that context, possibly due to working memory difficulties. We discuss the results in terms of information complexity, social interactions, and neural connectivity.

136.012 12 Strategic Influences On Face Processing in Autism Spectrum Conditions, Dyslexia and Typical Development.
C. A. Palmer*, K. Plaisted Grant and G. J. Davis, *University of Cambridge*

Background: The general issues of category-specific visual processing abnormalities and atypical early visual mechanisms are fiercely debated in the autism literature. Specifically, spatial frequency preferences and the face inversion effect are relevant to the current investigation. There is a wealth of literature to suggest that atypical processing strategies in autism spectrum conditions (ASC), including abnormal spatial frequency biases, may contribute to such findings. Face processing has been the focus of much autism research and there is mounting evidence of strategic differences in ASC individuals compared to typically developing controls (Teunisse et al., 2003). There are also thought to be visual disturbances associated with dyslexia and comparisons have been drawn between visual processing in these two sets of conditions. However, the same emphasis on strategic atypicality has not been applied to dyslexia. In this study, low-level perceptual strategies are assessed in ASC and dyslexia.

Objectives: To study the low-level visual strategies selected by participants with ASC, in comparison to those diagnosed with dyslexia and typically developing individuals. The relationship between the prevalence of autistic traits in general, and the processing strategy adopted is also explored.

Methods: A computer-based identity matching experiment was run on three groups of high-functioning adult participants: those with ASC, with dyslexia and typically developing individuals. There were two experimental sessions, testing the identification of three faces and three cars separately. Stimuli were spatial frequency modified, to investigate the low-level visual preferences exhibited by the groups under different experimental conditions. The images used were full spectrum, low-pass filtered, high-pass filtered and hybrids of low- and high spatial frequency components of different images. Stimuli could be presented upright or inverted. In addition, participants completed the Autism Spectrum Quotient (AQ) and the Advanced Raven's Matrices (APM).

Results: At the time of writing, data-collection is incomplete. However preliminary observation of control group data reveals an intriguing relationship between upright face identification performance in certain conditions and participants' score on the AQ. At this early stage some compelling contrasts can be observed between patterns of performance in the ASC and dyslexia groups.

Conclusions: In this experiment, face identification performance is related to the degree of autistic traits exhibited by a typically developing population. The relationship observed here is specific to rapid presentation conditions and is also sensitive to the image category, which suggests that it is the execution of particular processing strategies which is related to AQ. This relationship may extend into the ASC and dyslexia groups, or a distinct pattern of results may be observed in these participants due to additional processing atypicalities that overwhelm any influence of autistic traits as measured by the AQ.

136.014 14 The Role of Integration in the Memory Deficits of ASC.
L. Maister* and K. C. Plaisted-Grant, *University of Cambridge*

Background: The study of memory functioning in ASC reveals a complex pattern of strengths and impairments, and many mixed findings. However recent studies have begun to converge on some recurring themes. Firstly, findings suggest individuals with ASC seem not to utilise semantic information to aid their recall in the same way as neurotypical individuals. This often results in impairment, for example when recalling a list of semantically related items (e.g. Toichi and Kamio, 2003; Renner, Klinger and Klinger, 2004; Tager-Flusberg, 1991; Minshew and Goldstein, 1992). Individuals with ASC also appear to be impaired in processing relations between

items in memory (Gaigg, Gardiner and Bowler, 2008; Bowler, Gaigg and Gardiner, 2009). This could explain impairments seen in episodic memory and source memory, as recalling context requires relations between different elements of an event to be processed. Both the processing of inter-item relationships, and the use of semantic information to aid recall, requires integration of memory structures. Relational processing requires on-line integration of activated memory representations within working memory, both at the encoding and retrieval stages. Integration is also needed to enable semantic information to be used to aid encoding and retrieval processes; activated representations in working memory must be integrated with pre-existing long-term semantic memories. It is therefore possible that a more general impairment in integration of memories is underlying these difficulties seen in ASC. Objectives: This study aimed to investigate integration in ASC, both within working memory and between items in working memory and long-term memory. Task support was systematically varied to investigate whether any deficit was due to a problem in the self-initiation of integration or the actual integration process itself. Relationships between performance on these integration tasks, performance on other memory tasks and tests of executive function were then explored. Methods: The study compared the performance of a group of 16 children with high-functioning ASC to a group of 16 typically-developing children, matched on chronological age, verbal and non-verbal IQ. Firstly, the study investigated whether the mechanisms underlying basic integration of items within working memory were functioning correctly. Then, the ability to integrate activated items in working memory with existing long-term memory representations (both semantic and episodic) was explored. Integration was tested both with and without task support. Memory measures, including the free recall of related word lists, unrelated word lists and autobiographical memories, were taken to investigate the relationship between performance on memory tasks and integration abilities. Various tests of executive function were also carried out to assess their role in any impairment found. Results: At time of writing, data collection for an ASC-group was not complete. Conclusions: We predict that a deficit in memory integration may underlie some of the memory impairments seen in ASC.

136.015 15 An Understanding of Sharing, Following, and Directing Attention and Behaviour in Children with Autism. J. M. Normand* and B. D'Entremont, *University of New Brunswick*

Background: Social cognitive development begins early in life when children develop an understanding of others in terms of their intentions (concrete goals or purposes that guide behaviour). An understanding of others as intentional agents is displayed through the functional behaviours of sharing, following, and directing attention and behaviour. Previous cross-sectional research investigating these functional behaviours in children with autism spectrum disorder (ASD) has found that, for both these behaviours, children find sharing easier than following, and following easier than directing (Carpenter, Pennington, & Rogers, 2002). Furthermore, it appears that the attention functions were more challenging for children with ASD than the behaviour functions. Objectives: The objective of the present research was to test whether the findings of Carpenter et al. (2002) would generalize to an independent sample with ASD. The present study used tasks which were different from those used by Carpenter et al; however the tasks were designed to measure the same underlying constructs. It was hypothesized that the results would be similar to Carpenter et al.
Methods: Eleven children (10 males) with community diagnosed ASD participated. All children were seen individually for one session. A modified version of the Early Social Communication Scale (ESCS; Mundy, et al. 2003) was used to gather information on sharing attention, following attention, directing attention, and directing behaviour. Three imitation procedures provided assessment of following behaviour. A cross-sectional design was used. Pass/fail criteria were created for each task and group patterns were determined by ordering the tasks by the number of children who passed each task at the time of inquiry. Individual patterns of passing or failing each task were

compared to the group to identify how many children fit the group pattern.
Results: An overall group pattern was displayed by 90% of participants. Considering the attention function, more participants passed sharing attention than following attention and more passed following attention than directing attention. For behaviour, more participants passed directing behaviour than following behaviour. Comparing across functions, directing behaviour was found to be easier than sharing, following, or directing attention, while following behaviour was more difficult than all three attention tasks.
Conclusions: As predicted, our sample displayed the same pattern of sharing, following, and directing attention as Carpenter et al. (2002). In contrast to Carpenter et al., more children passed directing behaviour than following behaviour. Carpenter et al. found the opposite pattern. Also, while understanding attention was generally more difficult for our sample than understanding behaviour, at least one following behaviour task posed a significant challenge for our sample. The difference between these two studies could be due to the way directing and following behaviour were measured or to differences in sample characteristics, particularly verbal ability. Importantly, these findings suggest that different pathways to intentional and social understanding may exist for children with ASD depending on their developmental or verbal profiles.

136.016 16 Anticipatory Capacity for Social Interactions and Verbal Communication in Individuals with Autism. E. Poljac*[1], K. Dahlslätt[1], J. K. Buitelaar[2] and H. Bekkering[1], (1)*Radboud University Nijmegen*, (2)*Radboud University Nijmegen Medical Centre, Nijmegen Centre for Evidence-Based Practice*

Background: Already in 1943, Leo Kanner described eleven children having a major problem in relating themselves in an ordinary way to people and situations. Specifically, almost all these children failed to assume any anticipatory posture preparatory to being picked up. Contemporary literature provides ample scattered empirical evidence for the idea of deficits in anticipatory capacity in autism. This study is developed to systematically test whether individuals with autism have a general deficit in anticipatory capacity within and across different cognitive domains.

Objectives: The main objective of this study is to explore the possibility of deficits in anticipatory capacity accounting for the frequently reported cognitive dysfunctions within social cognition and verbal communication in autism. Specifically, we opt for a direct as possible comparison between the two fields of interest, aiming not only to gain insight into anticipatory capacity within each of the two areas, but also into the generalizability of the assumption across the two domains.

Methods: The study will be conducted in two stages differing mainly in the tested population. In the first stage, a healthy student population (n = 30) is included in a pilot that aims to test two newly developed eye-tracking paradigms, one within the action domain and the other within the language domain. After conducting the pilot, the second stage includes collecting the data from high functioning children with autism (n = 20) and their healthy controls (n = 20) matched on age (10 to 16 years) and IQ (> 70). In both stages, each participant takes part in two experiments. In Experiment 1, our action paradigm is applied, in which participants watch videos showing a person executing a series of object-related actions either sequentially interdependent or not (baseline). We measure anticipatory eye movements towards the object associated with the upcoming action. In Experiment 2, our language paradigm is applied, in which participants watch scenes while listening to sentences that differ in the degree of the constraining context allowing for anticipatory behavior. Images for scenes are taken from the action paradigm, in order to keep the two paradigms as comparable as possible. In both experiments, we compare eye-gaze frequencies and onset latencies between high and low anticipatory conditions.

Results: Data acquisition for the pilot starts in January 2010, with two main focus areas: (1) testing of both paradigms for their sensitivity to detect the desired (eye-movement and latency) effects reflecting

anticipatory capacity in general and (2) in autism in specific. The latter is operationalized by means of a correlation between the effects reflecting anticipatory capacity and the score on the Autism Quotient Scale (Dutch version). The pilot data will be used to adapt the two paradigms if needed, before testing the actual patient population.

Conclusions: The results of the pilot data showing the sensitivity of our paradigms to tackle anticipatory capacity in autism together with the preliminary data assessed in the actual patient population will be presented at the conference.

136.017 17 Deficit in Visual Temporal Integration in Autism Spectrum Disorders. T. Nakano*[1], H. Ota[2], N. Kato[2] and S. Kitazawa[1], (1)*Juntendo University School of Medicine*, (2)*Showa University School of Medicine*

Background: Individuals with autism spectrum disorders (ASD) are superior in processing local features. Frith and Happe conceptualize this cognitive bias as "weak central coherence," implying that a local enhancement derives from a weakness in integrating local elements into a coherent whole. The suggested deficit has been challenged, however, because individuals with ASD were not found to be inferior to normal controls in holistic perception, at least when it is required of them. In these opposing studies, however, subjects were encouraged to ignore local features and attend to the whole.

Objectives: To directly examine the ability to integrate elements into a whole image over time, we tested whether individuals with ASD are able to integrate local elements into a whole image by using slit-viewing.

Methods: Each subjects (ASD group: n=17, age 32.4 ± 8.2 years; control group: n=16, age 29.4 ± 6.9 years) named 40 figures three times, once for each of three blocks: in the first and the second block, pictures were presented behind the narrow slit (slit-viewing) at a fast and a slow speed, counterbalanced across subjects, and in the third block, whole pictures were presented in front of the slit at a fast speed (full-viewing).

Results: In the slit-viewing, the mean rates of correct answers in the ASD group (fast 46%, slow 48%) were strikingly lower than those in the control group (fast 77%, slow 75%) at both speeds, which was worsened by the absence of local salient features in the figures. By contrast, both groups successfully named almost all pictures in the full-viewing (ASD 96%, control 99%). Two-way ANOVA detected significant main effects of group ($F_{1,31}$=25.5, p<0.0001) and condition (F_2=119.0, p<0.0001), and significant interactions ($F_{2,62}$=16.2, p<0.0001).

Conclusions: The present results indicate that individuals with ASD have a clear deficit in integrating local visual information over time into a global whole, providing a direct evidence for the "weak central coherence" hypothesis.

136.018 18 Exploring Alexithymia in Autism Via Musically Induced Emotions. R. J. Allen*[1], P. Heaton[2] and E. Hill[1], (1)*Goldsmiths, University of London*, (2)*Goldsmiths College, University of London*

Background: It has been reported that due to the social evolutionary origins of human music-making, individuals with autism – who by definition have social deficits – are unable fully to appreciate music, especially the emotional content of music. At the same time, alexithymia (difficulty in identifying and describing feelings) is known to be a common condition in autism, and it seemed to us that attempts to measure the ability in autism to experience emotion in music might have been confounded with difficulties with self-reporting those emotions. This suspicion was strengthened by an initial, qualitative study (Allen et. al, 2009) which showed no qualitative difference in the importance of music in the lives of high-functioning adults with autism, compared with published studies on the general population.
Objectives: our aim was to measure and compare physiological responses to a standard set of musical items and to a set of environmental noise items (as control condition) in autism and control groups, to see whether and how these responses differed independently of the confound of alexithymia. We aimed also to compare these results with the self-reports of

emotional reactions to the music in the two groups, correlating this with conventional questionnaire measurements of alexithymia, to see how far alexithymia might explain any apparent autistic lack of responsiveness.
Methods: We used matched samples of 23 (autism group) and 24 (control) to measure galvanic skin responses to a set of 12 short music passages and 6 items of environmental noise. We also sought self-report of emotions evoked by the music, and administered standard normed questionnaires to measure alexithymia (TAS-20 and BVAQ).
Results: the gsr responses of our autism group were significantly lower than controls. However, their responses to environmental noise were proportionately lower as well, amd when allowance was made for this, there was no group difference in relative responsiveness to music. The autism group did use significantly fewer words to describe their emotional responses to music compared with controls, but this correlated strongly with, and was explicable in terms of, their lower scores on factor 3 ("poor insight") of the BVAQ.
Conclusions: our results are consistent with the hypothesis that in autism, the basic physiological emotional component of their reactivity to music is functioning normally, but that their ability to translate and verbalize these reactions into conventional emotional language terms is reduced, precisely in line with the extent of their alexithymia. This has possible implications both for developing a more objective measure of at least one aspect of alexithymia, and for treatment of alexithymia through associative learning between labelled items of music and the corresponding induced physiological states.

Ref: Allen, R., Hill, E., & Heaton, P. (2009). 'Hath charms to soothe...'. An exploratory study of how high-functioning adults with ASD experience music. *Autism, 13*(1), 21-41.

136.019 19 Eye Gaze Patterns of Young Children with Autism and the Broader Autism Phenotype During a Dynamic Social Interaction Task. L. Sepeta*, K. Quach, T. Hutman, M. Dapretto, M. Sigman, S. P. Johnson and S. Y. Bookheimer, *University of California, Los Angeles*

Background: Atypical facial fixation patterns have been discovered in older individuals with autism (Pelphrey et al., 2002); however, much less is known about facial fixation behavior in children with autism at 36-months of age and younger. The small body of research that exists suggests that atypical face processing and facial fixation behavior is evident even in young children with autism (Dawson et al., 2004; Klin & Jones, 2008; Webb et al., 2006). Given these findings, studying facial fixation patterns in the siblings of children with autism is important because these children are at a greater risk of developing autism, and thus this is a population that can be evaluated for signs of autism from birth.

Objectives: To examine the fixation behavior of 36-month-old siblings of children with autism (high-risk group) in comparison to typically developing (TD) children (low-risk group) during a social interaction task with a caregiver in an effort to improve characterization of autism and the broader autism phenotype (BAP).

Methods: We examined the facial fixation behavior of 36-month-old siblings of children with autism (n = 28) and a typically developing comparison group (n = 25). All 53 children were part of a larger study and were followed longitudinally starting at 6 months of age. At 36 months of age, the children were grouped into best-estimate clinical diagnostic categories (including Autism/ASD, BAP or TD)) using data from the ADOS-G, ADI-R, Mullen Scales of Early Learning, and behavioral observations. Each study participant sat in front of the eye-tracking monitor and engaged in a live interaction (peek-a-boo) with his/her caregiver via a closed-circuit computer monitor. Fixation patterns during the interaction were compared between clinical diagnostic groups.

Results: Children diagnosed with Autism/BAP (n=10) displayed an atypical fixation pattern, focusing less on the upper region of the face (eyes: $p < 0.05$) and more on areas around the face (hands: $p < 0.05$) than TD children in both the high-risk and low-risk groups (n = 41). The siblings of children with autism who were found to be typically developing (n = 19) showed similar fixation behavior to TD

control children (n = 22) for upper face, lower face, and hand regions (ps > 0.341).

Conclusions: Our findings suggest that young children diagnosed with autism and the BAP display atypical attention to faces when interacting with a caregiver compared to TD children in both the high-risk and low-risk groups at 36 months of age. Importantly, the results of this study demonstrate that differences in facial fixation behavior are not a general feature of children at risk for autism; rather, those high-risk siblings who were diagnosed as typically developing displayed typical fixation behavior. The results of the current study also indicate that there is a close relationship between social impairment and facial fixation behavior, supporting the hypothesis that gaze patterns at a very early age are related to social development. Consequently, eye-tracking technology within the context of the infant sibling research design is useful for characterizing early signs of autism and the BAP.

136.020 20 Is Source Memory Impairment Specific to Social Stimuli inHigh Funtionning Autism Spectrum Disorder?. E. Gilbert*[1], K. Morasse[2] and N. Rouleau[3], (1)*Centre de recherche Université Laval Robert-Giffard*, (2)*Hôtel-Dieu de Lévis*, (3)*Université Laval*

Background: For the past thirty years, studies have tried to characterize the memory profile of individuals with autism spectrum disorders (ASD). Findings from the literature suggest they show deficits or atypical processing in episodic memory and more specifically in memorizing the source of information. Since the last decade, source memory has been increasingly investigated in individuals with ASD. However, contradictory findings have been found and the nature of source memory impairment in this population is still inconsistent.

Objectives: The aim of the current study is to better understand source memory functioning in children with High Functioning ASD (HF-ASD). To achieve this, limitations of previous research were addressed by using a theoretically driven task and an appropriate comparison group.

Methods: A group of 21 HF-ASD boys aged from 7 to 17 years old and their individually matched controls were assessed. Groups were matched on age, gender and verbal abilities. Memory was assessed using a theory driven experimental task designed to measure source memory for self-other (internal-external) and temporal context (external-external) of studied words (Doré et al., 2007).

Results: Discrimination indexes and response bias indexes were calculated based on the Two High Threshold Theory (Corwin, 1994). Groups comparison showed that the HF-ASD group is lower than the control group in discriminating self versus other source of previously presented targets ($p < .05$). There are no group difference on the identification of the temporal context ($p = .21$). Group comparisons also demonstrate that the HF-ASD group have lower recognition abilities in episodic memory ($p < .05$). Response bias indexes were similar between the two groups thus suggesting that both groups adopt a conservative approach when uncertain.

Conclusions: Findings confirm evidences from other studies that episodic memory seems impaired in children with HF-ASD. More importantly, our results point out to a particular profile of source memory processing in HF-ASD children. Analyses have shown that self-other source memory is impaired but not memory for temporal context. This finding support that source memory deficits are not generalized but may be more important when the to-be remembered source involves social aspects. To our knowledge no studies have yet examine how source memory may be related to the social impairments in children with HF-ASD. This is of particular interest since social difficulties are a core deficit in HF-ASD. Further studies are actually in process in our laboratory to explore relations between source memory and social functioning in HF-ASD.

136.022 22 Speed of Responding in ASDs: A Look at the First Seconds of Processing. J. M. Bebko*, S. M. Brown and C. A. McMorris, *York University*

Background: Minshew (2009) characterized slow processing speed as a hallmark of autism spectrum disorders (ASDs). However, slow processing in children with ASDs has been inconsistently demonstrated across a variety of tasks. For example, on some tasks, such as the embedded figures task, children with ASDs have quicker response times compared to typically developing (TD) children. Previous studies have primarily examined reaction times as responses to stimuli that remain visually present for extended periods of time, such as in working memory tasks. Less is known about the speed of responding in tasks when stimuli only remain in view for very short exposure times (e.g., 100 msec). Using free and cued recall tasks, the current study examines if speed of responding in children with ASDs is different from TD children after a presentation of visual stimuli for a very short duration in an iconic memory task. The results will provide clarification for whether observed differences in speed of responding begin extremely early in processing, or emerge after the initial input stages.

Objectives: To provide insight into children with ASD's information processing skills: Specifically to examine if children with ASDs have longer response times at the earliest stages of information processing.

Methods: Fourteen children with an ASD (*M* = 122.57 months; *SD* = 24.83 months) and fifteen TD children (*M* = 114.07 months; *SD* = 20.56 months) participated in the present study. Participants completed two tasks, each following a presentation of a circular array of eight letters for a brief, 100 msec period: 1) a free recall task where participants were asked to recall all the items they could remember; and 2) a cued recall task, where an arrow was also presented to cue which single item they were required to report. In the second task, the time between the presentation of the stimuli and the cue (interstimulus interval) was varied.

Results: For each participant reaction times were calculated from the end of the presentation of the stimuli to the start of the participant's response, and response times were calculated from the start of the response to the end of the response. Data analysis is ongoing, and group differences are being evaluated for both correct and incorrect responses to examine possible speed-accuracy relations.

Conclusions: The results from this study will provide information about the first few seconds of information processing in children with ASDs compared to TD children. More specifically, if children with ASDs differ from TD children in their reaction and response times at this early stage of processing, it provides strong support for a general speed of processing deficit associated with ASDs. A finding of equivalent speed of responding would suggest that speed differences observed later in processing, such as in short term memory tasks, are due to downstream, higher level activities.

136.023 23 Temporo-Spatial Gaze Patterns in Autistic Children and Adults While Viewing Video Stories. T. Nakano[1], K. Tanaka[1], H. Ota[2], N. Kato[2] and S. Kitazawa*[1], (1)*Juntendo University School of Medicine*, (2)*Showa University School of Medicine*

Background: Eye-tracking has been used to investigate gaze behavior in individuals with autism spectral disorder (ASD) while viewing socially salient stimuli like faces, but results are not consistent across studies. The discrepancy might be due to difference in age groups and limitation of the fixation time analysis that has been used in most studies so far. We hypothesized that differences are most likely to be detected by taking sub-second temporo-spatial gaze patterns into account, because social salience in a scene dynamically changes from one place to another over time.

Objectives: To clarify sub-second characteristics of gaze behavior in children and adults with ASD, we examined temporo-spatial gaze patterns while they viewed ecological video stimuli.

Methods: Children with ASD (2-8 y.o., n=26), normal children (1-7 y.o., n=26), normal adults (>21 y.o., n = 27), and adults with ASD (>18 y.o., n=27) participated. Gaze positions were recorded with an eye-tracker, while they viewed a short video stimulus with sound, 77 s long. The video consisted of 12

short clips, each of which was taken from a film or a TV program for young children, and involved one, two, three, or more human characters. To quantify differences in temporal patterns of gaze movement, we calculated distance between gaze positions in every pair of subjects ($_{106}C_2$) in every frame (2327 frames), and applied multidimensional scaling (MDS) to visualize similarity of the temporo-spatial gaze patterns among 106 subjects on a two-dimensional plane (MDS plane). We further analyzed each frame whether there was any discrepancy in gaze distributions across groups.

Results: Normal adults and normal children formed two distinct clusters near the center of the MDS plane. Groups of autistic children and adults distributed in the periphery, each surrounding its age-matched control group. The results indicate that temporo-spacial gaze patterns were highly conserved within normal children, within normal adults, but varied in ASD subjects. Significant across-group differences in gaze distribution appeared, for example, when the subjects viewed two children that talked in turn, and when the subjects viewed a single child that announced her name. In the former case, gazes in normally developing children and adults moved between the two children in a highly conserved manner, but those in children and adults with ASD did not. In the latter case, normally developing children spent much more time in viewing the mouth than in viewing the eye, in marked contrast to the normal adults that concentrated on the eyes. In children and adults with ASD, there was no such preference to the mouth or to the eyes in viewing the scene.

Conclusions: We conclude that normally developing children share temporo-spatial gaze patterns that grew into those shared among normal adults. On the other hand, temporo-spatial gaze patterns were varied from subject to subject in both children and adults with ASD. Diagnostic application of the present temporo-spatial analysis using MSD merits further investigation in both age groups.

136.024 24 The Cognitive Interview for Witnesses with Autism Spectrum Disorder. K. L. Maras* and D. M. Bowler, *City University, London*

Background: The Cognitive Interview (CI) is one of the most widely accepted forms of police interviewing techniques as it elicits the most detailed, yet accurate reports from witnesses. Despite a substantial body of research which has demonstrated the effectiveness of the CI with different groups, including those with intellectual disabilities, the elderly, and children, no research to date has examined its effectiveness with witnesses with autism spectrum disorder (ASD) despite their very specific memory difficulties, particularly with regards to the episodic recollection of personally experienced events. Objectives: The aim of this study was to examine the efficacy of the CI for witnesses with ASD compared to their age and IQ matched typical counterparts.
Methods: Twenty-six adults with ASD and 26 matched typical adults viewed a video of an enacted crime. Following an unrelated filler task, witnesses were interviewed with either a CI or a standard Structured Interview (SI), which was identical to the CI but did not include CI mnemonics.

Results: The ASD and typical groups did not differ on the quantity or quality of their reports when interviewed with a SI, t (24) = 0.30, *ns*, however, when interviewed with a CI the ASD group were significantly less accurate than the typical group, t (24) = 3.55, p < 0.005, Further, accuracy within the ASD group when interviewed with a CI was reduced specifically for details that might be considered to be central to the event; i.e. those relating to persons, t (18) = 3.51, p < 0.005, and actions, t (14) = 3.66, p < 0.005, but was comparable to controls for more peripheral details relating to surroundings, t (24) = 0.26, *ns*, and objects, t (24) = 1.92, *ns*. Conclusions: Individuals with ASD are as accurate and provide as detailed eyewitness reports as do typical individuals when interviewed with a SI. However when interviewed with a CI, they are significantly less accurate than their typical counterparts. Findings indicate that investigative professionals should be cautious in relying on the CI to interview witnesses with ASD.

136.025 25 The Perception and Pose of Emotional Expressions in Adolescents with Autism. E. Back*[1], H. Hunt[1] and A. Lindell[2], (1)*Kingston University London*, (2)*La Trobe University*

Background: Research suggests that individuals with autism struggle to recognise and understand the emotional expressions of others, potentially leading to communication difficulties in everyday social interactions. Typically developing adults usually perceive stronger emotion in the left hemiface (predominantly controlled by the emotional right hemisphere) when observing photographs of models. Similarly, when presenting their own poses, they tend to offer the left hemiface to convey heightened emotional states (Nicholls, Wolfgang, Clode and Lindell, 2002).

Objectives: This study investigates how individuals with autism view emotional expressions in the hemifaces of others and how they portray their own emotional expression in lateral poses. It was predicted that typically developing individuals will select the left hemiface as being more expressive when observing pictures of models, whereas participants with autism may show a reduced, or reversed, asymmetry in their hemiface selections. Moreover, typically developing participants will portray their own emotional expressions using their left cheek whereas individuals with autism may show a sporadic selection of either left or right poses.

Methods: Seventeen adolescents with ASD aged between 12 and 15 years were individually matched on chronological age and Full Scale IQ to 17 adolescents without ASD. The first task assessed the perception of emotional expressions by showing participants a series of slides, each depicting a right and left cheek pose of six different models (Nicholls et al., 2002). The left and right pose of each model appeared side by side (counterbalanced) and was labelled A or B on a PowerPoint slide. The experimenter asked participants after each trial, "Which picture do you think is more expressive, A or B?" The second task involved asking participants to consider an imaginary setting such as, "you have just passed all of your school exams with straight A grades. Think about how you feel and pose for the picture."

Results: Repeated measures logistic regression was used to see whether participants' cheek preferences could be predicted on the basis of participants' autism group status. Age and IQ were also considered as independent variables. Findings suggested that participants with autism use the left hemiface to judge emotional expressions, in line with typically developing populations. However when presenting their own poses, participants with autism fail to perform in line with their peers without autism, and do not show a left hemiface preference.

Conclusions: Participants with autism used their right hemisphere as productively as typically developing participants when observing and processing the emotional responses of others. These findings provide support for the hemisphere hypothesis (Burt & Perrett, 1997), which suggests that the right hemisphere is central for the creation and examination of emotional expression. Although this study provides evidence for individuals with autism perceiving emotional expressions in a similar way to those without autism, results indicate that they offer their left hemiface less frequently than typically developing peers. This suggests they are less able to display their own facial expressions of emotion in a typical fashion and this could lead to difficulties in effectively communicating in social interactions.

136.026 26 The Role of Secondary Executive Function Demands in the Manifestation of Inhibitory Difficulties in Individuals with Autism. A. Moffitt*, K. E. Bodner, L. Brubaker, J. H. Miles and S. E. Christ, *University of Missouri*

Background: Executive function is postulated as one of the core areas of impairment in individuals with an autism spectrum disorder (ASD). Past laboratory-based research, however, has provided only limited support for this hypothesis. Indeed, when measured in isolation, aspects of executive function such as working memory and inhibitory control have often been found to be intact in ASD cohorts. It remains unclear, however, to what extent impairments may be more readily observed when concurrent demands are placed on multiple components of executive function.

Objectives: To evaluate whether ASD-related impairments in inhibitory control are exaggerated (and thus easier to detect) in the presence of additional demands on other aspects of executive function (i.e., working memory).

Methods: An eye movement task was used to assess inhibitory performance in 28 individuals with ASD (Mean age = 14.0 years) and an age-matched comparison group of 41 typically developing individuals (Mean age = 13.8 years). The eye movement task comprised two experimental conditions: In the prosaccade (baseline) condition, participants were asked to make an eye movement towards a peripheral luminance change (i.e., a brightened box) – a fairly reflexive response. In the antisaccade (inhibitory) condition, the same stimulus was again shown, but participants were asked to inhibit the reflexive saccade and instead generate a voluntary saccade in the opposite direction. To evaluate the impact of secondary load on inhibitory performance, each participant completed the aforementioned eye movement tasks in the presence of low and high secondary working memory demands.

Results: A mixed model ANOVA approach was used with group (ASD & control) serving as a between-subjects variable and inhibitory condition (baseline and inhibitory) and memory load (low and high) serving as within-subjects variables. Significant main effects of saccade condition and memory load were evident. As anticipated, participants generally responded slower in the inhibitory eye movement condition as compared to the baseline condition, $F(1, 67) = 118.38$, $p < .05$. The presence of high secondary working memory demands also resulted in slowed overall performance as compared to the low memory load condition, $F(1, 67) = 8.96$, $p < .05$. Most importantly, the 3-way interaction between inhibitory condition, memory load, and group approached significance, $F(1, 67) = 3.95$, $p = 0.05$. Increasing concurrent working memory load had little or no effect on inhibitory performance for the non-ASD comparison group, $t(40) = 0.65$, $p = .52$. In contrast, we found that an increase in working memory demands resulted in poorer inhibitory performance (an 8.90% increase in response time) for the ASD group, $t(27) = 1.94$, $p < .05$.

Conclusions: The current findings suggest that ASD-related impairments in cognitive abilities may be most apparent in situations requiring the coordination of multiple aspects of executive function.

136.027 27 To What Extent is Poor Theory of Mind Task Performance in Autism Due to Diminished Theory of Mind Competence? The Importance of Control Tasks. S. E. Lind* and D. M. Bowler, *City University, London*

Background: It is often assumed that theory of mind (ToM) task failure amongst children with autism spectrum disorder (ASD) is the consequence of reduced ToM *competence*. However, the majority of ToM tasks depend upon multiple cognitive functions for successful *performance*. Thus, failure on ToM tasks can potentially stem from deficits in cognitive functions other than ToM.

Understanding of the perception-knowledge relationship is one key component of ToM, thought to be diminished in ASD. However, previous studies have failed to unambiguously demonstrate such a diminution. For example, Baron-Cohen and Goodhart (1994) implemented a "see-know" task in which participants observed one doll *lifting* a closed box and another doll opening the box and *looking inside.* Participants were subsequently asked, *"Who knows what's in the box?"* (a correct answer being that only the doll who has had the relevant visual access will know what is inside). Children with ASD gave fewer correct responses than comparison children. However, a correct response requires not only an appreciation of the perception-knowledge relationship (i.e., ToM) but also the ability to (a) recall an action (e.g., Doll A opened the box and looked inside), (b) make an inference based on that action (e.g., Doll A must, therefore, know what is inside the box), whilst (c) reasoning about unobservable variables. Thus, children may fail this task for a number of reasons.

Objectives: The current study aimed to establish whether children with ASD have

difficulties with see-know tasks because of diminished ToM competence or difficulties with extraneous task factors. We adopted Baron-Cohen and Goodhart's (1994) see-know procedure and designed a control task with cognitive demands that closely mirrored those of the see-know task except with respect to the key variable of interest – i.e. ToM.

Methods: Participants were 40 children with ASD and 40 comparison children who were individually matched on chronological age (*M* ≈ 10.5 years) and verbal mental age (*M* ≈ 6.7). Each participant completed five test questions (e.g., "*John lifts up the box and Fiona opens the box and has a look. Who knows what's in the box?*") and six control questions (e.g., "*John and Fiona go to the beach. John lies down in the sun while Fiona goes swimming. Who gets hot?*").

Results: Participants with ASD performed significantly less well on the control questions than comparison participants, __ (1, *N* = 80) = 5.54, *p* = .04, _ = .26. After excluding children who failed the control task (ASD *n* = 11; comparison *n* = 3), it was found that children with ASD also performed significantly less well on the see-know test questions, Fisher's exact probability test, *p* = .02, _ = .31.

Conclusions: Although ToM competence is diminished in ASD, this is not the only reason individuals with ASD fail ToM tasks. Hence, previous research, which has not included adequate control tasks, may have overestimated the extent to which ToM competence is diminished in ASD. We recommend that future research on ToM includes carefully designed control tasks to rule out non-ToM sources of task difficulty.

136.029 29 Emotion Understanding in Children with Autistic Spectrum Disorders From a Longitudinal Perspective. S. Wiesendanger*[1], E. Thommen[2], B. Cartier-Nelles[3], A. Guidoux[3] and F. Pons[4], (1)*University of Applied Sciences Western Switzerland of Lausanne (EESP)*, (2)*University of Fribourg and University of Applied Sciences Western Switzerland of Lausanne (EESP), Switzerland*, (3)*University of Applied Sciences Western Switzerland of Lausanne*, (4)*University of Oslo*

Background: Emotion understanding has been extensively investigated during the last thirty years. It has been often demonstrated that children with autism encounter difficulties in expressing and understanding emotions (Baron-Cohen, 1993; Celani et al., 1999; Thommen et al., 2004). However, few studies have tried to examine the development of such understanding in autistic children,particularly longitudinally. Although some educational programs have been developed to improve these abilities (Howlin et al. 1999, Hadwin et al., 1996; Golan at al. 2008; Peng et al., 1992; Bennett et al., 1994; Pons et al., 2003), their evaluation is still in debate.
Objectives: The aim of our research was to follow longitudinally the evolution of emotional comprehension in children with autism. We are looking for an instrument sensitive enough to detect an evolution over time in their comprehension. The role of verbal and nonverbal factors in this development will be explored as well as their impact on individual trajectories.
Methods: An evaluation was carried on in two sessions separated by one year. Twenty eight children with autism (5- to 15-years old, M =10;6) participated in the study, all evaluated with the Wechsler Nonverbal Scale, the E.CO.S.SE (French equivalent of TROG) and diagnosed with the DSMIV. The assessment of emotional comprehension was based on the French version of the TEC (Test of Emotion Comprehension, Pons & Harris, 2005).

Results: The first test revealed that children with autism were able to recognize some of the basic emotions from pictures of people's faces. The TEC is highly correlated with the language test as evaluated by the E.CO.S.SE (r=.87) and less correlated with WNV (r= .51). The second test session is ongoing and will be discussed at the congress.

Conclusions: Implications from this research are multiple. First, the data on the evolution of emotional understanding in children with autism spectrum disorder is important for research and practice. Second, we will be able to give information on the sensitivity of the TEC to assess evolution in children's understanding of emotion. Third, our data

shows a greater correlation with verbal than non verbal abilities. We will examine if these factors predict evolution of emotion comprehension.

136.030 30 Executive Functions in Asperger's Disorder: An Empirical Investigation of Verbal and Nonverbal Skills. A. McCrimmon*[1], V. Schwean[1], D. Saklofske[1], J. Montgomery[2], D. Brady[1], K. Thorne[1] and Y. Hindes[1], (1)*University of Calgary*, (2)*University of Manitoba*

Background: Researchers have investigated the specific abilities of individuals with Asperger's Disorder (AD). One construct used in this effort is Executive Functioning (EF). While research has shown that this population performs more poorly than typically-developing matched controls on many EF tasks, there is a lack of consistency in these results (Calhoun, 2006; Hill, 2004). This is likely due to the use of inconsistent diagnostic criteria leading to incomparable studies (Klin, Pauls, Schultz & Volkmar, 2005). This study was designed to investigate if individuals with AD demonstrate a performance bias in favour of verbal Executive Functioning.

Objectives: To empirically determine if individuals with Asperger's Disorder demonstrate a performance bias in favour of verbal Executive Functioning.

Methods: The present study investigated EF in AD using a bottom-up method whereby several EF tasks were administered to 35 adolescents and young adults aged 16-21 with AD and 35 age- and gender-matched controls. VIQ and PIQ cutoffs of 85 as measured by the Wechsler Abbreviated Scale of Intelligence (WASI) were used to ensure cognitive abilities of all participants fell within the average or above average range. Two-step cluster analysis was used to derive subgroups of participants based upon performance on several subtests of the Delis-Kaplan Executive Functioning System (DKEFS). Diagnostic composition of these subgroups was examined to provide empirical evidence of a performance bias towards verbal EF functioning for the AD group.

Results: The participants did not differ in terms of VIQ, PIQ, or FSIQ. The two-step cluster analysis indicated that the data was best described by a two cluster solution. The first cluster was primarily comprised by individuals with AD (23 individuals with AsD, 8 controls) while the second primarily contained typically developing controls (9 individuals with AD, 24 controls). Performance on the EF measures between these groups was investigated by T-tests. Cluster 2's performance was significantly higher than cluster 1 on Trail Making 4, Verbal Fluency 3, Design Fluency 3, Color Word Identification 3, Word Context, and Tower. Performance did not differ on the Proverb subtest.

Conclusions: The performance of individuals with AD and typically developing controls on seven specific measures from the DKEFS was empirically examined. A cluster of participants consisting primarily of individuals with AD and a cluster consisting primarily of typically-developing control participants were derived on the basis of this performance. Although the performance of the individuals in cluster 2 was significantly above that of cluster 1 on six of the seven subtest components, the hypothesized verbal EF performance bias was not found. Rather, the clusters were differentiated on the basis of better performance on both verbal and visual subtests except for the Proverb subtest where performance did not differ between the groups. These results lend continued support for an overall deficit in EF abilities in individuals with AD.

136.031 31 From Test Scores to ASD Diagnosis: A Bayesian Approach. S. V. Huemer*, *University of California, Irvine*

Background: Our starting point was a database of test results from 487 children and adolescents containing scores from nine standardized measures of reading ability and comprehension. All subjects had either a diagnosis of autism, Asperger's, PDD-NOS, or dyslexia. Prior research indicates that children with ASD show deficits in comprehension greater than can be expected for their reading ability while children with dyslexia show deficits in reading ability greater than can be expected for their level of comprehension.

Objectives: Our goal was to find out whether the test results, independent from the actual diagnosis, could predict one of the four

diagnoses, how accurate these predictions would be and how well the model could distinguish between groups.

Methods: We used Matlab software to create two models. For the naïve Bayesian classifier model we trained the machine on 90% of the data (standard test scores and diagnosis) to predict the remaining 10%. Using a 10-fold cross-validation of the analysis, we compared the accuracy of our predictions to the truth values for all four groups combined as well as between ASD groups. For the multinomial logistic regression model, we transformed the standard test scores into z-scores and used 10 training sets each of which contained 75% of the data to predict a diagnosis for the remaining 25%. We then created a confusion matrix to force the model to decide on a diagnosis, normalized the data, and averaged over all the means.

Results: The naïve Bayesian classifier showed 48% accuracy for a prediction of diagnosis when data from all four groups were combined, 82% accuracy for a binary prediction of autism or dyslexia, 56% accuracy for a binary prediction of autism or Asperger's, and 56% accuracy for a binary prediction of autism and PDD-NOS (collapsed) or Asperger's. The multinomial logistic regression model showed an average performance hovering around 45% of correct predictions for all four diagnostic groups.

Conclusions: The naïve Bayesian classifier fared well above chance for predictions of a diagnosis from reading and comprehension scores when data from all four diagnostic groups were combined and when data from the two "extreme" groups on the reading vs. comprehension spectrum, autism and dyslexia, were compared. The model, however, hovered around chance when it came to a prediction among the ASD subgroups. The more refined multinomial logistic regression model performed well above chance to predict an accurate diagnosis of either autism, Asperger's, PDD-NOS, or dyslexia with a more even spread of predictive power between all four groups. Our results indicate that trends in academic performance, in our case reading and comprehension, are measurable and predictive of an ASD diagnosis. Future studies with similar models predicting a diagnosis based on test performance could be especially valuable when examining core ASD deficits, i.e. social cognition, communication, and language skills. Ultimately, results from these models could aid in the establishment of a clear definition of the phenotype and a systematic examination of a distinction between ASD subgroups.

136.032 32 Intact and Impaired Conceptual Reasoning Abilities in High Functioning Autism. R. X. Glosser*[1], D. L. Williams[2], C. A. Mazefsky[1], N. J. Minshew[3] and G. Goldstein[4], (1)*University of Pittsburgh-Center for Excellence in Autism Research*, (2)*Duquesne University*, (3)*University of Pittsburgh School of Medicine*, (4)*VA Pittsburgh Healthcare System*

Background:

We previously proposed a dissociation between intact concept identification and impaired concept formation in conceptual reasoning abilities in individuals with high functioning autism (HFA). Thus, they were found to do relatively well on sorting tests when the task was that of identifying a predetermined concept, but poorly on tasks such as the 20 Questions Test that required self-initiated concepts or full understanding of concepts as demonstrated by flexible use in changing circumstances. The present research extends this work to the area of verbal analogical reasoning in which the task is to identify analogical relationships among word pairs, such as part-whole or causal relationships (e.g., "handle is to cup as branch is to…tree, picture, house or desk" or "fire is to heat as poverty is to…hunger, beauty, color, or joy). The analogies test is a concept identification procedure because there are predetermined correct answers for the series of multiple-choice items.

Objectives:

The purpose of the current study was to determine if individuals with HFA would do as well as normal controls at verbal analogical reasoning but more poorly than controls on the concept formation tasks.

Methods:

30 individuals with HFA and 16 demographically and IQ comparable typically-developing individuals were administered a written analogies test evaluating analogies that had synonymous, opposite, functional, characteristic property, causality, sequential, and part-whole relationships. They also received the Wisconsin Card Sorting Test (WCST) and the 20 Questions task which required self-initiating of concepts in an effort to identify a target object. *t*-test comparisons were made to evaluate group differences. We hypothesized that individuals with HFA would do as well as controls on the analogies test but significantly more poorly on the WCST and 20 Questions tests.

Results:

There were no significant ($p<0.5$) differences between the autism and control groups for any of the analogies categories. There were significant differences for constraint-seeking and hypothesis testing questions from the 20 Questions Test and for the perseverative errors score from the WCST. Constraint-seeking questions are those that narrow the range of possible correct identifications (e.g., "Is it an animal?" or "Is it a vegetable?"), while hypothesis testing is essentially random guessing (e.g., "Is it a glove?").

Conclusions: The findings provide further support for the concept of a dissociation between intact concept identification and impaired concept formation abilities in individuals with HFA. This distinction appears to hold even in the case of abstract cognitive processes involved in analogical reasoning.

136.033 33 Memory for Detail in High-Functioning Children and Adults with Autism. J. M. Griebling*[1], C. A. Mazefsky[1], D. L. Williams[2] and N. J. Minshew[1], (1)*University of Pittsburgh School of Medicine*, (2)*Duquesne University*

Background: Individuals with autism demonstrate an enhanced ability to focus on and recall details of their surroundings compared to typical individuals. Several theories attempt to explain this preferential awareness of details in autism (e.g., enhanced local processing), but it is still poorly understood. Previous memory studies have established that individuals with autism are not initially learning more information compared to matched controls (Williams, Goldstein, & Minshew, 2005, 2006). Therefore, a potential explanation for the increased ability of individuals with autism to recall details could be that they have an enhanced long-term retention of details.

Objectives: To compare the long-term retention of story details between children and adults with high-functioning autism and typically developing controls.

Methods: Participants included 81 high functioning children with autism (mean age = 11.84, mean VIQ = 103.10, mean FSIQ = 104.68) compared to 32 typically-developing controls, and 48 high-functioning adults with autism (mean age = 26.33, mean VIQ = 105.42, mean FSIQ = 106.38) compared to 67 typically-developing controls. All controls were matched on age, verbal IQ, and full scale IQ. Independent samples t-tests were used to compare memory performance scores on the WRAML for children, and the WMS-III subtests Logical Memory I (immediate recall) and Logical Memory II (delayed recall) for adults. Both test administrations for children and adults included immediate recall of a story followed by a 30 minute delay, as well as a 48 hour delayed recall. Analyses utilized scores based on the total retention of details in the 48 hour delayed recall compared to their 30 minute delay and immediate recall scores. Lower scores indicate greater memory retention.

Results: Analyses of the children's performance on the WRAML indicate that the autism group retained significantly more details compared to both their 30 minute delay (autism = 0.74, control = 0.96, $p<0.01$) and immediate recall scores (autism = 0.62, control = 0.86, $p<0.001$). On the WMS-III, the adults with autism also retained more details than controls. This difference reached statistical significance when 48 hour delay scores were compared to their immediate recall scores (autism = 0.72, control = 0.86, $p<0.01$), but not compared to their 30 minute delay scores (autism = 0.92, control = 1.00, $p>0.05$).

Conclusions: The results indicate that individuals with autism demonstrate greater

long-term retention of memory for details of stories compared to typically-developing individuals. The result of no difference between the two adult groups when their 48 hour delayed recall scores were compared to their 30 minute delayed recall scores can be explained by a ceiling effect in the overall amount of memory retention by the 30 minute delay. In other words, there was a significantly greater amount of retention in the autism adult group compared to the control group in 48 hour delay versus immediate recall but no difference in the 48 hour versus the 30 minute delay; therefore, the 30 minute delayed recall indicates the point at which there was no additional significant memory loss for both groups.

136.034 34 No Difficulties in Extracting Subtle Emotional Cues From Social Contexts in Children with An Autism Spectrum Disorder. K. Evers*[1], J. Steyaert[2], I. L. J. Noens[1] and J. Wagemans[1], (1)*Katholieke Universiteit Leuven*, (2)*UPC-K.U.Leuven*

Background: Children with an autism spectrum disorder (ASD) are known to have difficulties in interpreting social interactions. They are generally found to have problems with processing facial emotional expressions, certainly when dynamic or more complex and naturalistic emotions are used. Since eye-tracking studies revealed atypical viewing behavior in ASD, good performances in some emotion processing tasks could be due to compensatory, more emotionally neutral mechanisms in individuals with ASD.

Objectives: We wanted to investigate the ability of children with ASD in extracting subtle emotional cues from a context and reading these expressions from dynamic facial expressions or word labels.

Methods: Two groups of 24 boys, individually matched for age (M = 11.79 y, range between 9.38 y and 14.04 y) and full scale IQ (M = 107.96, range between 83.25 and 132.25) were tested. Both groups were matched on group level for verbal IQ en performal IQ. One group had received a clinical diagnosis of ASD based on a multidisciplinary assessment and met DSM-IV-TR PDD criteria. Children with attention deficits or using medication were excluded. The typically developing group was representative for the general population. Each trial consisted of an auditory and visually presented social context ('story'), eliciting either a subtle or an intense expression of anger or happiness. This story was followed by a test screen, consisting of either two dynamic facial expressions or two word labels (stimulus type). The answer possibilities always consisted of a match and a mismatch item. The mismatch item had either the correct intensity, but incorrect emotion (emotion-mismatch-trial) or the incorrect intensity, but correct emotion (intensity-mismatch-trial). Participants had to indicate how the protagonist in the story felt.

Results: No large group differences were found. The ASD group performed more slowly, but not worse than the typically developing group. Task difficulty largely depended on the specific task requirements. As expected, subtle emotions and intensity-mismatch-trials were more difficult than intense emotions and emotion-mismatch-trials. A trend for a three-way-interaction between mismatch, intensity and group was found. Further analysis pointed out that in the subtle trials mismatch only seemed to have an effect in the typically developing group and not in the ASD group. Happiness was responded to more accurately than anger but only in the more difficult subtle trials, not in the intense trials. Dynamic facial expressions were responded to less accurately than word labels. Older children performed better than younger children. A learning effect was observed in both groups. No correlation was found between the score on the 'Development, Diagnostic and Dimensional Interview (3DI) subscale 'social interaction' and performances on this task.

Conclusions: We did not find large difficulties in extracting subtle emotions from an auditory and visually presented social context. Task difficulty and group differences depended on the specific task requirements. Slower responses and slightly less influences of task difficulty on performance could indicate rule-based response strategy in the ASD group. In the ASD group, we did not find a correlation between the score on the 3DI subscale 'social interaction' and performances on this task.

136.035 35 Sensory Integration From Different Perspectives. M. Boman*[1], G. R. Mancil[2] and Z. Mailloux[3], (1)*Kelly Autism Program at Western Kentucky University*, (2)*University of Louisville*, (3)*Pediatic Therapy Network*

Background: The complexity of the central nervous system is illustrated by the cascade of challenges faced by individuals with ASD, a neurological disorder that involves primary brain structures and functions (Bauman, & Kemper2003; Courchesne, Carper, & Akshoomoff, N.,2003). Increasingly, the literature describes the way in which these brain differences include sensory integration and praxis dysfunction (Crane, Goddard, & Pring, 2009; Dawson & Lewy, 1989; Dawson & Watling, 2000; Smith & Bryson, 1994; Deitz. & White, 2001) Minshew & Hobsen, 2008; Rogers & Williams 2007) report significant incidences of sensory sensitivities and sensory perception deficits in a sample of individuals with autism, suggesting neurological abnormalities in higher cortical sensory perception. Ben-Sasson et.al. (2009) report that 14 different studies show sensory differences between individuals with an ASD and neurotypical individuals with greatests difference in under-responsivity, followed by over-responsivity and then sensation seeking. However, practitioners struggle to understand and address these needs.
Objectives: The ultimate goal is for individuals with ASD and the people who care for them to understand and manage sensory integration needs and challenges, for increased life satisfaction and participation. Although problems in sensory integration are relatively common, these issues are often difficult to detect, understand and cope with. Traditional behavioral approaches and positive reward systems may be successful for some aspects of changing responses, but if sensory and motor planning issues underlie behaviors, they will be likely to continue to be exhibited in some form. When sensory integration issues are treated using behavioral strategies only, the entire problem is not addressed which can result in partial success, and even greater problems emerging in the future, Sensory seeking, sensory avoiding and anxiety or withdrawal responses to motor planning challenges can occur across environments and situations and must be understood to be sppropriately addressed. For this reason, an understanding of sensory integration functions must be considered when working with individuals with ASD.

Methods: Three case studies from the various perspectives of different care givers were investigated. These include: Sensory Integration from an Occupational Therapist/Executive Director from Pediatric Therapy Network in CA; Kentucky Autism Training Center Director and father of two children with sensory processing challenges, and the Director of the Kelly Autism Program at Western Kentucky University, servicing over 100 individuals with ASD.

Results: Sensory integration are viewed differently by the various service providers, but it is clear that educators must gain an understanding of sensory challenges that are exhibited by individuals with ASD. Currently, educators do not always understand these individuals and their sensory dysfunction. Many students are being restricted to time-out or even being suspended from school. Students as well as educators must be taught about these differences so that they can learn how to support then in the educational and community setting.

Conclusions: Through sensory modulation training, students with Sensory integration dysfunction can learn to regulate themselves. Educators should be trained to recognize these stressors so that they understand the support that they need to provide in order for these individuals to be successful. These case studies demonstrate the success that can be gained by providing sensory supports.

136.036 36 The Influence of Communicative Cues On Short-Term Memory in Children with ASD and TD. E. J. H. Jones*, K. M. Venema, R. T. Lowy and R. Bernier, *University of Washington*

Background:

Recent evidence suggests that for typically developing infants, communicative cues produce specific memory biases that may be central to their role in teaching interactions.

Specifically, the addition of communicative cues when an experimenter demonstrates the location of an item facilitates memory for the item and negatively impacts memory for the item's location in typically developing infants (Yoon et al., 2008). For children with Autism Spectrum Disorder (ASD), communicative cues can be difficult to interpret; however, little is known about their effect on memory.

Objectives:

To assess the effect of communicative cues on short-term memory for items and their locations in young children with ASD and Typical Development (TD).

Methods:

Data collection is ongoing; to date, 17 children with ASD (3 female, mean age = 7.0 years) and 16 TD controls (5 female; mean age = 6.2 years) have provided valid data. Children were diagnosed using the ADOS, ADI-R and expert clinical judgment; cognitive skills were evaluated with the Differential Abilities Scale-II. Memory was assessed using a board in which distinctive pegs could be placed in any of 25 locations. Key variables included: item memory – percentage of correctly chosen pegs; item-location memory – percentage of correctly chosen pegs placed in the correct location.

After ability to understand the instructions was assessed, children were administered the "Communicative" and "Non-Communicative" conditions in randomized order. In both conditions, children watched a female model sequentially place four pegs on the board, before covering them up. Children were then given an array of target and distracter pegs, and asked to reproduce the pattern of pegs on their own board. In the Communicative condition, the female model used child-directed speech, alternated her gaze between the child and the blocks, and pointed to the target items after they were placed on the board. In the Non-Communicative condition, a second female model used adult-directed speech, alternated her gaze between the blocks and a point off-camera, and did not point to the target items.

Results:

Preliminary Repeated Measures ANOVAs (alpha = 0.05) indicated that for the TD group, item memory did not significantly differ between conditions; item-location memory was significantly worse in the Communicative than the Non-Communicative condition. For the ASD group, both item and item-location memory were significantly worse in the Communicative than the Non-Communicative condition. Finally, the only significant group difference was poorer item memory in the Communicative condition for the ASD versus the TD group.

Conclusions:

As predicted, memory for the location of an item (but not the item itself) was negatively impacted by communicative cues during encoding for typically developing children. Thus, communication-induced memory biases may operate through early childhood. However, for children with ASD both item memory and item-location memory were negatively impacted by communicative cues. Possibly, increased difficulty in interpreting communicative cues has a global impact on encoding for children with ASD. The generality of these effects is a critical topic for further investigation, since there may be important implications for the use of communicative cues in teaching interactions with children with ASD.

136.037 37 The Mid-Band Spatial Frequency Bias in Face Recognition: A Cross-Syndrome Developmental Study of Autism and Williams Syndrome. H. C. Leonard*[1], D. Annaz[2], A. Karmiloff-Smith[1] and M. H. Johnson[1], (1)*Birkbeck, University of London*, (2)*Middlesex University*

Background: Previous research has suggested that autism may be characterised by a local bias in visuo-spatial tasks, including face processing. One possible cause of this could be a low-level bias towards high spatial frequencies. As typically-developing adults tend to rely on middle spatial frequencies for face recognition, a persistent bias towards high spatial frequencies in autism could result in reduced accuracy when recognising faces, or may represent a different strategy for achieving the same outcome. The current paradigm was adapted

to use across development and involved masking different spatial frequencies in face images. Lower accuracy when a particular spatial frequency band was masked would imply that this band was used during face recognition. Objectives: The current study compared the development of spatial frequency biases in face recognition in autism, Williams syndrome and typically-developing controls. The objective of this comparison was to determine if a mid-band bias was present in the two atypical groups and whether it emerged through the same developmental processes as in the typical population. Methods: Sixty-eight children (age range = 7 years - 15 years) were grouped as being typically-developing controls (TD; N = 36), or as having high-functioning autism (HFA; N = 18) or Williams syndrome (WS; N = 14). Children learned to recognise two faces and then determined which face had been masked during presentation in a 2AFC task. Masks covered the face images at either 8, 16 or 32 cycles per image (LSF, MSF and HSF respectively). Results: The use of each spatial frequency was plotted over developmental time for the three groups. In the TD group, age significantly predicted the use of HSFs (Adjusted R_ = 0.28, $p < 0.001$), with 7-year-olds relying on HSF information significantly more than 15-year-olds. The use of LSFs and MSFs were not predicted by age, and an adult-like bias towards the mid-band was evident by the age of 15. Interestingly, the HFA group followed an almost identical pattern, with HSFs being used more by 7-year-olds than 15-year-olds. The WS group, however, demonstrated a greater use of LSFs at 7 years and no change in the use of HSFs with age. Both disorder groups displayed the adult-like mid-band bias found in typical development by the end of the age range studied. Conclusions: The present study has demonstrated that children with autism can be as accurate at recognising faces as typically-developing controls, and that this outcome is achieved through similar developmental changes in spatial frequency biases. Children with Williams syndrome, however, achieve the adult-like mid-band bias through a very different developmental process. These data confirm the importance of comparing syndromes across a wide age range, as a focus on adults in the current study would have found no differences between the three groups. In conclusion, any featural bias found during face recognition in high-functioning autism is not due to a persistent bias towards high spatial frequencies. Future studies should address this issue in low-functioning autism in order to compare performance with the current data.

136.038 38 The Predictability of Eye Movements in ASD. M. Freeth*[1], T. Foulsham[2] and P. Chapman[3], (1)*University of Sheffield*, (2)*University of British Columbia*, (3)*University of Nottingham*

Background:

Individuals with Autism Spectrum Disorders attend to the natural world in a different manner to typically developing individuals. There is evidence that they displaying diminished interest in social stimuli (Jones & Klin, 2008; Klin et al. 2002) especially in the first few fixations when viewing complex scenes (Freeth et al., in press). Could the impact of visual saliency (low-level properties such as colour, intensity and orientation) account for any of these differences? Actions are often performed in a routinised, repetitive way by individuals with ASD. Is this style evident in their patterns of eye movements when natural scenes are viewed?

Objectives:

1. To discover whether individuals with ASD are influenced by visual saliency in a similar or different manner to matched controls when viewing naturalistic scenes.

2. To discover whether eye movement scanpaths are predictable over time and whether individuals with ASD are drawn to similar or disparate aspects of natural scenes.

Methods:

A series of natural scenes were presented in a free viewing task at Time 1 and Time 2 (approximately 6months apart) by 13 high functioning adolescents with ASD and 13 typically developing adolescents, matched on age and ability. The influence of visual

saliency was investigated using the Saliency Toolbox (Walther & Koch, 2006). Scanpath similarity was analysed using Mannan similarity scores and string edit similarity.

Results:

Preliminary findings suggest that visual saliency is more predictive of fixation location early in viewing than later in viewing in individuals with ASD, a finding that has previously been demonstrated in typically developing individuals, and replicated in this study. Visual saliency appears to influence eye movements to a similar extent in high-functioning adolescents with ASD and their typically developing peers. This was found when comparing fixations on the five most salient regions and the mean saliency at fixation. Scanpath analyses suggest that image properties predict fixation sequences in both typically developing individuals and those with ASD when comparing scanpaths at Time 1 and Time 2. However, within group similarity was found to be lower for individuals with ASD suggesting that individuals in the ASD group were more different from each other than individuals in the typically developing group.

Conclusions:

Initial results suggest that visual saliency does not influence the attention of individuals with ASD in a markedly abnormal manner. It is therefore unlikely that attention is being strongly captured by low-level properties of stimuli.

Viewing the same image twice resulted in similarly predictable scanpaths in the typically developing group and the ASD group demonstrating that it may be possible to characterise an individual's attention profile over time but that eye movements are not abnormally predictable in ASD. Comparison of scanpaths between individuals in the ASD group demonstrated greater within group heterogeneity than between individuals in the typically developing group. This finding highlights the importance of looking into individual differences in attention in ASD and suggests that individuals with ASD, as a group, may be more disparate than typically developing individuals.

136.039 39 The Relationship Between Executive Function and Social Competence Intervention (SCI) Outcomes Among Adolescents with An Autism Spectrum Disorder. S. E. Christ*[1], J. Stichter[2], K. Visovsky[1], A. Moffitt[1] and M. Herzog[1], (1)*University of Missouri*, (2)*Deartment of Special Education*

Background: Social skill deficits, including difficulties with social relationships and interactions, manifest in individuals with Autism Spectrum Disorders (ASD) as key signifiers of the disorder, with varying degrees of severity across the spectrum. From a theoretical standpoint, researchers have hypothesized that deficits in executive function may contribute to such social difficulties. Further, previous research suggests that cognitive behavioral interventions (CBI) are effective for addressing social competence deficiencies that impact day-to-day functioning for these individuals. The nature of the relationship between CBI-related improvements in everyday functioning and possible changes in executive ability however, remains unclear.

Objectives: To evaluate the possible relationship between intervention-related improvements in social competence and changes in underlying cognitive processes (e.g., executive function).

Methods: Fifteen children with High Functioning Autism or Asperger's Syndrome (mean age = 12.3 yrs; range = 11 to 14 yrs) participated in the Social Competence Intervention (SCI), a 10-week CBI-based intervention that was recently developed by one of the co-authors to improve social skills competence in individuals with ASD. It targets executive functioning, theory of mind and emotion recognition as key constructs in addressing social competence deficits. Two components of executive function (i.e., working memory and inhibitory control) were assessed at two time points: once prior to participating in SCI (Week 0), and then again shortly after completion of the intervention (Week 12). Digit and spatial memory span tasks were used to assess verbal and non-verbal working memory, respectively. Inhibitory control was assessed using a visual filtering task (Eriksen & Eriksen, 1974), which

required participants to respond to a centrally-presented visual stimulus while ignoring other distracting stimuli on the display.

Results: As anticipated, participation in the intervention was associated with a significant decrease in autistic symptomatology and other problematic social behaviors/issues (as measured by parents' reports on the Social Responsiveness Scale), $p < .001$. In addition, pre- to post-intervention improvements were also observed on several components of the working memory and inhibitory control tests. There was an overall improvement in forward span performance across both the verbal and non-verbal working memory tasks, $F(1,15) = 4.62$, $p < .05$. However, the intervention had no apparent effect on backward span performance, $F(1,15) < 1$, $p = .45$. On the inhibitory task, participants were more effective at resisting distracter interference post-intervention as compared to pre-intervention, $t(14) = 3.13$, $p < .05$.

Conclusions: The present findings provide preliminary support for the hypothesis that participation in the SCI program is accompanied by improvements in underlying neurocognitive processes such as executive control. Additional research with a larger sample size and inclusion of a non-intervention comparison group is still needed.

136.040 40 Unsystematic and Non-Optimal Large-Scale Search in Autism Spectrum Disorder. E. Pellicano*[1], A. D. Smith[2], F. Cristino[3], J. Briscoe[3], B. Hood[3] and I. D. Gilchrist[3], (1)*Institute of Education*, (2)*University of Nottingham*, (3)*University of Bristol*

Background: Recent theoretical accounts of autism have suggested that individuals with autism spectrum disorder (ASD) demonstrate a bias towards systematic and rigid analytic thought and behaviour. This behaviour manifests itself in everyday situations, with children with ASD taking the same route to school or carrying out tasks in an inflexible manner, and is purportedly driven by the need to construct or analyze the rules that govern systems. Here we investigate the microstructure of search and navigation behaviour in children with ASD in an effort to test whether their search behaviour reflects this apparent bias towards "systemizing".

Objectives: The aims of this study were threefold: (1) to assess whether children with ASD show superior large-scale search compared to typical children, as evidenced in small-scale contexts, (2) to identify differences in search strategies between clinical and comparison groups, especially with regard to the systematic or otherwise nature of search, and (3) to determine the relative consistency in search behaviour within individual children.

Methods: Twenty-one children with ASD aged between 8 and 13 years, and 21 typically developing children, of similar age, nonverbal ability, verbal ability, participated in an engaging, ecologically-valid large-scale search task. Children searched within a unique laboratory, an isolated space without landmarks, in which an array of search locations (LED lights) was embedded into the floor. On each trial, children were instructed to look for a (red) target by pressing the (green) switch at each location. Children completed a total of 40 trials. The distribution of target locations across trials was probabilistically manipulated so that they appeared on one particular side of the array for 80% of trials.

Results: Comparative analysis of the microstructure of the search behaviour of the two groups revealed striking differences in three respects. First, children with ASD were *less* sensitive to the spatial probability manipulation compared with typical children. Second, the search patterns that children with ASD followed were further from the optimal route than comparison children. And third, there was less internal consistency in the search patterns for individual children with ASD, further suggesting that they were searching in a *less systematic* fashion.

Conclusions: Previous studies have suggested that children with ASD show enhanced small-scale visual search and "systemising" behaviour. Contrary to these reports and to anecdotal evidence, we discovered that search and foraging behaviour in ASD is in fact disorganized and non-optimal. These findings have important

implications for current theoretical accounts and for our understanding of autistic individuals' everyday functional behaviour.

136.041 41 "Thinking in Speech" Amongst Individuals with Autism Spectrum Disorder (ASD): The Relations Between Inner Speech and Short-Term Memory, Executive Functioning, and Clinical Features. D. M. Williams*[1], C. Jarrold[2] and D. M. Bowler[3], (1)*City University*, (2)*University of Bristol*, (3)*City University, London*

Background:

"Inner speech" is critical for flexible thinking and behaviour (Zelazo, 2004). Yet, individuals with ASD sometimes report that their thoughts consist predominantly of visual images, rather than speech (Hurlburt, Happé, & Frith, 1996), which may contribute to their limitations in cognitive and behavioural flexibility (Russell, Jarrold, & Hood, 1999). However, recent experimental studies of inner speech in ASD have produced mixed results, with some studies observing appropriate use (e.g., Williams, Happé, & Jarrold, 2008; Winsler et al., 2007) and others observing reduced use (e.g., Holland & Low, 2009; Wallace et al., 2009).

Objectives:

The present study combined techniques and tasks used *across* several of the above studies. This allows us to clarify whether the discrepant results have been due to: a) the different techniques employed to measure inner speech use ("similarity effects" versus "articulatory-suppression"; see below), and/or; b) the different domains of cognition explored in each of the studies (e.g., memory versus executive functioning). Also, the study is the first to explore the association between inner speech use and severity of ASD features.

Methods:

Twenty high-functioning adults with ASD and 20 age- and ability-matched comparison participants (recruited as part of an on-going study in our laboratory) will complete two experimental tasks. Data collection is ongoing. Six participants with ASD and 4 (well-matched) comparison participants have been tested.

1) Inner speech in short-term memory: A serial recall task (similar to that used by Williams et al., 2008) was employed. In one set of trials, pictorial items had similar sounding names (phonological trials) and in another set they did not (control trials). If participants encode items using inner speech, rather than visual imagery, recall of phonological trials will be significantly poorer than recall of control trials [a "phonological similarity effect" (PSE)].

Participants completed each set of trials twice, once under baseline conditions and once under concurrent articulatory-suppression (repeating the word "Tuesday" throughout the presentation of stimuli). Articulatory-suppression selectively disrupts inner speech. If participants employ inner speech to mediate the experimental task, articulatory-suppression should reduce recall of control trials only (relative to baseline presentation), resulting in the disappearance of the PSE.

2) Inner speech in planning: Participants will complete the Tower of London task with and without articulatory-suppression. If participants employ inner speech to mediate their planning, performance will be significantly poorer under conditions of articulatory-suppression than under baseline conditions.

Results:

On the serial recall task, both groups show a large PSE under baseline conditions (Cohen's d = 2.31 amongst ASD participants; 2.10 amongst comparison participants), but not under articulatory-suppression (d = 0.13 amongst ASD participants; 0.18 amongst comparison participants). Amongst ASD participants, size of the PSE was strongly (negatively) associated with severity of ASD features, as measured by the Autism-spectrum Quotient (r_s = -.70). Tower of London data is yet to be collected.

Conclusions:

We will discuss the implications of the research results for a) our theoretical understanding of whether (or in what circumstances) people with ASD employ inner

speech, and b) intervention strategies designed to remediate behavioural and cognitive inflexibility.

136 Epidemiology

136.069 69 Autism Spectrum Disorders Among 4, 8, and 15 Year Olds in 2006-2007. L. King*, L. A. Carpenter, J. Charles, W. Jenner and J. Nicholas, *Medical University of South Carolina*

Background: Recent data from the Centers for Disease Control and Prevention indicate that approximately 1 in 150 8-year-old children are affected with an Autism Spectrum Disorder (ASD). However, little information is known about ASD among preschool and teenage children.

Objectives: The purpose of this study was to compare the prevalence and case characteristics among three age groups of children with Autism Spectrum Disorders (ASD) residing in a single geographic area at a single point in time.

Methods: Information was collected on 4-year old children (born in 2002), 8-year old children (born in 1998), and 15-year old children (born in 1992) residing in three South Carolina counties during 2006/2007 as part of an ongoing, population-based multiple source surveillance of Autism Spectrum Disorders in South Carolina. Data were analyzed to compare the prevalence of ASD across age groups and to evaluate case characteristics including educational placement, developmental concerns, and cognitive ability.

Results: The overall prevalence of ASD was 8.0 per 1000 among 4-year olds (1 in 125), 12.3 per 1000 among 8-year olds (1 in 81), and 7.7 per 1000 among 15-year olds (1 in 130). Approximately 20% of 4-year old children with ASD had an educational classification of Autism, compared to 47% of 8-year olds and 58% of 15-year olds. At age 4, 56% of children with ASD also had intellectually disability (ID), compared to 49% at age 8, and 42% at age 15. Approximately 99% of 4-year olds had documented developmental concerns before age 3, compared to 89% of 8-year olds and 85% of 15-year olds. 60% of the 4-year olds identified in our study had an existing formal diagnosis of ASD, compared to 73% of 8-year olds and 70% of 15-year olds. Median age of diagnosis was 2.8 years for the 4-year olds, 4.5 years for the 8-year olds, and 8.7 years for the 15-year olds. There was a delay between the median age of first evaluation to the median age of diagnosis ranging from 1 month for the 4-year olds, to 13 months for the 8-year olds, and 39 months for the 15-year olds.

Conclusions: Our results indicate that the prevalence of ASD was highest among 8-year olds compared to the 4-year olds and 15 year olds. We speculate that this may be due in part to increased awareness contributing to better documentation among the younger groups, and to changes in special education eligibility across the lifespan. The declining incidence of comorbid ID suggests that children with cognitive delays may be recognized sooner than those without such impairments. Younger children had a shorter delay between first evaluation and first formal diagnosis, suggesting possible improvements in recent years. However, younger children were also less likely to be served educationally under an Autism eligibility, suggesting possible delays in access to appropriate educational services despite early identification.

136.070 70 Epidemiological Study of Autism in Tianjin, China. C. Y. Wang*, *Nankai University*

Background: Recent studies have suggested a significantly higher prevalence rate for autism spectrum disorders (ASD). Kogan et al (2009) reported that about 110 per 10,000 children ages 3 to 17 in US have ASD, an increase over previous estimates. However, there is very few large scale epidemiological research about the prevalence and incidence of autism in China and there is no such a registry for autism to collect and store all the inpatient data from all public hospitals either. We collected and analyzed and reviewed all the hospital and school records of children diagnosed with autism in Tianjin, one of four provincial-level cities in China since early 1990s.

Objectives: This study aims to investigate the epidemiology of autism in children in Tianjin, China.

Methods: We collected all the inpatient data from all public hospitals and rehabilitation centers and schools in Tianjin and computerized them and conducted statistical analysis. Diagnoses were confirmed or ruled out following a multidisciplinary assessment including standard psychometric tests of IQ, Japanese S-M Social Living Ability Scale (SM), Child Behavior CheoKlist (CBCL), Sensory Integration Rating Scale, Children Temperament Scale (CTS), Toddler Temperament Scale (TTS), Gesell Development Schedules (GDS), Autism Behavior Checklist (ABC), Childhood Autism Rating Scale (CARS), International Classification of Diseases 10 Edition (ICD-10), Diagnostic and Statistic Manual of Mental Disorders (DSM-IV), Chinese Classification of Mental Disorders (CCMD-3), etc. The incidence and prevalence of autism have been calculated for the period of 1993 to 2008 using the population statistics available in the government for children less than 15 years old and less than 5 years old respectively in Tianjin City.

Results: 1769 children 0-14 years old with diagnoses of autism were identified from 1993 to 2008 in Tianjin City, including 1375 boys and 394 girls (the male to female ratio was 3.49: 1). 1316 children 0-4 years old were identified with autism from 1993 to 2008 in Tianjin City. The estimated incidence of autism was 5.3 per 10 000. The prevalence was 43.87 per 10 000 for children less than 15 years old for the same period.

Conclusions: The incidence rate is similar to those reported in Hong Kong, Australia and North America, but lower than Europeans. The prevalence is higher than that reported in Hong Kong, but still lower than those reported from year 2000 onward in North America and Europe. The results of this study supported the previous research on the ratio of male to female. Although it is possible that unidentified environment factors have contributed to an increase in autism, the timing of the increase suggests that it may be due to improved awareness, changes in diagnostic criteria, and availability of services, leading to identification of previously unrecognized young children with autism. It was also noticed that the diagnosed ages became younger in the past decades, so there is an urgent need for early diagnosis and intervention.

136.071 71 Finnish Prenatal Study of Autism and Autism Spectrum Disorders (FIPS-A): Design and Overview. K. M. Lampi*[1], P. N. Banerjee[2], M. Ikonen[1], S. Hinkka-Yli-Salomäki[1], H. Helenius[1], I. W. McKeague[3], A. S. Brown[2] and A. Sourander[1], (1)*University of Turku*, (2)*Columbia University/NYSPI*, (3)*Columbia University*

Background: Autism is a complex developmental syndrome of the central nervous system and is most likely the result of multiple etiologies with genetic and environmental contributions. Recently, the number of people with autism spectrum disorders (ASD) has been reported to rise. The rise in prevalence has been attributed, for example, to changes in diagnostic criteria, changes in surveillance or methodologically different or biased studies. However, we can not rule out the possibility that the true prevalence of ASD has actually increased at least in part because of environmental factors or other reasons yet to be discovered.

Objectives: The goal of this paper is to present the methods that will be used in the initiation of the Finnish Prenatal Study of Autism and Autism Spectrum Disorders (FIPS-A). The purpose of FIPS-A is to examine the relationship between developmental factors associated with ASD from the 10th week of pregnancy to the age of 6 years in a population-based cohort by capitalizing on the Finnish Maternity Cohort (FMC), which consists of all births in Finland, as well as national, centralized comprehensive registries containing data on medical diagnoses, pregnancy, perinatal and neonatal complications.

Methods: A nested case-control design using the FMC is being used to evaluate the relationship between prenatal serologic factors, mediating and moderating developmental antecedents, and risk of ASD. The sampling frame consists of all offspring born in Finland from 1987-2005.

Results: Total of 5036 cases of ASD were identified from the Finnish Hospital Discharge Register (FHDR) using diagnostic criteria from *International Statistical Classification of*

Diseases, 10th Revision (ICD-10). The FHDR includes both hospital admissions and outpatient care. All cases were matched with four controls from the Medical Birth Register (MBR) on date of birth, sex and birth place. Prenatal serum samples are obtained from each pregnancy, and the archived sera will be analyzed for biomarkers of potential environmental risk factors. Mediating relationships of these factors with other pre-/perinatal and neonatal events and effect modification by sex and other risk factors will also be examined. Additionally, the relationship between serologically documented prenatal factors and anthropometric measures, documented prior to the onset of autism, will be examined.

Conclusions: The FIPS-A capitalizes on several important features: a national birth cohort, a large sample size, archived prenatal sera, virtually complete case ascertainment and comprehensive national registries. Many of the potential etiologies being investigated are risk factors that are modifiable by public health measures, and are relatively common in the population. These approaches include: vaccination to prevent influenza, improved hygiene to reduce exposure to toxoplasma, thyroid supplementation to correct deficiency of this hormone, and measures to reduce cigarette use during pregnancy to diminish fetal exposure to nicotine. These studies of prenatal etiologies, and their relationship to pregnancy and birth complications, offer the promise to develop a fuller understanding of uncovering pathogenic mechanisms by which these exposures alter fetal brain development and lead to autism.

136.072 72 Parenting Stress Associated with Autism Spectrum Disorders, 2007 National Survey of Children's Health. L. A. Schieve*[1], S. Boulet[1], M. D. Kogan[2], M. Yeargin-Allsopp[1], C. A. Boyle[1], S. Visser[1], S. J. Blumberg[1] and C. E. Rice[3], (1)*Centers for Disease Control and Prevention*, (2)*HRSA*, (3)*National Center on Birth Defects and Developmental Disabilities*

Background: Previous studies suggest parenting a child with an autism spectrum disorder (ASD) is associated with high stress levels. Most studies were based on small clinical samples, few included non-ASD comparison groups, and analyses of underlying predictors of stress were limited. One past population-based study suggested that the association between parenting stress and ASD varied according to the child's special service needs, but further research is needed to fully explore this finding.

Objectives: To examine the association between having a child with an ASD and parenting stress and aggravation and to examine associations between parenting aggravation and family sociodemographic characteristics, health care access, and social supports among parents of children with and without ASDs.

Methods: Weighted prevalence estimates of parent-reported stress indicators, including a composite measure of aggravation in parenting, were assessed for parent respondents of 73,030 US children aged 4-17 years included in the 2007 National Survey of Children's Health. Parents who reported their children had ASDs currently were compared with 4 mutually-exclusive groups of parents of children without a current report of ASD. Within each group, risk factors for high aggravation were assessed.

Results: The proportion of parents of children with current ASDs who were in the high-aggravation range (36.6%) was comparable to the proportions for parents who reported their child had a past but not current ASD (35.2%), or had another non-ASD emotional, developmental, or behavioral problem (31.2%). Proportions of high aggravation were significantly lower for parents of children with other types of special health care needs (6.5%) and no special health care needs (5.1%). Among parents of children with current ASDs, variations in high aggravation were observed based on whether the child received family-centered care (26.1% high aggravation versus 46.3% for those without family-center care), received care within a medical home (defined based on American Academy of Pediatrics framework) (12.5% versus 48.4%), recently received mental health treatment (51.3% versus 23.3%), was uninsured during the past year (68.5% versus 35.0%), whether the parent had someone to turn to for emotional support (32.8% versus 53.8%), and parent-reported

ASD severity (27.3%, 41.6%, and 54.1% for mild, moderate, and severe ratings, respectively). After multivariable adjustment, independent associations were observed between high parent aggravation and child age <6 years (adjusted prevalence ratio [aPR]=1.7), child uninsured in past year (aPR=1.6), child not receiving care in a medical home (aPR=2.0), child recently received mental health treatment (aPR=1.8), parent lacks someone to turn to for emotional support (aPR=2.1), and child's current ASD rated as moderate/severe (aPR=1.4). While some of these same factors were associated with aggravation within the non-ASD groups, the association between lack of a medical home and parental aggravation was particularly noteworthy for children with current or past only ASDs reported.

Conclusions: Having a child with an ASD is associated with high stress levels; however, there is variability within health care and social support subgroups. Strategies to strengthen family-centered care and other components of the medical home construct might positively impact parent stress levels for children with ASDs.

136.073 73 Paternal Age and Autism Spectrum Disorder (ASD) Versus ADHD in the Offspring. L. Gabis*, R. Raz, Y. Kesner Baruch and B. Reichman, *Sheba Medical Center*

Background:

Previous studies reported increased paternal age in families with ASD as compared to general population. Those reports strengthened the genetic theory on the basis of autism pathogenesis and postulated that paternal age could be related to increased rate of spontaneous single gene mutations, however, a comparison to other disabilities was not performed.

Objectives:

To examine the paternal age distribution in families with ASD offspring and to compare it to the distribution of ADHD families and to general population.

Methods:

Interview and chart review of families from clinic visits and database at the Weinberg Developmental Center (WDC). Family histories of children with ASD were compared to an age and gender matched group of ADHD children, all being diagnosed using DSM-4 criteria. Those two groups were compared to family planning information from population survey performed by Health department.

Results:

Sig.*	Total	15-24	25-34	35-44	45-54	55-64	65plus		Paternal Age Class
P<0.001	268	8	143	104	11	2	0	N	
	100%	**2.99**	**53.36**	**38.81**	**4.10**	**0.75**	**0.00**	**%**	**ASD**
P=0.735	320	21	190	98	11	0	0	N	
	100%	**6.56**	**59.38**	**30.63**	**3.44**	**0.00**	**0.00**	**%**	**ADHD**
	1,187,330	110852	699572	335916	36493	3724	773	N	**Total**
	100%	**9.34**	**58.92**	**28.29**	**3.07**	**0.31**	**0.07**	**%**	**Population**

*** Significance of the Chi-square test, compared to the total population**

Conclusions: Tendency towards a higher paternal age in families with ASD was confirmed by our study. This tendency did not exist in families with ADHD and paternal age in this population was similar to general population.

136.074 74 Pharmacotherapy of ASD Children in 2006: Findings From the New Jersey Autism Study. J. Shenouda*[1], D. Rosivack[1], B. Peng[1], R. Baltus[1] and W. Zahorodny[2], (1)*New Jersey Medical School - University of Medicine and Dentistry of New Jersey*, (2)*University of Medicine and Dentistry of New Jersey*

Background: Though behavioral and educational interventions continue to be 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. Population-based analyses of pharmacotherapy provided to children with ASD may enhance appreciation of this type of intervention.

Objectives: This study was undertaken to estimate of the number, proportion and demographic distribution of children with ASD receiving pharmacotherapy with psychoactive

drugs, in the New Jersey metropolitan region, in 2006, to describe the number of children with ASD receiving polypharmacy and to define the frequency of psychoactive treatment by drug type, over time.

Methods: Data were collected as part of the New Jersey Autism Study (NJAS), a population-based ASD surveillance investigation carried out in Essex, Union, Hudson and Ocean Counties. 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. Current findings, representing 8-year olds (1998-born), in 2006, were compared to baseline findings for a cohort of 8-year olds born in 1992. The socioeconomic status (SES) of ASD cases was represented by the District Factor Group (DFG) ranking, a community-level index. Chi-square tests were used to test associations.

Results: 528 children with ASD, born in 1998, were identified from a total 8-year old population of over 30,000. 148 of the 528 ASD children (28%) were prescribed one or more psychoactive drug, at any time before or during their eighth year. 44 ASD children (8.3%) were prescribed two or more psychoactive drugs. Stimulants were the most frequently used drug-type, being prescribed to 80 children (15% of the total ASD cohort). 46 children with ASD (8.7%) were prescribed anti-psychotics, while anti-depressants were prescribed to 17 children (3.2%) and alpha-adrenergic agonists were prescribed to 15 children (2.8%). Anti-convulsant drugs were prescribed to 23 children with ASD (4.4%), while sedatives (2%) and other psychoactive drugs (10%) were prescribed less frequently. Overall, neither the frequency of psychoactive prescription, nor the distribution of prescribed medicines varied by sex, race or SES. However, boys with ASD were more likely to receive polypharmacy than girls with ASD ((9.3% vs 3.5%; $p<0.05$).

Conclusions: The proportion of ASD children in metropolitan New Jersey treated with psychoactive medicines and the pattern of drug-type use remained stable between 2000 and 2006. While stimulants continued to be the most frequently prescribed medicines, the proportion of children treated with stimulants decreased in the period. The frequent prescription of stimulants to children with ASD underscores the importance of attention deficits as an associated feature of ASD. Continued monitoring of children with ASD in the region by our population-based method may disclose trends in the frequency and pattern of psychoactive treatments provided to children with ASD.

136.075 75 Prescription Drug Rates Among Children with Autism Spectrum Disorders (ASD). S. L. Logan*, L. King, J. Nicholas, J. Charles, L. Carpenter and T. Hulsey, *Medical University of South Carolina*

Background: Autism Spectrum Disorder (ASD) is a neurologically based developmental syndrome that affects 1 in 91 children in the United States. Medications are often prescribed for correcting ASD associated problem behaviors, and evidence suggests rates of medication use among children of all ages with ASD are high and increasing. Studies show that 30%-60% of ASD children are currently taking or have within the past year been prescribed at least one psychotropic medication. Additionally, ASD children have substantially higher total healthcare costs, largely due to prescription drugs. However, the generalizability of these findings may be limited by the reliance on parent recall, volunteer participation, or previous diagnoses, and the lack of systematic diagnostic assessments.

Objectives: The aims of this study were to determine rates of prescription medications and comorbid conditions among children with ASD.

Methods: Our study population consisted of 8-year old children with ASD identified by the Centers for Disease Control and Prevention (CDC) sponsored South Carolina Autism Developmental Disabilities Monitoring

(SCADDM) Network. All Medicaid-eligible cases from the first three study years (2000, 2002, and 2004) that met DSM-IV criteria for Autistic Disorder (AD), Asperger Disorder (AS), or Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS) were linked to Medicaid to obtain a history of attention-deficit hyperactivity disorder (ADHD) and epilepsy diagnosis from birth through age 8, and a 2-year history of any prescription medications.

Results: A total of 306 children were included. Overall, 88% (270/306) were prescribed one or more medications, and over 50% (159/306) were prescribed 10 or more during the 2-year medication history (1999-2000 for study year 2000, 2001-2002 for study year 2002, and 2003-2004 for study year 2004). The number of prescriptions per subject was consistent across study years (median=10). Cases with a history of ADHD at any time between birth and age 8 increased from 28% in study year 2000 to 36% in study years 2002 and 2004, while cases with a history of epilepsy at any time between birth and age 8 decreased from 19% in study years 2000 and 2002, to 11% in study year 2004.

Conclusions: To the authors' knowledge, this is the first study to examine rates of medication use among ASD children that were identified by a population based surveillance project. Our findings suggest an even higher rate of medication usage than previously reported and support the need for further research in this area. These results will be beneficial for future comparisons and ultimately a better understanding of the impact of this disorder.

136.076 76 Prevalence of Autism Spectrum Disorders In a Population of Children with Intellectual Disabilities. J. Charles*, J. Nicholas, L. Carpenter, L. King and W. Jenner, *Medical University of South Carolina*

Background: The prevalence of Autism Spectrum Disorders (ASD) in the general population ranges from 1/100-1/150 and 40-60% of those have a diagnosis of Intellectual Disability (ID). However, there is less information about prevalence of ASD in the population of those affected with ID. The presence of a dual diagnosis has challenging implications for clinical diagnostic services, therapeutic intervention, service utilization and managing additional behavioral and psychiatric issues that are specific to the ASD population.

Objectives: The objective of this analysis was to determine the prevalence of ASD in a population of 8-year-old children with intellectual disabilities.

Methods: Data were analyzed from an ongoing active, population-based surveillance program conducted in South Carolina as part of the Centers for Disease Control and Prevention's Autism and Developmental Disabilities Monitoring Network. Prevalence data for ID and ASD among 8-year-old children from three points in time, 2002, 2004, and 2006 were analyzed for overall prevalence of ID and comorbid ASD, severity of ID and for the influences of gender and race/ethnicity. Chi-square analysis was used to determine significance of results.

Results: The prevalence of ID in this group of 8-year-old children was approximately 19 per 1000 or 1 in 53. Sixteen percent of children with ID had a comorbid diagnosis of ASD. For children with ID plus ASD, the overall prevalence was 3.1 per 1000 or 1 in 323. The prevalence ratio of males to females with ID plus ASD was 3.7 ($p<0.05$), and the prevalence ratio of blacks to whites was 1.5 ($p<0.05$). Among females with ID plus ASD, 66% were in the mild range, 22% in the moderate range, 10% in the severe range and 2% in the profound range. For males: 57% in the mild range, 26% in the moderate range, 12% in the severe range, and 3% in the profound range.

Conclusions: Results indicate that ASDs affect 16% of 8-year-old children with intellectual disabilities. A significant number of boys with ID have comorbid ASD suggesting that routine ASD screening may be appropriate in this population. Given the relative frequency of ASD among children with ID, tailored assessment and intervention approaches may be needed. These results emphasize the need for increased attention for a subgroup of the ID population having a comorbid diagnosis of ASD.

136.077 77 Response Inhibition to Emotional Facial Expressions in Children with Autism Spectrum Disorders. K. F. Jankowski*[1], J. Phillips[1], G. L. Wallace[2], L. Kenworthy[1], R. Oliveras-Rentas[3] and B. Yerys[4], (1)*Children's National Medical Center*, (2)*National Institute of Mental Health, National Institutes of Health*, (3)*Ponce Center for Autism*, (4)*Children's National Medical Center, George Washington University*

Background:

Past research has demonstrated relatively intact response inhibition in individuals with autism spectrum disorders (ASD). Response inhibition studies using the Go/NoGo paradigm typically use letters and simple shapes as stimuli. However, several Go/NoGo studies use emotional facial expressions as stimuli in order to explore the influence of social content on response inhibition. Only one study has implemented the Go/NoGo task in ASD using facial emotions, which were limited to anger and happiness (Geurts, Begeer, & Stockmann, 2009). While the study failed to demonstrate differential response inhibition between children with ASD and typically-developing controls (TYP), it is unknown if these findings generalize to additional negative facial expressions, such as sadness and fear, which several studies show to be atypically processed by individuals on the autism spectrum.

Objectives:

To expand on ASD research of response inhibition of social stimuli by including additional negative facial emotions.

Methods:

37 children from two groups (25 ASD; 12 TYP) matched on age (7-12 years), IQ (70+), gender ratio, and socioeconomic status completed an E-prime emotional Go/NoGo response inhibition task. The task consisted of two block types (Go and NoGo trials) across three facial emotions (fear, sadness, and happiness). Neutral faces were paired with the Go or NoGo emotional stimuli within each block type.

Results:

False alarm (FA) rates and mean response time (RT) did not differ significantly across emotion condition or diagnostic group. However, the ASD group had a significantly greater mean standard deviation of RT during NoGo trials, $F(1,35)= 4.82$, $p< 0.05$. Due to this extreme variability, an Intra-individual Coefficient of Variation (ICV) was calculated for each participant. There were significant ICV group differences in NoGo trials, $F(1,35)= 4.28$, $p< 0.05$, and in fear trials, $F(1,35)= 4.12$, $p= 0.05$, demonstrating significantly greater variability in the ASD group during fear NoGo trials.

Conclusions:

Processing emotional stimuli does not significantly influence response inhibition accuracy or central tendency (i.e., mean RT) in children with ASD or TYP. However, children with ASD demonstrate significantly greater variability, as captured by the ICV, in their ability to inhibit responses to fearful faces. This finding has methodological implications, as it provides a quantifiable index of the phenotypic heterogeneity that is often discussed qualitatively in ASD research. It also demonstrates variability in an attentional bias to fearful stimuli in ASD.

136.078 78 The Association of Maternal Infection Requiring Hospitalization During Pregnancy and Autism Spectrum Disorder: An Explorative Danish Cohort Study. H. Ó. Atladóttir*[1], P. Thorsen[2], L. Østergaard[3], D. E. Schendel[4], S. Lemcke[5], M. Abdallah[6] and E. Parner[7], (1)*Institut of Public Health, Department of Epidemiology*, (2)*Atlanta*, (3)*Skejby Hospital*, (4)*Centers for Disease Control & Prevention*, (5)*Aarhus University Hospital*, (6)*Aarhus University*, (7)*University of Aarhus*

Background: Maternal infection during pregnancy has been suggested to cause adverse fetal brain development.
Objectives: Estimate the association between maternal exposure to hospitalization for infection during pregnancy, and diagnosis of ASDs in the offspring.
Methods: This population based cohort study included all children born in Denmark from January 1, 1980, through December 31, 2005, a total of 1,612,342 children. Diagnoses of ASDs were obtained from the Danish National Psychiatric Register.

Diagnoses of maternal infection were obtained from the Danish National Hospital Register. Data was analysed using Cox proportional hazards regression.
Results: A total of 10,133 children were diagnosed with ASDs. No association was found between maternal infection and diagnosis of ASDs in the child when looking at the total period of pregnancy; any maternal infection: adjusted HR=1.13 (CI: 0.96-1.34). However, admission to hospital due to maternal viral infection in the first trimester: adjusted HR=2.98 (CI: 1.29-7.15), and maternal bacterial infection in the second trimester: adjusted HR=1.43 (CI: 1.08-1.88), were found to be associated with diagnosis of ASDs in the offspring.
Conclusions: We observed no overall association between a variety of maternal infections requiring hospitalization during the total length of the pregnancy and diagnosis of ASDs in the child. However, the results support prior hypotheses concerning early prenatal viral infection increasing the risk of ASDs.

136.079 79 ASD Diagnosed and Then Ruled out by Community Professionals in a Population-Based Study. J. Baio[1], L. D. Wiggins*[2] and C. E. Rice[1], (1)*National Center on Birth Defects and Developmental Disabilities*, (2)*Centers for Disease Control and Prevention*

Background: Autism spectrum disorders (ASDs) are developmental disabilities that affect social, communication, and behavioral development and are often associated with intellectual disabilities (ID). Although ASDs are generally accepted as life-long conditions, recent studies indicate that 10-20% of children once diagnosed with an ASD no longer meet diagnostic criteria when evaluated several years later. However, it is uncertain whether the likelihood of ruling out an ASD diagnosis after confirming an ASD diagnosis is increasing over time and what factors predict a change in ASD classification.

Objectives: We used a population-based surveillance dataset to examine changes in ASD diagnoses, specifically examining whether a community professional excluded an ASD diagnosis that had previously been confirmed by the same or another community professional during surveillance years 2000 to 2006. We also examined whether cognitive functioning or the original ASD subtype noted predicted a change in ASD classification and alternative diagnoses given when an ASD was ruled out.

Methods: Participants were identified from the Autism and Developmental Disabilities Monitoring (ADDM) Network. Study clinicians applied a standardized coding scheme based on DSM-IV-TR to information contained in health and educational records of children with conditions associated with ASDs (e.g., language and cognitive delays) to determine surveillance case status. Clinicians also recorded diagnostic impressions of community professionals who authored each report; which included confirming ASD diagnoses, ruling out ASD diagnoses, and giving alternative diagnoses such as language delay.

Results: A total of 4,958 children had surveillance records reviewed; 1,394 of these children had a known age of first ASD diagnosis. Of these 1,394 children, only 63 (5%) had an ASD diagnosis ruled out after an ASD diagnosis was confirmed. Children without ID were more likely to have an ASD ruled out after an ASD was confirmed than children with ID (p=.012, OR=2.84; 95%CI=1.26-6.45). The likelihood of having an ASD ruled out after an ASD was confirmed increased from 2000 to 2006 (p=.009; OR=2.42; 95%CI=1.23-4.67); this increase was limited to children without ID (defined as IQ>70; p=.005; OR=7.75; 95%CI=1.84-32.54). Original ASD subtypes among children who later had an ASD ruled out were autistic disorder (37%), general ASD or PDD-NOS (33%), subtype not specified (25%), and Asperger's disorder (5%). The most common diagnoses given when an ASD was ruled out were language delay or disorder (38%) and ADHD (22%).

Conclusions: We found fewer children with an ASD ruled out after an ASD was confirmed than recent reports, indicating stability in ASD diagnoses in this population. However, the likelihood of rejecting an ASD after confirming an ASD increased over time for children without ID. The subtype of autistic disorder was just as common as the subtype of

general ASD or PDD-NOS in children who later had an ASD ruled out; suggesting subtype is less influential in predicting changes in ASD classification than cognitive functioning. Our results also suggest that ASDs may sometimes be difficult to accurately distinguish from language delay or disorder and ADHD since these diagnosed were commonly confirmed when an ASD was ruled out.

136.080 80 Association Between Assisted Reproductive Technology and Autism Spectrum Disorders. P. A. Davis*[1], K. Hollenbach[2], K. Schmidt[1], C. Ferrone[1] and M. L. Bauman[3], (1)*MassGeneral Hosptial for Children/Harvard Medical School*, (2)*University of California, San Diego*, (3)*MassGeneral Hosptial for Children/Harvard Medical School; Boston University School of Medicine*

Background:
There has been a dramatic upswing in the number of autism diagnoses among children beginning in the early 1990's. A recent prevalence report indicates that 1 in 91 children ages 3 to 17 have such a disorder. The increasing incidence in Autism Spectrum Disorders (ASD) is potentially associated with the increasing use of Assisted Reproductive Technology (ART) to achieve pregnancy. In the United States, 1.2% of the 2005 U.S. birth cohort was born following ART treatment (CDC, 2008). Despite the lack of a systemic surveillance effort on the safety of ART, convincing evidence that ART treatment increases the risk of adverse outcomes, including developmental disabilities, among conceived children has begun to emerge.

Objectives:
To examine the relationship between ART and the occurrence of ASD.

Methods:
Reproductive history information was analyzed from all subjects enrolled in the Autism Treatment Network (ATN) Clinical Research Registry. The ATN is a group of 15 hospitals and medical centers dedicated to improving medical care for children and adolescents with autism spectrum disorder through treatment research. Participating institutions administer standardized protocols and assessments and contribute this data to a national database. Those enrolled in the registry are between the ages of 2 and 17.6 years and have met ASD criteria on both the DSM-IV and the Autism Diagnostic Observation Scale at an established ATN site.

Results: Of the 1491 autism spectrum disorder patients enrolled in the ATN, 94% (n= 1401) provided information on whether their pregnancy was conceived naturally or through use of assisted reproductive technology (ART) and were used as the basis for analysis. One hundred sixty-six subjects (11.8%) conceived through use of ART. This rate was significantly higher than the 1.2% of US births conceived using ART in 2005 ($z = 36.4$; $p < 0.0001$). ASD was further defined as Autism, Asperger Syndrome or PDD/NOS, and percentage of pregnancies conceived using ART among each group was 12.5%, 12.1% and 10.2%, respectively. Women in the study who conceived using ART had a mean age of 32.1 ± 6.6 as compared to women who conceived naturally (29.6 ± 5.9 years)($t=4.9$; $p < 0.001$). Similarly, mean paternal age was higher among those whose pregnancies were conceived using ART (34.2 ± 7.0 years) as compared to those whose were not (32.1 ± 6.6 years)($t = 3.7$; $p = 0.0002$). Among the ATN registry, there was no gender difference between those conceived naturally or through use of ART, with 15.6% and 14.5% female registrants, respectively ($z = 0.37$; $p = 0.71$).

Conclusions:
This study demonstrates a strong association between ASD and ART. Further studies on ART-conceived children with ASD are warranted.

136.081 81 Associations Between Maternal Affective Disorders and Specific Characteristics in Children with Autism Spectrum Disorder. R. A. Vasa*, C. Anderson, J. M. Thorn, A. R. Marvin, G. Sarphare, K. Law and P. Law, *Kennedy Krieger Institute*

Background: Elevated rates of affective disorders have been consistently reported in family members of children with autistic spectrum disorder (ASD). Evidence shows that the onset of parental depression and anxiety predates the birth of the child with ASD. A small number of studies suggest a link between maternal depression and specific child ASD characteristics, such as

higher cognitive functioning. These data suggest that common genes or endophenotypes may underlie autism and familial affective disorders. Further research on this relationship carries implications for delineating ASD subgroups as well as developing targeted interventions.

Objectives: To examine the relationship between maternal affective disorders and specific characteristics of autism spectrum disorder (ASD) in their children in a large sample of families participating in a national online ASD research project.

Methods: Mothers completed online questionnaires regarding their own as well as their affected offspring's psychiatric history. Relationships between maternal mood disorder status (history of depression or bipolar disorder vs. no history of mood disorder) and characteristics of their eldest child with ASD were explored. Multivariate regression analyses examined whether each maternal affective disorder predicted the following ASD outcomes: high cognitive functioning, child emotional disorders, and multiplex family status.

Results: 5.6% of participating mothers reported receiving a diagnosis of bipolar disorder by a health professional, while 32.4% reported being professionally diagnosed with major depression, dysthymia or a hormonally-based depressive disorder. Seventy percent of mothers with a professional diagnosis of depression had their initial onset of depression prior to having children; this group endorsed higher rates of depression recurrence, psychiatric hospitalization, suicidal behavior, and family history of affective disorder. Maternal depression was associated with a diagnosis of Asperger's Disorder, older child age at ASD diagnosis, child psychiatric comorbidities, and multiplex family status. Maternal bipolar disorder was more strongly associated with all of these same characteristics, as well as child comorbid bipolar disorder and a child IQ of 116 or above.Conclusions: Maternal affective disorders predict a specific profile in children with ASD. These data suggest that common pathophysiological mechanisms may underlie these two types of disorders.

136.082 82 Breastfeeding and Autism. P. G. Williams* and L. L. Sears, *University of Louisville*

Background:

Breastfeeding has long been considered the preferred diet for infants, both with regard to nutritional value and the protection provided against infection and allergies.
Breastfeeding rates have increased fairly steadily over the last 40 years. The Ross Mothers Survey cites national breastfeeding rates at 6 months increasing from 18.9% in 1992 to 33% in 2002. Kentucky is among the states with the lowest overall rates of breastfeeding with approximately 14% of babies being breastfed at 6 months in 2002.

The few studies which have looked at breastfeeding and autism suggest either lower or similar rates of breastfeeding in children with autism as compared to controls. A 1989 study by Tanoue noted earlier weaning rates in children with autism compared to typically developing children. A 1988 study by Burd et al yielded similar rates of breastfeeding for 50 children with Pervasive Developmental Disorders and controls. Schultz et al (2006) used data from the Autism Research Internet Study to conclude that no breastfeeding was associated with increased odds of having autism when compared to breastfeeding for more than 6 months. However, a recent study by Kenet et al (2007) identified significant differences in the brain development of rat pups which were exposed to polychlorinated biphenyls (PCB's) through nursing and in utero. The authors theorized that PCB's in breast milk might act as an environmental risk factor for autism.

Objectives:

Our objective was the investigation of rates of breastfeeding among children diagnosed with autism.

Methods:

Our study was an interview study which looked at medical issues associated with autism. Of those interviewed, information on breastfeeding was available for 45 children with autism as compared to 68 age and

gender matched controls with other developmental disabilities. Chi square tests were performed to compare data between the two groups.

Results:

The percent of ASD patients who were breastfed at 6 months was 37% as compared to 13% of controls (p of 0.003).

Conclusions:

In contrast to previous studies, our interview study yielded significantly higher rates of breastfeeding in subjects with autism as compared to controls with other developmental disabilities. The control rate of breastfeeding at 6 months was similar to the general rate for Kentucky, but the rate of breastfeeding in children with autism was nearly 3 times higher. The Kenet study pointed to possible concerns associated with substances in breast milk. While PCB's were banned in the late 1970's, these substances are very slowly degraded and maintain a significant presence in breast milk. Infants breastfed for more than 3 months have as much as a 6.6 fold increase of plasma PCB concentrations compared to those who were not breastfed. The authors hypothesized that exposure to PCB's in breast milk might act as an environmental trigger, disrupting brain development and resulting in autism for those already genetically predisposed. While the known breastfeeding benefits still outweigh risks, our study points to the need to further investigate rates of breastfeeding in autism and evaluate potentially harmful substances in breast milk.

136.083 83 Clinical and Neuro-Psychological Profile of Autism in Saudi Arabia: A Systematic Approach. A. Almuslamani*, L. J. Al-Sharif, D. S. Khalil, J. M. Shinwari, H. Khalak, N. A. Al Tassan, B. F. Meyer, M. Nester and M. Aldosari, *King Faisal Specialist Hospital and Research Center*

Background:

Autism Spectrum Disorders (ASD) represents a group of complex developmental disorders which is seen in all ethnic groups across all nations. The majority of available information regarding ASD is derived from developed countries. The available data from developing countries are mostly in the form of case series or retrospective review of records. A systematic approach is highly needed in developing countries to gain more insight of ASD across cultures. In addition, some cultures have unique characteristics such as high rates of consanguinity and endogamy which make them attractive for genetic studies highlighting the need of an improved understanding of ASD in such cultures. A systematic evaluation, clinical and neuro-psychological profiling and pheno-typing might also give more value to such studies by exploring phenotype-genotype association.

Objectives:

Our major aim was to set-up a systematic hospital-based registry of ASD patients with a detailed demographic, clinical, and neuro-psychological data to provide the basis of a future country-wide registry.

Methods: This is a report from an ongoing approved research project of studying clinical and molecular characteristics of ASD in Saudi Arabia. We present our analysis of 100 subjects who have been enrolled thus far. The diagnosis of ASD was established by two independent evaluations by experienced clinicians utilizing DSM-IV criteria. Neuro-psychological studies were performed by an experienced neuro-psychologist with over 20 years of experience in evaluating children with developmental disabilities. Children were also evaluated by a multidisciplinary team specialized in evaluating children with ASD. In addition, many individuals underwent evaluations using Autism Diagnostic Observational Schedule (ADOS) module I and / or Autism Diagnostic Interview – Revised (ADI-R). The use of ADOS and / or ADI-R will become standard once their translation and adaptation are completed.

Results:

The mean age of enrolled patients was 8.2 years (range 2-19). Male-to-female ratio was 4:1. 73% of fathers and 70 % of mothers had a college degree or higher. Parents were first or second degree cousins in 41%, while 18% were from the same

extended family. 29% of the subjects had a sibling with ASD. Language regression was reported in 39%. Neuro-psychological profiles showed that 70 % had delay in their cognitive or developmental abilities with severe delay accounting for 18 %, moderate delay for 30 % and mild delay for 22% of the total sample. Self-injurious behaviors were reported in 42% while hyperactivity was reported in 32%. 12 % of subjects had seizures.

Conclusions:

There are many similarities between our sample and the published reports on the clinical characteristics of ASD. There are notably unique features of our sample that might prove to be valuable. We think that systematic data collection of ASD patients from developing countries will serve as an important source of furthering our understanding of the clinical as well as the biological aspects of ASD worldwide.

136.084 84 Factor Structure of the Q-CHAT, a Revised Screening Instrument for Autism Spectrum Conditions in Toddlers Between 18 - 24 Months. C. Allison*[1], G. Pasco[1], S. J. Wheelwright[1], T. Charman[2], C. Brayne[1] and S. Baron-Cohen[1], (1)*University of Cambridge*, (2)*Institute of Education, University of London*

Background:

Recent evidence suggests that the structure of autistic traits varies along more than one single underlying continuum.

Objectives:

To evaluate the dimensional structure of a revised version of the Checklist for Autism in Toddlers (the Quantitative - Checklist for Autism in Toddlers [Q-CHAT]) in the general population.

Methods:

The Q-CHAT was sent to parents of 18 – 24 months olds from two general populations in the Eastern Region, UK. Exploratory Factor Analysis (EFA) (using MPlus) was run on the first sample (N=754) to obtain the factor structures with up to six factors using the robust Weighted Least Squares Mean and Variance (WLSMV) estimator. Poorly and negatively loading items were dropped until all remaining items loaded ≥0.35 on each factor. EFA was re-run on the second sample (N=819), followed by Confirmatory Factor Analysis (CFA) on the remaining 17 items to confirm the factor structure.

Results:

The EFA revealed two possible factor structures. The two factor solution separated social from non-social items (RMSEA=0.095). The three factor solution reflected the domains of social interaction, communication and repetitive and stereotyped behaviours (RMSEA=0.051). The CFA confirmed that the three factor solution (CFI=0.92, TLI=0.93, RMSEA=0.055, WRMR=1.338) marginally fit the data better than the two (CFI=0.838, TLI=0.855, RMSEA=0.077, WRMR=1.759) factor structure. The social and non-social factors in the two factor solution were only weakly correlated (r=0.14, p=0.001), indicating that these domains are largely independent. In the three factor solution, the social interaction factor was not correlated with the repetitive and stereotyped behaviour factor.

Conclusions:

No evidence was found to support a single continuum of autistic traits; rather the data support at least a bi-dimensional approach underlying autistic traits in toddlers. Ongoing work is testing the sensitivity and specificity of the Q-CHAT in a total population.

136.085 85 Gene-Environment Related Epidemiological Research On Autism in Jamaica. M. H. Rahbar*[1], K. A. Loveland[2], M. Samms-Vaughan[3], E. Boerwinkle[4], J. Bressler[4], D. del Junco[5], D. A. Pearson[2], P. Assassi[5], S. Pellington[3], M. L. Grove[4], K. Bloom[5], C. Beecher[3], K. Brooks[6] and M. Ardjomand-Hessabi[5], (1)*University of Texas School of Public Health*, (2)*University of Texas Medical School at Houston*, (3)*The University of the West Indies*, (4)*The University of Texas School of Public Health*, (5)*The University of Texas Health Science Center at Houston*, (6)*Tropical Metabolism Research Institute*

Background:

Autism Spectrum Disorders (ASDs) are complex lifelong neurodevelopmental and behavioral disorders manifesting in infancy or

early childhood, characterized by impairments in social interaction and communication, and by repetitive, stereotyped behavior. The prevalence of 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.

Objectives:

In collaboration with researchers at the University of West Indies (UWI) in Kingston, Jamaica, we are conducting this study to compare ASD case-finding and case-ascertainment approaches. Additionally, we are investigating whether environmental exposures to mercury, lead, arsenic and cadmium play a role in autism. Furthermore, we are assessing the role of select polymorphisms in glutathione-**S**-transferase (GST) genes, and their potential interactions with the aforementioned heavy metals in relation to ASD.

Methods:

This is an age and sex matched case-control study. We are administering the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview-Revised (ADI-R) to 225 children in the UWI's Jamaica Autism Database who have previously been identified as being at risk for ASD using the Childhood Autism Rating Scale (CARS). Our goal is to identify 150 children with an ADOS-ADI-R confirmed ASD. For each case, we will also identify an age and sex matched control using the Social Communication Questionnaire (SCQ). We also administer a pre-tested questionnaire to assess demographic and socioeconomic information, parental history, and potential exposure to heavy metals through food or occupation of parents. At the end of the interview, we collect 5 mls of whole blood, 2 mls of saliva, and hair samples to be analyzed in the US. Using conditional logistic regression, we assess the role of GST genes, and their potential interactions with heavy metals in relation to ASD.

Results:

A preliminary analysis of the ongoing Jamaica Autism Database identifies 411 children with ASD during 1996 - present. About 83% of cases are male resulting in a sex ratio of 4.9:1 (Male:Female ratio). Approximately half of the ASD cases are younger than or equal to 8 years, making them eligible to participate in our study. Our Jamaican team members received ADOS and ADI-R training in the US. Our Genetics team visited UWI in October 2009 to provide training for the collection, processing and shipment of biological specimens.

Conclusions:

This study will lay out the foundation for the first epidemiological study of ASD in an Afro-Caribbean population. Although we have not yet completed our data collection, we have gained significant insight in conducting epidemiological research on autism in other cultures. For example, despite our target population being from an English speaking part of Jamaica, we have experienced some subtle cultural differences between Jamaica and the US that may require attention with respect to the administration of particular components of the ADOS. In addition, we have gained significant insight in potential logistical challenges with respect to transportation of specimens from other countries into the US. We believe our experience will be useful to other researchers.

136.086 86 Parental and Grandparental Ages in the Autistic Spectrum Disorders. C. D. Steer, J. Golding* and M. Pembrey, *University of Bristol*

Background:

A number of studies have assessed ages of parents of children with autistic spectrum disorders (ASD), and reported both maternal and paternal age effects. To our knowledge, no study has determined whether the ages of the preceding generation are associated.

Objectives:

To assess whether parental age effects are secondary to the ages of the grandparents

Methods:

We compared the parental and grandparental ages of children in the population-based Avon Longitudinal Study of Parents and Children (ALSPAC), according to their scores in regard to 4 autistic trait measures and whether they had been given a diagnosis of ASD.

Results:

Mean maternal and paternal ages of ASD cases were raised, but this appears to be secondary to a maternal grandmother age effect (P=0.006): OR=1.66[95%CI 1.16,2.37] for each 10-year increase in the grandmother's age at the birth of the mother. Trait measures also revealed an association between the maternal grandmother's age and the major autistic trait – the Coherence Scale (regression coefficient b=0.142, 95%CI=0.057,0.228;P=0.001). After allowing for confounders the effect size increased to b = 0.217[95%CI 0.125,0.308](P<0.001) for each 10 year increase in age.

Conclusions:

Although the relationship between maternal grandmother's age and ASD and a major autistic trait was unexpected, there is some biological plausibility, for the maternal side at least, given that the timing of female meiosis I permits direct effects on the grandchild's genome during the grandmother's pregnancy. An alternative explanation is the meiotic mismatch methylation hypothesis, presented here for the first time. Nevertheless the findings should be treated as hypothesis generating pending corroborative results from other studies.

136.087 87 Prevalence Rates of Autism Spectrum Disorders Among the Old Order Amish. J. L. Robinson*[1], L. Nations[1], N. Suslowitz[2], M. L. Cuccaro[3], J. Haines[2] and M. Pericak-Vance[1], (1)*University of Miami Miller School of Medicine*, (2)*Vanderbilt University*, (3)*University of Miami School of Medicine*

Background:

The prevalence rate of Autism Spectrum Disorders (ASD) appears to be steadily increasing. The latest report from the Center for Disease Control estimates the rate of ASD is 1 in 91 children (Kogan, 2009), up from 1 in 150 in 2007. Understanding the seeming changes in ASD prevalence require careful exploration of genetic and environmental factors. A method that has proven useful in dissecting the etiology of complex diseases is the study of isolated populations. One population isolate that has been studied extensively is the Amish, with well over 250 genetic studies. Expanding studies of autism to the Amish may provide important information about etiology. A crucial first step in this process is a feasibility study to determine ASD prevalence rates in this population.

Objectives:

This study presents preliminary data on the estimated prevalence of ASD among the Amish in two Amish dominant counties as part of a larger epidemiological study. All children between ages 3 to 21 in those counties will be screened for the presence of an ASD.

Methods:

Screening occurred in Holmes County, Ohio and Elkhart-Lagrange County, Indiana, two of the largest Amish communities in the United States. Trained clinicians ascertained door to door using a published Amish Directory as a guide. Families were approached and asked to participate in a brief interview regarding their children. Two primary screening instruments were used: the Social Communication Questionnaire (SCQ) and the DSM-IV-TR Checklist (a tool created by the authors). A Vaccination History and a brief family history including questions specific to the ASD phenotype were also taken. Children screening positive on either the SCQ or DSM-IV-TR Checklist were seen for a more comprehensive clinical evaluation by two licensed psychologists. This evaluation included the Autism Diagnostic Observational Schedule (ADOS) and Autism Diagnostic Interview (ADI).

Results:

From September 2008 to October 2009, 1899 Amish children were screened in the two

Amish communities. A total of 25 children screened positive for ASD on either the SCQ or the DSM-IV-TR checklist. A total of 14 screened positive for ASD on both screeners. Of those 25 children, 14 were evaluated and seven children were confirmed as having a diagnosis of ASD using the ADI and/or ADOS, and clinical judgment. Interestingly, four of the seven only met ASD criteria on the ADOS but not the ADI. Three of the four who were not diagnosed by the ADI only missed criteria on the Behavioral Domain, which may be attributable to the reporting style of Amish caregivers.

Conclusions:

Preliminary data have identified the presence of ASD in the Amish community at a rate of approximately 1 in 271 children using standard ASD screening and diagnostic tools although some modifications may be in order. Further studies are underway to address the cultural norms and customs that may be playing a role in the reporting style of caregivers, as observed by the ADI. Accurate determination of the ASD phenotype in the Amish is a first step in the design of genetic studies of ASD in this population.

136.088 88 Season of Birth and Risk of Autism in a Finnish National Birth Cohort. P. N. Banerjee*[1], K. M. Lampi[2], M. Ikonen[2], S. Hinkka-Yli-Salomäki[2], S. Niemelä[2], H. Helenius[2], I. W. McKeague[3], A. S. Brown[1] and L. A. Sourander[2], (1)*Columbia University/NYSPI*, (2)*University of Turku*, (3)*Columbia University*

Background: There is much interest in the theory that environmental factors following a seasonal pattern, (e.g., temperature, viral infection, availability or consumption of certain foods at specific times of the year), and acting during the prenatal or perinatal period, could be related to autism spectrum disorders (ASD). An environmental risk factor is hypothesized to act either directly or through interaction with other environmental or genetic factors, and adversely influence infant brain development. Findings from previous studies investigating this theory have been inconsistent. Methodological limitations of studies of season of birth in ASD, such as the use of clinical rather than population-based samples or small sample sizes may explain some inconsistencies in the findings. Additional factors contributing to variable findings include differences in (1) types of comparison groups (sibling controls vs. population-based controls) used; (2) diagnostic criteria applied; (3) definition of seasonality (e.g. months included in "winter") used; (4) hemispheric region study in which the study was conducted (5) statistical analysis.
Objectives: The objective of this study was to address many of the limitations of previous studies by using a large, national, population-based sample to investigate the association between seasonality and all subtypes of ASD. Birth *month* of individuals diagnosed with each ASD diagnostic subtype (Infantile Autism, Asperger's Syndrome and Pervasive Developmental Disorder), rather than "*season*", which may be defined differently in various regions, was examined for deviation from the monthly pattern of birth of children in the general population without autism.
Methods: All ASD cases born in 1990-2002 were identified from the Finnish Hospital Discharge Register (FHDR). Information concerning total births in Finland in 1990-2002 was obtained from the Finnish Medical Birth Registry (FMBR). Descriptive Chi-Squared "goodness-of-fit" tests, adjusted for year of birth, were conducted to examine how well observed frequencies of births of children with ASD differed from expected frequencies. Females and males were analyzed separately in order to examine any differences by gender. Poisson regression analyses will be used to test the data against a sinusoidal function.

Results: Preliminary results examining all births revealed a deviation in birth pattern in the months of June (p=.01) and October (p=.06) for all three subtypes of ASD. There was an association between a decrease in births of females diagnosed with all ASD subtypes (p=.04) in the month of June. There was an increase in males diagnosed with infantile autism born in October (p=.05), and the month of December approached significance (p=.08).
Conclusions: These results suggest that environmental exposures may contribute to increased risk of ASD in males. The finding

that females born in June are at decreased risk of being diagnosed with ASD warrants further exploration.

136.089 89 AUTISM Spectrum Disorder: The BRAZILIAN Research Capacity. M. C. Teixeira[1], M. T. Mercadante[2] and C. S. Paula*[3], (1)*Mackenzie P University*, (2)*Federal University of São Paulo*, (3)*Universidade Presbiteriana Mackenzie*

Background:

In the last decade, there has been a growth of research in the field of Autism Spectrum Disorder (ASD) in Latin America. Recently, the Brazilian Ministry of Health created a working group to develop health policy strategies to deal with these disorders, but the real Brazilian research capacity is still unknown.

Objectives:

The present study is a systematic literature review aiming to identify all scientific production covering publications of Brazilian authors about ASD in the period 2002 to 2007.

Methods:

This literature review includes the following scientific databases: (1) the National Library of Medicine and the National Institutes of Health (PUBMED); (2) Scientific Electronic Library Online (SciELO) and (3) Literature Latin American and Caribbean Health Sciences (LILACS). They are considered the most important Brazilian health databases.

Results:

A total of 53 papers about ASD in the period 2002 to 2007 were identified. The majority of articles were produced by authors from the Southeast Brazil and from public universities. The main research topics were: communication and familial relationship, followed by the phenotype and endophenotype. Most of the articles were based on small samples sizes and epidemiological studies were extremely rare. Over 40% of papers were published in journals with some level of impact factor that varied between 0.441 and 3.211. In addition, there were identified 117 dissertations/theses about ASD; 82.9% were master thesis.

Conclusions:

This literature review shows that Brazilian researchers are interested in the ASD theme and that there is a potential for the future in Brazilian research community. However, a big piece of the Brazilian scientific production is concentrated in dissertation/thesis and based on small samples. Additionally, the minority of papers was published in journals with high impact factor and there are important lacks in certain areas.

Thus, these results suggest the need for epidemiological studies with larger sample sizes, which would contribute to better local evidence in the public health perspective.

136.090 90 Demographic Distribution of Children with Autism Spectrum Disorder in Qatar. O. M. Ghoneim*, R. A. Al-Okka and S. J. Al-Naimi, *Qatar University*

Background: The prevalence rate of children with Autism Spectrum Disorder (ASD) has increased significantly worldwide from 1/10000 in the early 90's to 1/150 in 2009. The rise in ASD rate has concomitantly raised the awareness about the disorder, and increased the demands for more research, support services, recreational resources and highly trained special education professionals. Moreover, it brought the call to action in individual countries to further investigate the local prevalence rate as well as the detailed demographic distribution of children with ASD within each country. In developing countries, this is still a challenging task. No information about ASD rate or distribution is available in the Gulf countries, including Qatar.
Despite the fact that the state of Qatar has started the initiative of setting the world autism awareness day (WAAD), rate and demographic distribution of children with ASD in Qatar is yet to be established. There is no central ASD database to quantify and maintain all children with ASD within the country. Quality and magnitude of adequate health care services, specialized education centers, appropriate family support and recreation resources are truly reflected by the lack of such central database.

Objectives:

1. To determine the rate and demographic distribution of children with ASD living in Qatar in the last five years.

2. To quantify the needs of educational, medical, and social support services for children with ASD and their families living in Qatar.

Methods: Centers/schools provide services for children with ASD in Qatar were identified. The target centers/schools were contacted by phone/fax/emails and official copy of the research proposal was submitted. Field visits to individual centers/schools were executed and information about the number and the demographics of children with ASD were collected. The data collected were categorized according to five demographic distribution variables; nationality, gender, age, educational language and hosting Institutions. Data entry and data analysis were conducted using Scientific Package for Social Sciences (SPSS) software.

Results: Nine centers/schools were identified as possible service providers for ASD children (18 years old or younger) in the state of Qatar. Total numbers of ASD children currently living in Qatar and the total number of ASD children lived in Qatar in 2004 will be presented. The collected demographic data of children with ASD according to the five measured variables will also be presented.

Conclusions: A central list of children with ASD and their demographic distribution was established in Qatar for the first time. The presented results represent promising foundation base to be incorporated into adequate educational, medical, and family support services in the state of Qatar.

136.091 91 Frequency of Interventions to Children with ASD in the Pre-School Period: Findings From the New Jersey Autism Study. D. Rosivack*[1], J. Shenouda[1], B. Peng[1] and W. Zahorodny[2], (1)*New Jersey Medical School - University of Medicine and Dentistry of New Jersey*, (2)*University of Medicine and Dentistry of New Jersey*

Background: A growing body of evidence supports the early identification of Autism Spectrum Disorders (ASD) and the provision of timely interventions to children with ASD. While early interventions hold promise for language, cognitive and social improvement, there is scant data describing the frequency with which Early Intervention Program (EIP) and pre-school services for disabled students (PSD) are provided to ASD children. Analysis of the extent to which these core early intervention services are provided is necessary to determine if these services are being employed to their full potential and to better understand their role in assisting children with ASD.

Objectives: This study investigated the number, proportion and demographic distribution of children with ASD receiving services prior to kindergarten through EIP and/or as a result of PSD classification, in a large metropolitan, population-based sample and analyzed demographic differences among children receiving such services.

Methods: Data were collected as part of the New Jersey Autism Study (NJAS), an ASD surveillance investigation carried out in Essex, Union, Hudson and Ocean Counties. Using an active case-finding method established by the Centers for Disease Control and Prevention (CDC), ASD surveillance data were developed for children who were born in 1998 and resided in the surveillance region in 2006. NJAS data were based on review, analysis and independent ASD case-determination derived from information contained in health and education records. Demographic information and case-specific data, including the use of early intervention services and the classification of children for PSD services were analyzed. The socioeconomic status (SES) of children with ASD was represented by the District Factor Group (DFG) ranking, a community-level index. Statistical analysis was performed using Chi-square tests.

Results: In a population of over 30,000 8-year old children, 528 children were identified as having ASD. 206 of these children (39.3%) received EIP services and 374 of the ASD children (70.8%) were served under a PSD classification. Overall, the receipt of EIP services and PSD classification did not vary significantly by gender. While PSD classification did not vary by race, White

children with ASD received EIP services more frequently than non-White children (p<.003). Additionally, the frequency of children with ASD from high-SES communities receiving EIP services (p<.01) and classified as needing PSD services was significantly higher than those from children residing in mid or low-SES communities (p<.02).

Conclusions: Despite a growing awareness of ASD in the context of a well-developed pediatric health system, a significant majority of children with ASD residing in our surveillance region did not receive EIP services before the age of 3. Non-White children were less likely to receive EIP services than White children. While nearly three-quarters of all ASD children were identified for PSD services, participation in EIP and PSD programs was strongly associated with SES. The relatively low participation of ASD children in EIP and observed disparities in EIP and PSD program participation call for the broad implementation of innovative identification programs for children under age 3 and redoubled efforts to identify and intervene with socially-disadvantaged children at risk for ASD.

136.092 92 Identification of Asperger Disorder (AD): a Pilot Study in Gipuzkoa, Spain. J. Fuentes*[1], A. Altxu[2], N. Tamayo[3], A. Porcel[3], I. Isasa[3], I. Gallano[4], R. Canal[5] and M. Posada[6], (1)*Policlinica Gipuzkoa and GAUTENA*, (2)*APNABI*, (3)*Policlinica Gipuzkoa*, (4)*GAUTENA*, (5)*University of Salamanca*, (6)*Carlos III Health Institute*

Background:
Two ways of enhancing appropriate identification of Asperger Disorder (AD) include broad screening of target populations with specific tests, and routine surveillance by pediatricians.

Objectives:
To assess the efficacy of the CAST (Childhood Asperger Screening Test) as a screening instrument among 4 and 6-year-old children in Gipuzkoa, a county of 680.000 inhabitants in the Basque Country of Spain. The region is known for GAUTENA, a 31 year-old comprehensive community program for autism-spectrum disorders (ASD), which provides an appropriate setting for whole-population studies
Methods: The CAST was translated into Spanish and Basque, adapted to cultural factors, and reverse translated to ensure accuracy. All public pediatric clinics in the county participated in the study (N=33). Parents were invited to complete the CAST during routine visits between June 2007 and May 2008. The responses were classified, following published criteria, into "HIGH likelihood" of AD (score of 15 or more); "MEDIUM likelihood" (12-14 points), and "LOW likelihood" (11 or less).

The HIGH cases were re-interviewed by phone, using a novel CAST decision-tree manual. Cases still classified as HIGH after phone screening were clinically assessed with the ADI-R, ADOS-G and Vineland Scale. To identify possible false negatives, the Social Communication Questionnaire (SCQ) was sent to all HIGH and MEDIUM cases, and to a 10% random selection of LOW cases.

Case identification was compared to all cases with birthdays falling within the same age period who had already been referred to GAUTENA, and to files in the Special Education Registry and the Psychiatric Registry of the Basque Health System.
Results:
The mean response rate across clinics was 18% (range 1-77%), yielding 2,012 screened children (13.0% of the eligible population). There were 18 children in the HIGH likelihood score (0,89% of the sample); 48 (2.3%) cases in the MEDIUM range, and 1,925 (95.6%) in the LOW range. The subsequent phone interview of HIGH cases allowed elimination of 77% of them, reducing the need for further work up. Three children not previously identified in GAUTENA met criteria for AD following the CAST and clinical assessment (one case was CAST-false negative, but entered assessment because of concern of his pediatrician). The SCQ did not identify any false negatives among the eliminated HIGH (N=18), the MEDIUM (N=48), and the random sample of LOW cases (N=192).

Conclusions:

A prevalence of 1 in 670 in a sample of 2,012 children ages 4 and 6 was found in Gipuzkoa, Spain. This rate falls within the range described for Finland (1 in 400) and Canada (1 in 1,000). The CAST can be incorporated into routine pediatric practice and may help enhance timely identification of AD cases. Training of pediatricians will be needed to ensure accuracy, and subsequent phone review of those scoring above cut-point will simplify clinical practice and reduce unnecessary costs.

136.093 93 Incidence and Time Trends in Autism Spectrum Disorders - a Finnish Cohort Study. M. Ikonen*[1], P. N. Banerjee[2], S. Hinkka-Yli-Salomäki[1], K. M. Lampi[1], H. Helenius[1], I. W. McKeague[3], A. S. Brown[2] and A. Sourander[1], (1)*University of Turku*, (2)*Columbia University/NYSPI*, (3)*Columbia University*

Background: Incidence and time trends of autism spectrum disorders (ASD) have been explored in several studies in different populations. Both public and scientific debate of the increased incidence of these conditions has recently achieved considerable interest. Some studies also indicate this might be part of a broader epidemiological phenomenon among child neuropsychiatric disorders.

Objectives: The purpose of the study is to explore how the number of new ASD cases diagnosed in Finland has changed in twenty years of time. We will examine cumulative incidence in a population-based cohort study and evaluate possible trends over time. We aim to analyze trends of incidence in different diagnostic subgroups based on *International Statistical Classification of Diseases, 10th Revision (ICD-10)*, as well as to examine possible trends of gender distribution.

Methods: For the present study, we used the population-based birth cohort of the Finnish Prenatal Study of Autism and Autism Spectrum Disorders (FIPS-A), which is a large, register-based study of ASD in a national birth cohort. The study cohort includes all children born in Finland from 1987-2007. Data on ASD outcomes were obtained from the Finnish Hospital Discharge Register (FHDR). In this study, we included all registered diagnosed cases of childhood autism, Asperger´s syndrome and pervasive developmental disorder (PDD) or pervasive developmental disorder – not otherwise specified (PDD-NOS) using diagnostic criteria from *ICD-10*. Incidence rates for different subgroups of ASD were calculated for five 4-year time periods: 1988-1991, 1992-1995, 1996-1999, 2000-2003 and 2004-2007.

Results: Incidence was determined for ASD for the total 20-year study period and for five 4-year intervals. In the total study period, 4586 cases (3575 male, 1011 female) were diagnosed with childhood autism, Asperger´s syndrome or PDD/PDD-NOS. Incidence was age-adjusted to the determined population at risk (0-15 years of age). The incidence of ASD for the total study period was 23/100 000/year. Preliminary results indicate that for childhood autism, age-adjusted incidence seems to be significantly higher between years 1996-1999 compared to other intervals. For other diagnostic subgroups, incidence rates seem to be more stable over time.

Conclusions: Preliminary results suggest that there seem to be significant differences in the cumulative incidence rates across different time periods for ASD. Age- and gender-specific results of time trends will be examined further for diagnostic subgroups.

136.094 94 Maternal Education as a Differentiating Factor for Willingness to Participate in ASD Diagnostic Evaluations. M. Khowaja* and D. L. Robins, *Georgia State University*

Background: With its goal to reduce costs and increase accessibility, healthcare reform has become a popular topic of discussion among US citizens. Maternal education has been linked to decreased access and utilization of healthcare, due to factors such as level of understanding and exposure to information about risk factors of diseases and prevention initiatives, level of information processing, and having the knowledge to communicate effectively with healthcare providers.

Objectives: As part of a large screening study, parents are offered a free diagnostic evaluation; some decline to participate. This study examined whether the decision to

decline a free diagnostic evaluation differed by maternal education.

Methods: Parents in the metro-Atlanta area completed the M-CHAT at their child's well-baby visits (n=10,046). Of them, 115 screened positive on the M-CHAT, participated in and screened positive on the M-CHAT Follow-up Interview, and were offered a free diagnostic evaluation. Sixty-four mothers of the at-risk children completed the evaluation (82%), whereas 14 did not participate (18%); 37 were excluded due to physical handicaps that precluded completing the evaluation, not reporting maternal education, someone other than the mother as the respondent, or being unable to contact the family to schedule the evaluation (i.e., phone out of service). Individuals who declined evaluation included those who were not interested, were non-responsive to phone calls, or withdrew from the study. Maternal education was classified as High (HME; n=49) for mothers who attained at least a Bachelor's degree and Low (LME; n=29) as attaining anything less than a Bachelor's degree.

Results: Of the 64 who completed the evaluation, 44 were classified as HME and 20 as LME, whereas for the 14 who did not complete an evaluation, 5 were classified as HME and 9 as LME. A chi square test revealed significant group differences in maternal education for those who completed an evaluation and those who declined, $\_^2(1)=5.368$, $p=.021$. Sixty-nine percent of the parents who accepted the offer for a free diagnostic evaluation of their child were in the HME group and 64% of those who refused to participate were in the LME group.

Conclusions: The decision to participate in a free diagnostic evaluation after having being informed about one's child being at risk of a developmental delay was related to maternal education. Other factors may contribute to declining to participate, including cost of transportation (although in this study parents were offered compensation for such expenditures) and difficulty taking off time from work. However, given that level of maternal education, which is often used as a marker for socioeconomic status, is related to exposure to and understanding of preventative healthcare information, these findings suggest that changes in policy (e.g., universal screening) might not be enough to affect all families. Although universal screening is an excellent first step, individuals must first be educated on the importance of and their rights to healthcare, and specifically on the benefits of early detection of autism and other developmental delays. Without understanding these benefits, specialized healthcare services might be underutilized, particularly by families from low SES backgrounds.

136.095 95 MCHAT Screening for Autism in Hispanic Toddlers; Fail Rates of the 23 Item Instrument. N. J. Rosen*[1], G. Windham[2], M. Anderson[3], K. S. Smith[1], R. B. Coolman[4] and S. J. Harris[4], (1)*California Department of Public Health*, (2)*CA Department of Public Health*, (3)*Impact Assessment, Inc.*, (4)*Santa Clara Valley Health and Hospital System*

Background:

The American Academy of Pediatrics recommends screening for autism spectrum disorders (ASD) as routine pediatric practice. Surveillance of ASD has consistently shown lower prevalence rates among Hispanics than Whites, the reasons for which are not clear but may include differences in recognition or diagnosis. Few studies have examined screening methods within the Hispanic population in the United States. To investigate ASD prevalence rates and appropriate screening methods in this population, we initiated a universal screening program in a county healthcare system serving primarily low income Hispanics.

Objectives:

Screen children born in 2006 attending well-child pediatric visits at two county pediatric clinics, and for this report, to examine fail rates of M-CHAT items in Hispanics compared to other ethnic groups.

Methods:

The Modified Checklist for Autism in Toddlers (M-CHAT) was given to parents of children aged 16-30 months at their clinic appointment, in English or Spanish, as requested. These were scored on-site and

results were provided to pediatricians for further review or referral. Among subjects who failed the M-CHAT based on M-CHAT cut-off values, we calculated the proportion who failed for each of the 23 items. We compared these by factors including ethnicity and language using the chi-square test (p-value <0.05 indicating statistical significance.) Results:

Overall, 26% failed the M-CHAT, which was significantly higher in Hispanics (28%) than Non-Hispanics (17%), so we examined whether specific items contributed disproportionately to this difference. Examining the first failed instrument only, we compared Hispanics with positive screens (n=403) to Non-Hispanics (n=58). Of the six "critical" questions on the instrument, the only significant difference in was for item 15, which Hispanics were less likely to fail than Non-Hispanics, 6.5% vs. 13.8%, respectively (p=0.04). Children of Hispanic ethnicity had significantly more fails on items 4 (p=0.01), 10 (p=0.02), and 17 (p=0.02), and significantly less fails on items 18 (p=0.02), and 22 (p=0.02) than Non-Hispanics. Within the Hispanic population we compared fail rates of items by instrument language. Hispanics who chose a Spanish translation were more likely to fail items 3 (p=0.001), 4 (p=0.04), and 21 (p=0.01), but less likely to fail item 22 (p=0.006), than those who chose the English version. There was little difference in item fail rates by maternal education.

Conclusions:

This population's M-CHAT fail rate is twice that found in other studies of similar aged children. This may be due to a higher prevalence of ASD in this primarily Hispanic population, or to differences in interpretation of the instruments by these parents. The higher and lower fail rates on specific M-CHAT items among Hispanics may indicate these questions do not carry the same cultural relevance for Hispanics as for others. For example, item 4 asks if the child plays peek-a-boo, which may not be a common game in this population. Items with differing fail rates for Hispanics using the Spanish translation may indicate differences created upon translation of the original instrument. Further examination of ASD screening in Hispanics and refinement of screening methods and instruments are needed to help serve this growing population.

136.096 96 Pitocin and the Risk for Autism Spectrum Disorder. M. Rissenberg*, *Center for Neuropsychology*

Background: Version:1.0
StartHTML:0000000201
EndHTML:0000003781
StartFragment:0000002441
EndFragment:0000003745
SourceURL:file://localhost/Users/marian/Desktop/Research/Pitocin%20Study/Imfar2010Abstract.doc

A broad body of research points to a central role for the neuropeptide oxytocin (OT) in autism spectrum disorder (ASD). This includes evidence that depletion of central OT results in deficits in social affiliative behaviors in animals, that administration of OT reduces repetitive behaviors and improves social cognition in individuals with ASD, and increases trust and the stress-protective effect of social contact in controls, that plasma OT is decreased in individuals with ASD, and that there is an association between ASD and the gene for the OT receptor (Otr). In addition, early exogenous exposure to OT has been shown to effect both brain OT and social behavior later in life. The use of Pitocin, a synthetic form of OT, for the induction and augmentation of labor has increased in parallel with the dramatic increase in ASD in recent decades. Several authors have suggested a link, but a small number of studies of individuals with autism have yielded inconsistent results.

Objectives: Version:1.0
StartHTML:0000000201
EndHTML:0000002710
StartFragment:0000002440
EndFragment:0000002674
SourceURL:file://localhost/Users/marian/Desktop/Research/Pitocin%20Study/Imfar2010Abstract.doc To examine the relationship between the use of Pitocin during labor and the risk for the development of ASD in the child.

Methods: Version:1.0 StartHTML:0000000201 EndHTML:0000003392

StartFragment:0000002440
EndFragment:0000003356
SourceURL:file://localhost/Users/marian/Desktop/Research/Pitocin%20Study/Imfar2010Abstract.doc

: Subjects were children aged 6 to 16, seen in a private practice setting between 2000 and 2008, who were referred for neuropsychological evaluation of academic, behavioral or social emotional difficulties. Birth histories were obtained by parent interview. Diagnosis was based on DSM-IV criteria. Of 93 children, 15 were diagnosed with ASD (autism, Asperger's syndrome or PDD NOS), 42 were diagnosed with attention deficit/hyperactivity disorder (ADHD), 21 were diagnosed with anxiety or depression (PSY) and 15 had no psychiatric diagnosis but some cognitive-based learning issues (COG).

Results: Version:1.0 StartHTML:0000000201
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EndFragment:0000003119
SourceURL:file://localhost/Users/marian/Desktop/Research/Pitocin%20Study/Imfar2010Abstract.doc

The percentage of children whose mothers were administered Pitocin during labor was significantly greater in the ASD group (67%) than in the three other groups (ADHD 31%, PSY 19%, COG 27%), and the rate for the general population (about 26%). Analysis using Pearson Chi-Square demonstrated a significant relationship between diagnosis and OT exposure.

Conclusions: Version:1.0
StartHTML:0000000201
EndHTML:0000002688
StartFragment:0000002439
EndFragment:0000002652
SourceURL:file://localhost/Users/marian/Desktop/Research/Pitocin%20Study/Imfar2010Abstract.doc The results suggest that administration of Pitocin during labor increases the risk for autism spectrum disorder.

136.097 97 Pregnancy Complications and Obstetric Suboptimality as Risk Factors for Autism Spectrum Disorders in Children of the Nurses' Health Study II. K. Lyall*[1], D. L. Pauls[2], D. Spiegelman[1], A. Ascherio[1] and S. L. Santangelo[2],

(1)*Harvard School of Public Health*, (2)*Massachusetts General Hospital*

Background: The results of numerous studies suggest pregnancy and obstetric complications may be associated with autism spectrum disorders (ASD). However, it is unclear whether certain individual complications confer a higher risk than others, or whether associations differ by diagnostic subgroup. Further, the mechanisms underlying such associations are unknown.

Objectives: To examine specific pregnancy and obstetric complications in association with risk of autism spectrum disorders as a group and by diagnostic subgroup in a large United States cohort.

Methods: Participants from the Nurses' Health Study II, a prospective national cohort with reproductive, medical, and health information collected through biennial mailed questionnaires since 1989 and information on autism spectrum disorders collected in 2005. Logistic regression was used to obtain crude and adjusted odds ratios for ASD, and by diagnostic sub-group (autism, Asperger syndrome, or other ASD).

Results: 793 cases occurred among 66,445 pregnancies. Overall, pregnancy and obstetric complications were positively associated with risk of ASD (OR 1.49, 95% CI 1.26, 1.77, p <.0001 for pregnancy complications and 2.76, 95% CI 2.04, 3.74, p <.0001 comparing individuals with 4 or more obstetric suboptimality factors to those with none). Associations were similar by diagnostic subgroup. In particular, gestational diabetes was consistently associated with a significantly increased risk of ASD whether considering results in primary or sensitivity analyses or by diagnostic subgroup (OR in primary analysis = 1.76, 95% CI 1.34, 2.32, p <.0001). Sub-optimal parity and sub-optimal age at first birth were also individual factors associated with ASD.

Conclusions:

Consistent with previous research, general pregnancy complications were associated with autism spectrum disorders as a whole.

Additional work will be required to more fully assess the role of gestational diabetes.

136.098 98 Quantitative Evaluation of Sociologic Factors That Can Lead to Apparent Increases in Autism Prevalence. M. LaMadrid*, C. Brown and T. Deisher, *Sound Choice Pharmaceutical Institute*

Background: The prevalence of autism ('autism spectrum disorder') has risen dramatically from less than 1 per 2500 before 1980 to 1 per 91 children in 2007. The autism literature commonly cites three sets of sociologic factors, namely changes in diagnoses, enhanced professional and parental awareness, and Special Education funding incentives, as being largely responsible for the increased autism prevalence. Previous work quantifying diagnostic changes suggest that this cause does not explain the rise in autism prevalence in the US. The quantitative validity of the other sociologic factors has not been evaluated.

Objectives: To quantitatively measure the contributions of increased awareness and Special Education funding to the rise in ASD prevalence.

Methods: A review of autism prevalence literature, publicly available documents such as the US Statistical Abstracts, documents from Department of Education, Yahoo group sites, and other relevant databases was conducted. US autism/ASD prevalence rates from peer-reviewed publications were combined and averaged if more than one prevalence was published for a given birth year. When prevalence was measured for a range of years, point prevalence was obtained by taking the midpoint of the years. Professional awareness was measured through historical counts of the number of professionals who can diagnose autism and the number of peer-reviewed publications related to autism, as listed in Pubmed. Peer reviewed autism publications were normalized to the total number of annual peer reviewed publications, in order to account for confounding variables such as increased ease of publishing due to word processing advances or expanded numbers of scientific journals. Non-professional awareness (e.g., parental) was measured through Yahoo autism groups usage. Software was written to automatically download Yahoo group websites and extract the number of messages in Yahoo groups devoted to autism. The number of messages was normalized to the total number of Yahoo health (but non-autism) group messages in order to account for general increased computer usage and Yahoo groups. The history of autism funding by the Department of Education was reviewed and the funding amounts normalized to spending on general education.

Results: The US autism prevalence had a fold change of approximately 37 from birth years 1977 to 2000. The normalized number of autism diagnosing professionals had a fold change of 2.48 from 1977 to 2002. The normalized number of autism publications had a fold change of 3.3 from 1977 to 2002. Increased parental awareness was not significant until the late 1990s. Federal funding for Special Education was disbursed starting only in 1995, and had a normalized fold change of 2.24 from 1995 to 2006.

Conclusions: Increases in professional and parental awareness and increase in federal funding for autism do not adequately explain the rise in autism prevalence.

Stress and Age: A Comparison of Asian American and Non-Asian American Parents of Children with Developmental Disabilities Including Autism. W. Huang*[1], D. DeLambo[2], W. Chung[3] and D. Homa[2], (1)*Regional Center of the East Bay*, (2)*University of Wisconsin at Stout*, (3)*Eastern University*

Background: Little is known about ethnic differences in stress experienced by parents of children with autism.

Objectives: **This study examined parental stress differences between Asian American and non-Asian American parents of children with developmental disabilities (DD) including autism.**

Methods: **Participants (N=48) were administered the Parental Stress Index and a demographic information survey.**

Results: **Both groups reported high stress levels. However, Asian American parents experienced a significantly higher level of stress that was related to children's**

characteristics of disability than their non-Asian counterparts. Results also indicate that while the age of children with DD was negatively correlated with parental stress for non-Asian American parents, the age of parents was negatively correlated with parental stress for Asian American parents.

Conclusions: Implications of the findings for social service professionals are discussed.

Human Genetics Program

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136.099 99 Hypocholesterolemia in Autism Spectrum Disorder. E. Tierney*[1], I. Bukelis[1], J. Teng[1], C. Wheeler[1], W. E. Kaufmann[1], C. Wassif[2], S. K. Conley[3], R. W. Y. Lee[1] and F. D. Porter[4], (1)*Kennedy Krieger Institute*, (2)*NIH*, (3)*NICHD/ NIH*, (4)*National Institutes of Health/NICHD*

Background: Studies of metabolic function (metabolomic studies) in fragile X syndrome and Rett syndrome have been helpful in understanding cellular dysfunction that leads to autism spectrum disorder (ASD) profiles. Studies have extended to Smith-Lemli-Opitz syndrome (SLOS), an autosomal recessive disorder due to an inborn error of cholesterol metabolism that is caused by mutations of the 7-dehydrocholesterol reductase gene (*DHCR7*) encoded on chromosome 11q12-13. SLOS has an estimated incidence among individuals of European ancestry of 1 in 20,000 to 1 in 60,000 births and a carrier frequency of 1%. In SLOS, insufficient cholesterol is synthesized and the precursor sterols 7-dehydrocholesterol (7DHC) and 8-dehydrocholesterol (8DHC) accumulate. Approximately 50% of individuals with SLOS met the diagnostic criteria for autism (Tierney 2001, Sikora 2006) and approximately three-fourths met criteria for ASD, suggesting a consistent relationship with ASD and SLOS (Sikora 2006). In Autism Genetic Resources Exchange (AGRE) multiplex families, a high degree of hypocholesterolemia was detected (Tierney 2006) and hypocholesterolemia occurs at 10 times the expected rate. Cholesterol has multiple biological functions, some of which could plausibly contribute to ASD. Cholesterol is an important building block for the body's cell membranes and myelination of the central nervous system, is a major component of lipid rafts, modulates oxytocin receptor function, modulates ligand binding activity and G-protein coupling of the serotonin1A (5-HT1A) receptor, and is the precursor for neurosteroid production.

Objectives: To determine the relationship of both physical and behavioral phenotype to plasma and cerebral spinal fluid (CSF) sterol levels in individuals with SLOS.

Methods: Autism features, cognitive abilities, adaptive skills, and anatomical severity in 23 individuals with mild to moderate SLOS were correlated with plasma and CSF sterols.

Results: In SLOS, 56% had autism and 70% had ASD. Regression analyses with sterol levels and the scores of Autism Diagnostic Interview-Revised, IQ, adaptive behavior, and anatomical severity demonstrated that plasma and CSF 7DHC levels were the most significant correlates of social and nonverbal autistic symptom characteristics and that sterol ratios (7DHC+8DHC/ total sterols) were the most significant correlates of anatomical severity.

Conclusions: Using clinical assessment tools and metabolomic studies, we have been able to distinguish distinct neurobehavioral phenotypes among young persons with SLOS, and determined that ASD related behaviors in SLOS may be a functional consequence of the abnormal biochemistry in the brain and specifically due to the accumulation of 7DHC. Thus, in SLOS and non-SLOS hypocholesterolemic ASD, autistic symptoms may be potentially amendable to therapeutic interventions that increase cholesterol and reduce 7DHC levels. A study is being performed with AGRE multiplex non-SLOS hypocholesterolemic individuals to determine if there is a distinct physical and behavioral phenotype that represents an etiologically independent subgroup (endophenotype). In a community sample of mostly simplex families, a study is being performed to behaviorally characterize the hypocholesterolemic individuals and determine if cholesterol supplementation is safe and helpful for ASD-related behaviors.

136.100 100 Mutation and Expression Analyses of the Ribosomal Protein Gene RPL10 in An Extended German Sample of Patients with Autism Spectrum Disorder. G. Pakalapati[1], A.

Chiocchetti[1], E. Duketis[2], S. Wiemann[1], F. Poustka[2], L. Breitenbach-Koller[3] and S. M. Klauck*[1], (1)*German Cancer Research Center (DKFZ)*, (2)*Goethe University*, (3)*Paris-Lodron University*

Background:

Autism spectrum disorder (ASD) has a strong genetic background with a higher frequency of affected males suggesting involvement of X-linked genes and possibly also other factors causing the unbalanced sex ratio in the etiology of the disorder. Syndrome pathogenesis is associated with abnormal brain development and manifests in several specific brain regions, especially cerebellum, amygdala and hippocampus. Positive linkage findings in genome wide screens and association studies identified susceptibility regions and genes on the X chromosome.

Objectives:

The ribosomal protein L10 gene (*RPL10*) located in Xq28 was identified as a candidate susceptibility gene for ASD through RNA *in situ* hybridization experiments. We detected high expression of *RPL10* in mouse hippocampus. A first screen in 317 cases with autistic disorder, 21 cases with Asperger syndrome, and 7 cases with PDD-NOS representing 296 families revealed two missense mutations, L206M and H213Q, in two independent male-male affected sib-pair families (Klauck et al. 2006, Mol Psychiatry 11, 1073-84). In the follow-up study presented here, further 175 patients (145 autistic disorder, 27 Asperger syndrome, 3 PDD-NOS) representing 169 independent families have been screened to enlarge the study group. To understand the involvement of RPL10 in the pathogenesis of ASD, the *RPL10* mRNA level in patients with ASD and controls was quantified.

Methods:

All seven exons of the *RPL10* gene and the intronic snoRNA U70 have been screened by direct sequencing for mutations. *RPL10* transcript levels were tested by quantitative RT-PCR on RNA extracted from lymphoblastoid cell lines (LCL) of different probands.

Results:

In the follow-up sample the H213Q mutation inherited from the carrier mother was identified in a male patient from a simplex family. The two different mutations, L206M and H213Q, are both located at the yet uncharacterized C-terminal end of the RPL10 protein, a constituent of the large ribosomal subunit. RPL10 itself is known to have impact on differential gene expression in yeast and man. Functional analyses in yeast revealed that both amino acid substitutions L206M and H213Q, respectively, confer hypomorphism with regard to the alteration of the translation process while keeping the basic translation functions intact. No statistical significant difference in *RPL10* expression levels was found by testing 12 autistic patients including 2 patients from the two families carrying the H213Q mutation, 8 relatives of autistic patients and 7 controls. Moreover, the H213Q mutation has no effect on *RPL10* expression in this cell system.

Conclusions:

The mutations identified may have a modulating effect on translation processes of synaptogenesis in neuronal development with impact especially on those cognitive functions that are mediated through the limbic system. Alterations due to the inherited mutation at the transcript level may be too subtle to be identified in the LCL system. In future, the functional impact of both mutations in its hemizygous state on the X chromosome will be further analyzed by *in vitro* and *in vivo* modeling.

136.101 101 Maternal Cytokine Gene Regulation in the Pathogenesis of Autism. H. Fernandes*[1], M. Ramanathan[1], F. Limson[1], S. Shah[1] and N. M. Ponzio[2], (1)*UMDNJ / New Jersey Medical School*, (2)*UMDNJ - New Jersey Medical School*

Background: Activated cells of the immune system secrete cytokines that influence brain development and behavior. Studies show that pro-inflammatory cytokines such as Interferon – gamma (IFN-gamma) and Tumor Necrosis Factor – alpha (TNF-alpha) are elevated in patients with autism spectrum disorders (ASD). Genetic polymorphisms in the regulatory regions of cytokine genes

have a positive or negative influence on the level of protein produced. Single nucleotide polymorphisms (SNP's) in the promoter regions of cytokine genes including IFN-gamma, TNF-alpha, IL-1, IL-6 and IL-10 affect the level of transcription of the protein. Numerous studies have documented the dysregulation of cytokines as etiological factors in children with ASD, but there has been far less focus on the parents of autistic children.

Objectives: The aim of the study is to investigate the genetic polymorphisms in cytokine regulatory genes of mothers and correlate the presence of SNP's in mothers and their autistic children.

Methods: Genomic DNA, from 46 paired specimens from mothers and their autistic children were obtained from the Autism Genetic Research Exchange (AGRE) database. Mothers were selected using the following criteria: a diagnosis of allergies and/or GI problems in their children; evidence of an overactive immune system. Seventeen regulatory SNPs from seven pro-inflammatory and anti-inflammatory cytokines were detected in a multiplex PCR, using the LifeCodes cytokine SNP assay (Tepnel/GenProbe). The cytokines analyzed included TNF-alpha, IFN-gamma, TGF-beta, IL-1, L-6, IL-10 and IL-12. The SNPs were identified and detected by hybridization to beads on the Luminex bead array. Control samples were obtained from mothers who had neither autistic characteristics nor produced any offspring diagnosed with autism.

Results: Significant differences in the frequency of SNPs were observed between controls versus mothers and controls versus autistic children in the following pro-inflammatory cytokines: IFN-gamma, IL-1, IL-6, IL-12 and the anti-inflammatory cytokine, IL-10. In contrast the TNF-alpha SNP was significantly increased only in mothers when compared to controls. Overall, the pattern of SNPs detected in autistic children and their mothers favored a pro-inflammatory environment.

Conclusions: The results of this study suggest that both mothers and their autistic children exhibit cytokine immunogenetic profiles that trend towards a pro-inflammatory phenotype.

136.102 102 Phenotypic Outcome of Aetiologically Relevant Copy Number Variation in Autism Spectrum Disorders. A. K. Merikangas*[1], E. Heron[2], R. J. Anney[2], S. Brennan[1] and L. Gallagher[1], (1)*Trinity College Dublin*, (2)*Trinity College Dublin, Ireland*

Background:

Copy-number variation (CNV) is the most prevalent type of structural variation in the human genome. Studies of CNVs in neuropsychiatric disorders, including Autism Spectrum Disorders (ASD) have demonstrated the potential promise of CNVs as a window into their genetic susceptibility. These structural anomalies, including inversions, translocations, duplications and deletions have been identified as being associated with ASD in numerous studies. Some research has proposed a strong association of de novo copy number mutations with autism, whereas other studies have addressed the overall CNV burden in cases when compared to control subjects, and still other research has implicated CNVs at specific cytoband locations (e.g. deletions at 16p11.2 and 22q11.2 and duplications at 15q13) as being associated with ASD. Moreover, the evidence suggests that recurrent CNVs have impact on broader phenotypic manifestations such as learning disability, physical characteristics, and seizures as opposed to the strict autism phenotype.

Objectives:

The primary object of this study was to investigate the phenotypic outcome of CNVs. We hypothesized that individuals carrying CNVs with prior evidence of aetiological significance would be more likely to present with general developmental anomalies that might aid in the description of associated syndromes.

Methods:

All subjects were diagnosed with the Autism Diagnostic Interview-Revised (ADI-R) and Autism Diagnostic Observation Schedule

(ADOS). Singletons derived from simplex and multiplex families were included. Subjects with known karyotypic abnormalities or genetic disorders were excluded. Genotyping of DNA was completed on the Illumina Infinium 1M SNP microarray. CNVs were called using combinations of the QuantiSNP, iPattern and PennCNV calling algorithms, and stringent quality control criteria were applied. As data relating to early development and physical features was not obtained systematically in this cohort, items in the ADI-R reflecting developmental delay were selected. Where available, IQ data, parental age and body measurement data were also included in the analysis.

Results:

Prevalence of developmental anomalies, IQ categorization and parental age in the group with aetiologically significant CNVs compared with those without known aetiologically significant CNVs will be presented.

Conclusions:

The association of broader phenotypic manifestations such as learning disability, physical characteristics, and seizures with ASD and specific genetic variants may provide additional support in elucidating the aetiology of this highly heritable and complex disorder. The results of this study may also suggest new targets for candidate region genetic studies and future research.

136.103 103 Glutathione Pathway Genes and Risk for ASD. M. D. Fallin*[1], K. Bowers[1], C. Newschaffer[2], J. P. Bressler[3], Q. Li[1] and D. Avramopoulos[4], (1)*Johns Hopkins School of Public Health*, (2)*Drexel University School of Public Health*, (3)*Kennedy Krieger Institute & Johns Hopkins School of Public Health*, (4)*Johns Hopkins School of Medicine*

Background: Autism is a highly heritable disorder, with estimates that as many as 10-15 or more genes may contribute to genetic risk either additively or interactively. Inability to effectively combat oxidative stress has been suggested as a mechanism of autism pathophysiology, and glutathione is the most important antioxidant in the brain. Therefore, we have investigated whether genetic variation in genes related to glutathione may contribute to the risk of autism through independent or multi-gene interactive models.

Objectives: To determine whether single nucleotide polymorphisms (SNP) in genes related to glutathione metabolism are associated with autism risk either independently or interactively.

Methods: Glutathione genes were ranked by weighted criteria that addressed each gene's biological relationship with glutathione, location in autism linkage regions, levels of expression in brain, and degree with which their expression correlated with expression of other glutathione genes. SNPs were then selected for the top scoring genes by selecting tag-SNPs, functional SNPs, and SNPs in conserved regions. Single-SNP odds ratios for variants in 41 glutathione genes were estimated in case-parent trios from AGRE families using the genotype- Transmission Disequilibrium Test (gTDT). Models of multi-SNP interactions and resulting odds ratios were estimated using the trio logic regression method within a conditional logistic regression framework. Logic regression is an adaptive methodology that evaluates whether Boolean combinations of covariates predict risk and selects a final model via permutation testing. We evaluated models with up to four interacting SNPs.

Results: Single-SNP associations were observed for four genes including Cystathionine Gamma-Lyase (CTH), Alcohol Dehydrogenase 5 (ADH5), Gamma-Glutamylcysteine Synthetase, Catalytic subunit (GCLC), and Glutaredoxin 3 (GLRX3). In addition, a three-SNP joint effect was observed for genotype combinations of SNPs in GLRX, GLRX3 and CTH, with an odds ratio of 3.78 (2.36, 6.04).

Conclusions: SNPs in two genes, including CTH and GCLC are directly involved in glutathione metabolism, while ADH5 and glutaredoxins are also involved in anti-oxidation within the glutathione pathway. These results suggest that variation in genes involved in counterbalancing oxidative and nitrosative stress may contribute to autism. This includes marginal effects for some genes as well as interactions between these and other genes along this pathway.

136.104 104 Interaction Between Gluathione Genes and Maternal Oxidative Stress On Risk for ASD. K. Bowers*[1], C. Newschaffer[2], J. P. Bressler[3] and M. D. Fallin[1], (1)*Johns Hopkins School of Public Health*, (2)*Drexel University School of Public Health*, (3)*Kennedy Krieger Institute & Johns Hopkins School of Public Health*

Background: Autism may arise from contributions of both genes and environment, especially exposures during the perinatal window. Inability to effectively combat oxidative stress has been suggested as a mechanism of autism pathology and glutathione is the most important antioxidant in the brain. Therefore, variation in glutathione-related genes may contribute to autism risk, and these effects may be modified in the presence of maternal conditions capable of inducing oxidative stress during in utero development.

Objectives: To investigate gene-environment interaction between glutathione-related genes and potentially stressful fetal environments as measured via maternal conditions known to cause oxidative stress.

Methods: Glutathione genes were ranked by weighted criteria that addressed each gene's biological relationship with glutathione, location in autism linkage regions, levels of expression in brain, and degree with which their expression correlated with expression of other glutathione genes. SNPs were then selected for the top scoring genes by selecting tag-SNPs, functional SNPs as well as SNPs in conserved regions. Two domains of stressful fetal environments, altered mitochondrial function (AMF) and impaired immune function (IIF) were characterized based on maternal health conditions known to relate to oxidative stress. The AMF category included conditions that may stress mitochondrial function, leading to an increased production of oxidants and included: endocrine disorders, respiratory disorders, cardiovascular disease (CVD), and hypertension. The IIF category included: migraines, asthma, allergies, immune deficiencies, autoimmune disorders as well as irritable bowel syndrome and disease. Tests of genetic associations in the presence of gene-environment interactions with either of these environmental domains (AMF and IIF) were performed in case-parent trios from the AGRE sample for 308 SNPs in 41 glutathione-related genes using a nested likelihood ratio test (LRT) comparing models with SNP and environment and interaction terms to those with only environment terms. Odds ratios for interaction between gene variants and stressful fetal environments were estimated using conditional logistic regression (CLR) models. Genotype odds ratios for groups stratified by environment were also estimated for those SNPs with significant LRT results.**Results:** Statistically significant associations in the context of stressful fetal environments were observed for a number of SNPs in genes related to glutathione metabolism, including DPEP1, ADH5, ABCC6, CTH, and multiple isoforms of GGTLA and GSTs. The maternal conditions that contributed most to these joint gene-environment effects were those associated with AMF, including endocrine disorders, respiratory disorders, CVD and hypertension. Of note, SNPs in DPEP1, LTC4S, GGTLA1, GGTLA4 each had significantly interacting SNPs. In addition to their role in glutathione metabolism, they are each involved in cysteinyl Leukotriene synthesis. Cysteinyl leukotrienes have a role in inflammation in addition to serving as messengers and modulators during development.
Conclusions: These results suggest that risk associated with variation in glutathione genes may interact synergistically with a fetal environment resulting from medical conditions and/or exogenous factors experienced by mothers of affected children. Genes related to cysteinyl leukotriene synthesis emerged as potential candidate genes for autism, given their role in oxidative stress, inflammation as well as messengers during neuronal development.

136.105 105 Genome-Wide SNP Genotyping Reveals Novel Autism Candidate Genes within a Microdeletion On Chromosome 14q23. A. J. Griswold*[1], D. Ma[2], S. J. Sacharow[3], J. L. Robinson[1], J. Jaworski[1], H. H. Wright[4], R. K. Abramson[4], J. L. Haines[5], J. Gilbert[1] and M. Pericak-Vance[1], (1)*University of Miami Miller School of Medicine*, (2)*Hussman Institute for Human Genomics*, (3)*University of Miami*, (4)*University of South Carolina School of Medicine*, (5)*Center for Human Genetics*

Background: Autism is a highly heritable neuro-developmental disorder affecting approximately 1 in 150 individuals and characterized by deficits in reciprocal social interaction, communication and patterns of repetitive behaviors and restricted interests. While monogenic causes of rare syndromic forms of autism such as Rett Syndrome and tuberous sclerosis have been identified, and large chromosomal abnormalities have been detected in 5-7% of autism patients, these fail to explain a significant portion of the heritability of autism. Chromosomal abnormalities do suggest that copy number variations of genes involved in neurological development and synaptic formation likely contribute to the etiology of the disorder.

Objectives: The goal of this study is to identify large (>300kb), potentially pathogenic CNVs contributing to autism by SNP genotyping in autism trios.

Methods: Genotyping was performed using the Illumina Human 1M Beadchip on 635 autism cases and immediate family members from 600 families. To identify and call CNVs, the PennCNV algorithm implementing a hidden Markov model (HMM) was used. CNVs identified that were greater than 300kb in size and overlapped one or more genes were selected for further analysis by comparison to the Database of Genomic Variants (DGV) and functional classification of genes. CNVs not in the DGV and likely involved in neurological function and development were considered to be potentially pathogenic and investigated further. CNVs of greatest interest were validated using TaqMan Copy Number Assays.

Results: We identified a total of 48 de novo CNVs greater than 300kb using this approach. Of those, 21 were single copy duplications of which only two were not present in the DGV and were shown to be involved in neuronal processes. These CNVs occurred in previously identified autism candidate regions on chromosomes 15q11 and 17p13. Of the 27 single copy deletions, only four were not present in DGV and were involved in neuronal processes. These included previously identified autism related microdeletions at 16p11, deletion of the autism candidate gene ASDL on 22q13, and loss of CHRNA7 on chromosome 15q13. In addition we identified a novel 1.5Mb de novo deletion on chromosome 14q23 in a patient with autism, macrocephaly, and spherocytosis. A deletion in this region has previously been reported in a patient with spherocytosis and mental retardation, and includes novel autism candidate genes MTHFD1, a folate metabolism gene previously implicated in neuropsychiatric disorders such as bipolar disorder and schizophrenia, and PLEKHG3, a gene expressed predominantly in the brain and involved in Rho-GTPase signaling in neurons.

Conclusions: In conclusion, genome-wide SNP analysis is a viable way to identify CNVs related to autism. By filtering only those that are large and affect neuronal genes, we have focused our analysis to potentially pathogenic CNVs. This approach has replicated the presence of previously reported autism CNVs and supports the role of CHRNA7 in autism. Moreover, we have identified two additional potential candidates in MTHFD1 and PLEKHG3. Further analysis will be necessary to better understand the roles of these genes in the etiology of autism.

136.106 106 Identification of Rare Coding Variation in Autism Spectrum Disorders by Deep Resequencing. G. Cai*, T. Sakurai, J. Keaney and J. D. Buxbaum, *Mount Sinai School of Medicine*

Background: Multiple rare variants play an important role in the etiology of autism spectrum disorders (ASD). The study of rare variants has proven to be more important for identifying pathological mechanisms and for the conceptualization of new therapeutic targets.

Objectives: To identify rare variants in ASD by direct resequencing large numbers of ASD candidate genes.

Methods: As part of our long term strategy, methods for large scale variant detection are being developed, including methods of sample pooling, target enrichment, and high-throughput sequencing (HTS).

Results: In our pilot study we assessed 13 genes in 288-576 unrelated ASD cases using rapid, optimized Sanger sequencing. Our strategy was to screen for de novo nonsense (or missense) variants. Candidate genes were selected based on a potential role in ASD etiology, including synaptic cell adhesion molecules, genes in the 2q37 region, and other genes. While we identified nonsense changes in two genes, none were de novo. More recently, we have expanded our studies to larger numbers of genes using a pooling strategy and HTS on the Illumina platform. Careful pooling (10 fold to 50 fold) was carried out using three rounds of quantification. We are comparing Agilent, Nimblegen, and Raindance methods for target enrichment, followed by HTS. We are also comparing three platforms for rare variant calling. Raindance has some theoretical limits but proves useful in the case of a lower number of amplicons. The comparative studies are ongoing.

Conclusions: Deep resequencing studies represent the next phase in gene discovery in ASDs. By the careful comparison of available methods, we are identifying cost effective and efficient methods for rapid rare variants discovery in ASD.

136.107 107 Heterogeneity in Autism Spectrum Disorders (ASD): Linkage Analysis of Four ASD Subsets Defined by ADI-R Clustering. E. Moore*[1], V. Hu[2] and Z. Talebizadeh[1], (1)*Children's Mercy Hospital and University of Missouri-Kansas City*, (2)*The George Washington University Medical Center*

Background: Numerous susceptibility genes and chromosomal abnormalities have been associated with autism spectrum disorders (ASD), but most discoveries either fail to be replicated or account for a small effect. Inconclusive results could be in part a reflection of the heterogeneous phenotype of autism, suggesting the need to employ strategies to identify more homogeneous groups of subjects. Recently a new ASD phenotypic sub-classification was reported by employing clustering analyses on ADI-R data, the gold standard autism diagnostic assessment tool (Hu et al., 2009). According to this classification, four distinct phenotypic subgroups were identified: (G1) severe language impairment, (G2) milder symptoms across all domains, (G3) notable savant skills, and (G4) intermediate phenotype. Objectives: The objective of our study was to address clinical heterogeneity in ASD at the genomic level and to determine if the subject stratification method based on ADI-R clustering will reduce phenotypic heterogeneity and improve linkage analysis. Methods: Data for approximately 10,000 Single Nucleotide Polymorphism (SNP) markers derived from the Affymetrix 10K SNP array for 426 families was downloaded from the AGRE website. The SNP data were sorted into separate files for each of the four sub-categories. Four group-related main lists were prepared by selecting families having at least one autistic member belonging to one of the four groups (G1, G2, G3, or G4). In multiplex families, affected siblings that were not in the same phenotypic subgroup were then removed to reduce intra-family heterogeneity (G1s, G2s, G3s, and G4s). Further stratification was done based on the affected individual's gender. This intense subject stratification method resulted in 16 distinct lists for linkage analysis. Non parametric linkage was calculated using MERLIN package. The linkage disequilibrium command in MERLIN was used to remove unlikely genotypes and to rule out the possibility of false positive results. Results: When the combined (non-subtyped) samples were analyzed, the highest LOD score obtained for 426 families was 2.8, P=0.0002 at 10q23. It is expected that lowering sample size results in reducing the detection rate. Interestingly, when applying our subject stratification method, despite the sample size reduction, in several instances the LOD score either improved compared to no grouping or new group-specific suggestive linked regions were detected. An example of such group-specific results is CNTNAP2. Suggestive linkage to CNTNAP2, a candidate gene for autism and language impairment, was detected for group 1 autistic females, a severely language impaired ADI-R subtype. A positive suggestive linkage was also identified with the SEMA5A gene for group 4 only (LOD=1.9, p=0.002, 138 families). This group-specific linkage result is intriguing because a recent genome-wide association study identified SEMA5A as a new autism

susceptibility gene. Furthermore, expression of SEMA5A is reduced in autistic subjects compared with controls using both blood and brain samples. Conclusions: Our results indicate that applying such a phenotypic sub-classification method will improve the detection power in genome-wide linkage studies by reducing heterogeneity in ASD study subjects. It also provides further evidence for both inter- and intra-family heterogeneity. Our study demonstrates a novel and effective method to address the heterogeneity in ASD.

136.108 108 A Preliminary Investigation of Parent and Clinician Agreement in the Diagnosis of An Autism Spectrum Disorder. T. De Jesus, L. Kalb* and K. Patel, *Kennedy Krieger Institute*

Background: Discord between a parent of a child with an Autism Spectrum Disorder (ASD) and their diagnostic clinician may lead to a host of poor child outcomes. This agreement is particularly important when it comes to the child's autism spectrum diagnosis. However, the typical rate of parent and clinician diagnostic agreement and the factors that influence this concord are presently unknown.

Objectives: The goal of this study was to investigate the level of parent and clinician ASD diagnostic agreement. Our secondary goal was to examine several child, family, and clinician factors that may influence this agreement.

Methods: Cross-Sectional data from one-hundred and fifty four children, ages one to seventeen, were used for the study. Parental report of the child's ASD diagnosis was obtained from a registration form that was completed while parents were consenting to a database project at an outpatient autism clinic.Clinical diagnosis was extracted from a chart review of the patient medical records. Our chart review protocol promoted the methodological strategies proposed by Gilbert and colleagues (1996) that enhance data quality. For instance, we gave emphasis to evaluations that utilized the Autism Diagnostic Observation Schedule (ADOS; Lord, Rutter, DiLavore, & Risi, 1999), were most recent, and were part of an interdisciplinary team evaluation. When the appropriate document was identified, two reviewers independently determined the clinician's diagnostic conclusion. If these reviewers were discrepant, a master's level practitioner re-reviewed the medical record and resolved the final diagnosis; although, this was often unnecessary given the inter-rater agreement was 89% (Kappa=.85). Logistic regression models were then employed to examine the association between parental (marital status, low family income), clinician (physician vs. psychologist), and child (age, race/ethnicity) factors and diagnostic agreement.

Results: Overall, 84% of parents agreed with clinicians that their child was on the autism spectrum (sensitivity=75%, specificity=96%, ROC=.85), while 70% of these families reported the same ASD-specific diagnosis. Results from the logistic models revealed that non-white families (OR .45, $CI_{.95}$ = .21, .95) and a parent (OR .06, $CI_{.95}$ = .01, .33) or clinician (OR .13, $CI_{.95}$ = .02, .70) report of "Autism Spectrum Disorder" significantly ($p<.05$) decreased the likelihood of concordance.

Conclusions: Results from our analysis yielded a moderate to high level of accord concerning the child's specific ASD diagnosis (e.g., PDD-NOS) and a high level of agreement regarding whether the child has an ASD or not. We also found that non-white families and a diagnosis that was provided outside of the *DSM-IV-TR* (AMA, 2000) (e.g., "Autism Spectrum Disorder") increased the risk for dissonance. Although this data holds clinical and research utility, it is presently unclear why parental report did not match the results from the child's diagnostic evaluation. We suspect this could be a product of poor communication, disagreement, variability in the diagnostic presentation, and recall bias. Implications and new avenues for research will be discussed.

136.109 109 Transcriptional Analysis of Cytokines in the Cerebral Cortex of Autistic Patients. M. C. Mott*, M. F. Casanova, G. R. Fernandez-Botran, L. Sears, C. R. Tillquist and F. Crespo, *University of Louisville*

Background: Autism is an idiopathic pervasive neurodevelopmental disorder associated with an altered immunological

response evidenced by a neuroinflammatory process in the CNS of autistic individuals. Cytokines are involved in the regulation of inflammatory responses, and increased levels of certain cytokines have been demonstrated in the sera, cerebrospinal fluid, peripheral blood mononuclear cells and brain tissue in patients with autism spectrum disorder (ASD). Genotypic analyses of polymorphic sites in some cytokine genes of autistic individuals have yielded significant results, but the picture is still incomplete. Cytokine transcriptional analyses in autism should provide a better understanding of the potential role of the immune system in this disease. Objectives: The main objective of the current study was to perform transcriptional profiling of a panel of cytokine and chemokine genes in different regions of post-mortem brain tissues of autistic subjects and controls. Methods: Post-mortem brain tissue samples were provided by the Autism Tissue Program. After RNA extraction, transcriptional profiling was performed by reverse transcription - real time PCR in 5 cortical regions: BA 4, 9, 17, 22 and 46. Results: Preliminary analysis revealed that cytokine (TNF_, IL-6, TGF_1), and chemokine (IL-8) transcripts were increased in all brain regions (especially BA 46, dorsolateral prefrontal cortex) except BA 22 (superior temporal gyrus/Wernicke's area) in autism as compared with controls. Conclusions: This study reveals an up-regulation of cytokine and chemokine expression in autism in many cortical regions. We plan to expand the cytokine and chemokine panel and the sample size; but the current data suggest a heterogeneous regulation of cytokine gene transcription in autistic brains, where different brain regions show a differential inflammatory response.

136.110 110 Oxytocin Biology and Social Impairments in Autism Spectrum Disorders. K. J. Parker*[1], R. A. Libove[2], S. Hyde[1], P. Liao[1], J. M. Phillips[1], J. Hallmayer[1] and A. Y. Hardan[2], (1)*Stanford University*, (2)*Stanford University School of Medicine/Lucile Packard Children's Hospital*

Background: Impairments in social functioning are the defining, core feature of autism spectrum disorders (ASD). Although it is accepted that ASD are neurodevelopmental disorders, no widely applicable genetic or neurochemical markers with diagnostic or prognostic utility have been identified. Researchers have theorized, however, that the neurobiological systems critical for social functioning in healthy individuals are promising candidates for investigation in autism. One such candidate is oxytocin (OT), and several lines of evidence support its potential role in ASD. OT and its receptor (OTR) are critically involved in social behavior and social cognition, whereas OT and OTR impairments induced pharmacologically or through genetic manipulation produce diverse social deficits in animals. Importantly, preliminary research in multiple patient populations suggests that certain OTR single nucleotide polymorphisms (SNPs) increase risk for autism, and that plasma OT levels are lower in autistic compared to typically developing control children.
Objectives: We hypothesize that the degree of impairment in social functioning is associated with genetic OTR polymorphisms (e.g., rs53576) previously associated with autism. As part of our larger research program, we also hypothesize that variability in plasma OT concentrations is associated with differences in social functioning.
Methods: Participants included children with autism and typically developing control children. An extensive behavioral phenotype battery was completed on all subjects, and included the Social Responsiveness Scale (SRS). Autism diagnosis was based on the Autism Diagnostic Observation Schedule, Autism Diagnostic Interview Revised, and expert clinical opinion. Blood samples were collected from all subjects for DNA extraction and genotyping of OTR SNPs using standard SNP genotyping methods. Plasma aliquots were frozen for subsequent quantification of OT concentrations, and data will be presented if available.
Results: To date 90 participants have enrolled and completed the study procedures, including 43 children with ASD and 47 control children. We have analyzed SNP genotypes from the OTR for these subjects. In our initial analysis we did not detect any difference in overall social functioning for any of the OTR SNPs under investigation. However, our preliminary data indicate that the homozygous AA genotype of the OTR rs53576 is associated with increases in some social deficits as measured by the

SRS in comparison to either the AG or GG genotypes. In contrast, in the control population this AA genotype is not associated with increased social deficits.
Conclusions: These preliminary data suggest that in autistic individuals carrying the AA genotype of rs53576 may increase vulnerability to social impairments. These findings are in agreement with prior studies examining this SNP in measures of social functioning and suggest that variability in the OTR may modulate social behavior in autism. While our preliminary findings need to be replicated in a larger cohort, it is possible that a better understanding of OT biology may lead to improved prognostic and possibly therapeutic approaches in autism.

136.111 111 Genome-Wide Association Analysis of Susceptibility Genes in Autism Using with a Gene-Centric Approach. T. R. Magalhães*[1], J. Casey[2], C. Correia[1], F. Sequeira[1], M. Espada[1], S. Ennis[2], A. M. Vicente[1] and A. G. Project[3], (1)*Instituto Gulbenkian de Ciência/Instituto Nacional de Saúde Dr. Ricardo Jorge*, (2)*National Center for Medical Genetics/UCD*, (3)*Autism Genome Project*

Background: GWAS focus at the SNP-level. This is the most sensible approach if the causal variants are in LD with the same SNP for every individual; but if the causal variant is in LD with the same gene but to different SNPs, the most sensible approach is Gene-centric. Also, the noise introduced by different genetic backgrounds, which hinders the signal, is usually not factored into GWAS analysis. We suggest a GWAS analysis method that obviates these constraints. This method clusters individuals based on genetic similarity, applies an appropriate genetic association test to each cluster, ranks SNPs based on the results of the test, selects genes corresponding to top ranking associated SNPs, and then evaluates the gene overlap between population clusters. This approach will uncover otherwise missed signal if: 1) the causal variant is associated to different SNPs in different populations because of different LD patterns, 2) the causal variant is different in different populations due to a divergent evolution history.
Objectives: To find genes associated with autism, applying a Gene-centric approach to the AGP data and factoring the genetic background of the individuals into the analysis.
Methods: The AGP data set consists of 1399 trios, genotyped over 1072820 SNPs, using the Illumina technology. 18,946 genes are defined using the Illumina-based assignment. We cluster the probands based on genetic similarity in two steps: 1) run Eigensoft to obtain PCs, and 2) apply the Hopach algorithm to PCs. We then proceed to select genes in four steps: 1) apply a family-based TDT test (Plink) to each cluster-based population, 2) rank each gene by TDT p-value, 3) select the top 1000 ranked SNPs in each population, 4) select genes with top ranks SNPs in multiple populations (R). Currently we are analyzing the haplotypes of relevant gene's regions (Beagle) and investigating their differential distribution in parents vs. children (R).
Results: Our method produces eight clusters; the individuals recruited in Portugal are mostly placed into one cluster; the individuals recruited in Ireland are placed into its own cluster. This was expected since these two populations are historically the most isolated of the AGP sites. Self-reported ancestry validates the clustering results. An FST analysis for all pairs of clusters supports the results. One hundred and seventy genes were selected because:1) two or more clusters have one single SNP ranking in the top 1000 TDT-p values; we select the gene corresponding to this SNP, 2) four or more clusters have SNPs ranking in the top 1000 TDT p-values in any SNP mapping to the gene, and 3) three or more clusters have SNPs ranking in the top 1000 p-values, in a region we have defined as contiguous-high-ranked-SNPs. Included among the selected genes are axon guidance, CNS development, and autism related genes. Currently we are thoroughly analyzing the genes, investigating haplotype differential distribution in parents vs. children.
Conclusions: A Gene-centric approach and factoring genetic background into GWAS analysis uncovers genes which might be associated with autism disease; these genes would not be selected by the most commonly used TDT SNP-centric approach.

136.112 112 Prediction of SRS From Genotype in Autism. G. Guzzetta[1], G. Esposito[2], G. Jurman[1], P. Venuti[2] and C. Furlanello*[1], (1)*Fondazione Bruno Kessler - FBK*, (2)*University of Trento*

Background: Autism Spectrum Disorder (ASD) symptoms are heterogeneous and hard to discriminate in distinct subtypes. Although candidate loci have been recently identified by integration of large ASD cohorts (Wang et al. 2009), new bioinformatics methods are needed to cope with high individual variability. The l1-l2 regularization is a feature selection technique capable of generating a specific signature in biologically complex settings. It was applied to detect markers of transcriptional response of neuroblastoma to hypoxia (Fardin et al. 2009), and proposed for predicting quantitative phenotypes traits from high dimensional genetic data (Guzzetta et al 2009). Here we studied its first large scale application to whole genome association data from the AGRE research program.

Objectives: We aim to predict Social Responsiveness Scale (SRS) levels by means of a new bioinformatics platform for quantitative phenotype prediction. Although currently there is a limited coverage of the SRS phenotypes in the AGRE cohort, this is a powerful set of indicators that can be used to determine individual trajectories, the ultimate goal for our analysis. Here we set a bioinformatics experiment in which all unfiltered variant positions in the genome are used as potential markers and training is based on extreme value cases.

Methods: Given the 2,883 AGRE samples genotyped by the Broad Institute with the Affymetrix 5.0 platform (399,197 SNPs), we first identified 803 individuals with only ADI or ADOS-confirmed autism diagnosis and 1446 healthy controls not tested for ADI. Individuals having a teacher-administered SRS questionnaire were then selected, leaving 144 cases and 19 controls. We considered the highest 17 and lowest 18 SRS total scores (respectively, only cases and only controls). A linear l1l2-regularization regression model was trained on all features, using the SRS total score as target. The experiment protocol was based on the 10x5 FDA's MAQC-II procedure (5-fold cross-validation repeated 10 times). For the l1l2 parameter set having the best average R^2 score computed from CV test portions, we evaluated the Area under the Curve (AUC) for classification from real predictions (Wilcoxon Mann-Whitney) and ranked the weights corresponding to each selected SNP.

Results: AUC was 0.723 (95% CI: 0.684-0.768), with a fit of R2 = 0.237 (95% CI: 0.155-0.331). The same 51,744 SNPs were consistently selected in all experiments. Ranked by regression weights, the top 30 markers all had an average position higher than 150. Of these, 24 belong to only four regions: 3p12.2 (3), 8q21.11 (10), 11p12 (3), 11p14.1 (5), Xp11.4 (3). Near loci on chromosomes 8 and 11 had been previously identified for SRS by Duvall et al (2007). Within the top 500 SNPs, we also found 12 SNPs at loci 5p14.1 (2), 14q21.1 (4) and Xq21.1 (6) indicated as candidate markers for autism (Wang et al 2009).

Conclusions: This study represents the first application of a regression method to an autism-related quantitative phenotype. When trained on extreme values of the SRS score, the l1l2 method fairly discriminated cases from controls and explained 23.7% of variance. Moreover, selected markers were stable and consistent with literature. Top ranked markers are being investigated.

136.113 113 Genomic Imprinting of the X-Linked Gene Transketolase-Like 1 in Mouse and Human. A. M. I. Nesbitt*[1], J. J. LoTurco[1], D. H. Skuse[2], R. J. O'Neill[1] and M. J. O'Neill[1], (1)*University of Connecticut*, (2)*Institute of Child Health*

Background: Imprinting of X-linked genes has been hypothesized to contribute to the 4-fold male:female sex bias in autism. This hypothesis emerged from studies of Turner syndrome, where girls with a maternal X (45,Xm) show greater propensity to social impairment and have a higher rate of autism compared to 45,Xp females and the general population. Using a mouse model for Turner syndrome to search for X-linked imprinted genes, we and others identified the X-linked *Xlr3/4* locus as being imprinted. However, no imprinted orthologs of these genes have been found in humans. Since imprinted genes often exist in clusters, we expanded our search of this region of the X chromosome to identify genes that are imprinted in both mice and humans.

Objectives: To examine expression in developing brain of candidate imprinted X-linked genes and compare relative expression from parental alleles in human and mouse using quantitative PCR techniques.
Methods: Allele-specific quantitative real-time PCR was used to examine expression of X-linked genes in neonatal mouse and fetal human brain sub-regions.
Results: We have identified *Transketolase-like 1* (*TKTL1*) as an X-linked imprinted gene in both humans and mice. In human, differential expression of *TKTL1* varied from two to five-fold, showing sub-region specificity. *Tktl1* expression in mouse neonatal neocortex showed higher levels in 39,Xm and 40,XY mice compared to 39,Xp and 40,XX.
Conclusions: *TKTL1* exhibits imprinted expression in both humans and mice. *TKTL1* codes for a transketolase enzyme, which operates in the pentose phosphate pathway (PPP). One function of the PPP is maintaining glutathione in a reduced state by reduction of NADP to NADPH. Since aberrant glutathione levels have been found associated with autistic spectrum conditions, the effect of *Tktl1* expression on the state of glutathione in the developing brain is of current interest to our laboratory.

136.114 114 In Vitro and In Vivo Functional Characterization of the ENGRAILED 2 ASD-Associated Haplotype. J. Choi[1], S. Kamdar[1], P. G. Matteson[1], L. Brzustowicz[2] and J. H. Millonig*[1], (1)*UMDNJ-Robert Wood Johnson Medical School*, (2)*Rutgers University*

Background: Risk for ASD is likely due to both genetic and non-genetic environmental factors, with epigenetic regulation of genes providing a possible interface between genetic and environmental factors. Our previous research has focused on the homeobox transcription factor, ENGRAILED 2 (EN2). The common alleles (underlined) of two intronic EN2 SNPs, rs1861972 (A/G) and rs1861973 (C/T), are significantly associated with ASD (518 families, P=.00000035). Subsequent association, LD mapping, and re-sequencing identified the associated rs1861972-rs1861973 as the most suitable candidate to test for function. Objectives: The goal of these studies is to determine: i) whether the ASD-associated A-C haplotype is functional, and ii) if epigenetic differences function in concert with the A-C haplotype to affect EN2 regulation. Methods: In vitro functional differences were determined by Electrophoretic Mobility Shift Assays and transient transfections of luciferase reporters into primary mouse cerebellar neurons. Affinity purification followed by Mass Spectroscopy was used to identify the proteins binding specifically to the A-C haplotype. qRTPCR was employed to measure transgene levels in vivo and EN2 mRNA levels in cell lines and post-mortem samples. Bisulfite sequencing determined the methylation status of the EN2 promoter.
Results: In vitro studies using primary neuronal cultures determined the A-C haplotype results in an ~200% increase in expression (P<.0001) due to the preferential binding of transcription factors. Additional experiments demonstrated both the A and C alleles are necessary and sufficient for enhancer function. Proteomic experiments identified a seven-protein complex that binds specifically to the A-C haplotype. To extend our analysis to an in vivo system, transgenic mice were generated for the A-C and G-T haplotypes. The A-C haplotype results in ~215% increase in mRNA levels (P<.001). Environmental factors can also affect gene expression by altering epigenetic regulation. Six significant CpG islands flank human EN2, suggesting the gene may be regulated by differential methylation. We investigated this possibility by treating human neuronal cell lines with a methylation inhibitor (AZA) and a methyl donor (SAM). AZA treatment resulted in hypomethylation of the EN2 promoter and increased expression while SAM treatment results in hypermethylation and decreased levels (P<.001). EN2 levels were then quantitated in 90 human post-mortem samples. EN2 is significantly increased in affected individuals compared to controls (P<.01). Affected individuals with an A-C/A-C or A-C/G-T genotype express EN2 at the highest levels. We then investigated whether epigenetic differences could contribute to increased EN2 levels. Initial analysis indicates the EN2 promoter is methylated in unaffected individuals, while in affected individuals the same CpG dinucleotides are unmethylated.
Conclusions: These data demonstrate the A-C haplotype is functional and consistently

results in increased expression. EN2 is also epigenetically regulated and hypomethylation results in increased expression. Our post-mortem data demonstrate increased expression for EN2, and suggest the rs1861972-rs1861973 haplotype and promoter methylation function in concert to regulate EN2 levels.

136.115 115 Population- and Family-Based Studies Suggest An Epigenetic Role for the MTHFR Gene in the Etiology of Autism. X. Liu*[1], F. Solehdin[2], I. L. Cohen[3], M. Gonzalez[4], E. C. Jenkins[3], S. M. Lewis[2] and J. J. A. Holden[5], (1)*Queen's University*, (2)*University of British Columbia*, (3)*NYS Institute for Basic Research in Developmental Disabilities*, (4)*New York State Institute for Basic Research in Developmental Disabilities*, (5)*ASPIRE, Queen's University*

Background: Abnormal DNA methylation patterns have been associated with neurodevelopmental disorders, including autism. Two variants in the methylenetetrahydrofolate reductase (*MTHFR*) gene have previously been shown to affect DNA methylation levels, and both have been shown to be associated with autism susceptibility in case-control studies.

Objectives: Test for association between two functional SNPs in the *MTHFR* gene with autism spectrum disorders (ASDs).

Methods: The C677T (*rs1801133*) and A1298C (*rs1801131*) polymorphisms were studied in 205 North American families with a single child with an ASD (simplex: SPX). Both family-based and case-control association studies were performed.

Results: Case-control comparisons revealed a significantly higher frequency of the low-activity 677T allele (*P=0.0004*), higher prevalence of the 677TT genotype (*P=0.0016*), marginally higher frequency of the 1298A allele (*P=0.059*) and a trend towards increased prevalence of the 1298AA genotype (*P=0.124*) in autistic probands from SPX families versus controls. Analysis of combined genotypes revealed a significantly higher frequency of the double homozygous 677TT/1298AA genotype (*P=0.007*) and the 677T-1298A haplotype (*P=0.0004*) in affected individuals relative to controls. Family-Based Association Testing (FBAT) demonstrated significant transmission disequilibrium of both SNPs, with an excess transmission of the 677T (*P=6.5 X 10-5*) and 1298A (*P=0.015*) alleles and the 677T-1298A haplotype (*P=9.1 X 10-5*) from parents to affected offspring.

Conclusions: The results of both the population-based and family-based studies suggest that reduced *MTHFR* activity serves as an epigenetic risk factor for autism in families with isolated cases.

136.116 116 Positive Association of Engrailed 2 (EN2) Gene with Autism in the Indian Population. B. Sen*[1], A. S. Singh[1], S. Sinha[1], A. Chatterjee[1], S. Ahmed[2], S. Ghosh[3] and R. Usha[1], (1)*Manovikas Kendra Rehabilitation & Research Institute for the Handicapped*, (2)*Assam Autism Foundation*, (3)*Indian Statistical Institute*

Background: *Engrailed 2* (*EN2*) is located on chromosome 7q36.3, a genomic region linked to ASD and developmental language disorder, and has been implicated in the patterning of cerebellum during development. Studies on $En2^{-/-}$ mice indicate the role of *En2* in midbrain and cerebellum development as these mice display cerebellar hypoplasia, reduction in Purkinje cells with markedly reduced cerebellum and alterations in cerebellar serotonin levels. They also show impaired motor learning in the rotarod and complex socio-behavioral changes. Such deficits are reminiscent of symptoms observed in autistic individuals. *Engrailed* genes are necessary for serotonergic neuron development and defects in the serotoninergic system have been implicated in autism. Therefore, *EN2* is considered a candidate gene for autism.

Objectives: The main focus is to investigate genetic association of *EN2* with autism in the Indian population.

Methods: Autistic probands were recruited following DSM-IV criteria and CARS as the diagnostic instrument. The markers included are rs6150410 [9bp Ins/Del variant] and rs34808376 [GC/- Ins/Del polymorphism] in the *EN2* promoter, rs3735653 (C/T) in exon 1, and two SNPs rs1861972 (A/G) and rs1861973 (C/T) in the intron. Genotyping was carried out by RFLP analysis following PCR. We used TDTPhase from the UNPHASED programme suite (version 2.403) for family-based association analysis. Pairwise linkage

disequilibrium (LD) was computed with Haploview (version 4.1). "TFSearch" was used for identifying putative transcription factor binding sites.

Results: Since the two intronic SNPs are in absolute LD in this population, only one marker, rs1861973 was included for statistical analysis. We observed significant preferential transmission of the C allele of rs1861973 (hence A allele of rs1861972) from parents to the affected offspring (LRS=6.63, GS=0.006). Interestingly, the bias was highly significant for female offsprings (LRS=7.36, GS=0.0025). The study also revealed over-transmission of the Ins allele of rs6150410 (LRS=3.68, GS=0.03) and C allele of rs3735653 (LRS=3.4, GS=0.044) from mothers to affected sons. Significant transmission of the Ins allele from fathers to affected sons was noted for rs34808376 (LRS=3.4, GS=0.04). Comparatively strong LD was observed between different pairs of markers except for rs34808376 and rs3735653. The haplotype analysis demonstrated association of haplotypes formed between rs34808376-rs1861973 markers with autism. Based on these results, we investigated whether the SNPs impart any regulatory role during transcription. We identified a putative Sp1 transcription factor binding site in case of rs1861973 when the autism-associated C allele was present. In case of the Ins allele of rs6150410, we observed generation of three additional putative transcription factor binding sites.

Conclusions: The present study confirms in the Indian population previous results identifying the *EN2* intronic SNP rs1861973 as an autism risk allele in other populations, and extends these results by identifying a sex-specific allelic transmission pattern that confers especial risk in females – a finding not reported earlier. Specific maternal/paternal transmission bias indicates possibility of genomic imprinting in the etiology, and imprinted regions have been identified in chromosome 7q. Bioinformatic analysis suggests that rs1861973 may exert its effect via transcriptional regulation of *EN2*. The current study suggests sex-specific involvement of *Engrailed 2* gene in autism pathology in the Indian population.

136.117 117 Linkage On Chromosome 7 for Language Onset in Utah Pedigrees. M. Villalobos*, D. Cannon, G. Miles, J. Miller, N. Wahmoff, R. Robison, W. M. McMahon and H. Coon, *University of Utah*

Background: Language onset is an integral part of an ASD diagnosis. Previous studies have examined the genetic linkage of language onset in ASD and found linkage on both chromosomes 7 and 15 (Bishop, 2009).

Objectives: The aim of the present study was to conduct a linkage analysis using language onset for chromosome 7 in our sample of multiplex and extended pedigree families with ASD.

Methods: Participants were members of 70 pedigrees having at least 2 family members with ASD. A total of 653 family members were genotyped using the Center for Inherited Disease Research 6k Illumina Linkage Panel 12. 178 genotyped family members had language onset data (age at first words and age at first phrases) from the ADI-R. Of these affected subjects, 92 had delayed onset of words and 102 had delayed onset of phrases. Although there was substantial overlap (78 subjects showed delay for both words and phrases), 24 subjects showed only phrase delay, and 13 showed only delay of words. Linkage analyses were done using MCLINK multipoint linkage software. We performed nonparametric multipoint linkage analyses considering the traits as both qualitative and quantitative variables.

Results: Language traits showed some evidence for linkage on chromosome 7 at 121 – 135 cM. This is the location of a linkage peak found in our families for clinical affection status, and also using the Social Responsiveness Scale (SRS). However, linkage using the language variables at this location was diminished (HLOD=0.60 at 129 cM for word delay; HLOD=1.46 at 129 cM for phrase delay) in comparison to the clinical variables (HLOD=1.97 at 129cM for diagnosis; HLOD=2.55 at 133 cM for SRS). In contrast, linkage signals were stronger for the language variables in a more centromeric region at 55 cM – 68 cM (HLOD=1.96 at 57 cM for word delay; HLOD=1.54 at 63 cM).

This region was not of great interest for clinical diagnosis in our families (HLOD=0.51 at 62 cM for diagnosis; HLOD=1.12 at 57 cM for SRS). Analyses using the language variables as quantitative traits are in progress.

Conclusions: Our peak at 121-135 cM using clinical diagnosis and SRS is consistent with multiple previous findings on chromosome 7 for autism diagnosis and language onset in autism. However, in our families the use of language delay variables did not strengthen this signal. Interestingly, the language variables suggest a peak on 7p at 55 cM – 68 cM. This peak overlaps with our previous study of a single 6-generation extended autism pedigree (Allen-Brady, et al., 2009), and also with several genetic studies of ADHD (Bakker, et al., 2003; Neale, et al., 2008; Zhou, et al., 2008). Our results suggest that language onset may provide a useful tool to identify chromosomal regions that may contain autism susceptibility loci.

136.118 118 Genomic Copy Number Variation in Pediatric Patients with Autism Spectrum Disorders. E. A. Varga*[1], D. Lamb-Thrush[2], C. Astbury[2], R. Pyatt[2], S. Reshmi[2], J. Gastier-Foster[2] and G. E. Herman[1], (1)*The Research Institute at Nationwide Children's Hospital*, (2)*Nationwide Children's Hospital*

Background: Microarray-based comparative genomic hybridization (aCGH) is increasingly utilized in the genetic evaluation of children with autism spectrum disorders (ASDs). There is some controversy regarding the use of oligonucleotide arrays in clinical practice, as testing with this level of resolution may increase detection of likely benign copy number variation (bCNV) or CNV of unknown significance (uCNV), but not necessarily pathogenic CNVs (pCNVs).
Objectives: To describe our clinical laboratory experience in offering aCGH testing for an indication of ASD and determine if choice of array platform impacts number of bCNVs, uCNVs and pCNVs reported.
Methods: Our cytogenetics and molecular genetics laboratory performed aCGH on 530 unique subjects for a clinical indication of ASD between 1/1/2007 and 6/30/2009. Various aCGH platforms were used including bacterial artificial chromosome (BAC) arrays containing 600, 1887, and 4670 probes and an oligonucleotide (oligo) array containing 105,000 probes. To interpret the significance of CNVs, we evaluated the size and type of the rearrangement (deletion vs. duplication), inheritance and gene content. Insights were gained from the literature where possible and from databases, including the Database of Genomic Variants, the UCSC Genome Browser, and an internal institutional CNV database.
Results: Of 530 subjects, 320 (60%) were tested on a BAC aCGH and 210 (40%) were tested on an oligo aCGH platform. Four subjects were tested to clarify abnormalities identified previously on chromosome analysis and were excluded from subsequent analysis. Of the 526 subjects remaining, 129 (25%) had a reported CNV. Fifty-two of these (40%) were interpreted as a bCNV; 57 (44%) had at least one uCNV; and 20 (16%) had at least one pCNV. Twenty-one subjects (16%) had >1 reported CNV. Significantly more abnormalities were reported on oligo aCGH compared to BAC array (68/210 vs. 61/320, $p<0.001$), likely due to the fact that significantly more bCNVs were reported on oligo vs. BAC array (32 vs. 20, $p<0.001$). The number of reported uCNVs and pCNVs did not differ between array types (uCNV= 29 oligo vs. 28 BAC, $p>0.10$; pCNV= 7 oligo vs. 13 BAC, $p>0.50$). Recurrent pCNVs included a duplication (dup) and two deletions (del) of 22q11.21 (DiGeorge region); del and dup1q21.1, and 2 duplications of Xq28 including the *MeCP2* gene. Other pCNVs contained genes previously implicated in autism including, but not limited to, *NRNX1, NLGN4, SHANK3, ELN*, and *CNTN4*.
Conclusions: Our findings suggest that both BAC and oligo aCGH testing of subjects with ASD is beneficial to identify pCNVs, which may assist in genetic counseling. Further investigation of uCNVs, found in a large proportion of our population, may help delineate genes and molecular pathways which play a role in ASD susceptibility. Our laboratory experience confirms that more bCNVs may be reported on oligo array compared to BAC arrays.

136.119 119 ITGB3 Gene Variants Double the Risk of An Autism Spectrum Disorder Diagnosis. R. Sacco[1], F. Lombardi[1], P. Curatolo[2], B. Manzi[2], R. Militerni[3], C. Bravaccio[4], C. Lenti[5], M. Saccani[5], K. Fontaine[6], F. Rousseau[6], P. Lewin[6] and A. M.

Persico*[1], (1)*Univ. Campus Bio-Medico*, (2)*Tor Vergata University*, (3)*II Univ. of Naples*, (4)*University Federico II*, (5)*Univ. of Milan*, (6)*IntegraGen*

Background: Genetic factors provide significant contributions to the etiology of autism spectrum disorders. The ITGB3 gene, located on human chr. 17q21.32, encodes integrin beta 3 (also known as glycoprotein IIIa or GP IIIa), the beta subunit of the platelet membrane adhesive protein receptor complex GP IIb/IIIa. The integrin beta 3 (*ITGB3)* and serotonin transporter (*SLC6A4)* genes were both identified as quantitative trait loci (QTLs) for serotonin blood levels. Alleles at the ITGB3 and SLC6A4 loci may contribute to autism susceptibility.
Objectives: We aimed at assessing the association between ITGB3 gene variants and autism spectrum disorders. In addition, we also analyzed the influence of ITGB3 gene variants on serotonin plasma levels.
Methods: Our sample includes 281 simplex and 12 multiplex families, encompassing 306 patients with an autism spectrum disorder. Nine SNPs spanning the ITGB3 locus were genotyped using SNPlex and TaqMan technologies. Family-based association analyses were performed using FBAT and UNPHASED.
Results: One ITGB3 haplotype is significantly associated with autism (HBAT, global $P<0.05$) and doubles the risk of affection (O.R.=2.11, $P<0.01$). The "risk" and "protective" haplotypes differ only by a single SNP, rs12603582, which analyzed by itself reaches P-values of 0.071 and 0.056 with FBAT and TDT, respectively. Effects of ITGB3 alleles and ITGB3-SLC6A4 interactions on serotonin blood levels do not reach statistical significance ($P=0.12$).

Conclusions: Family-based association analysis shows that in our sample one ITGB3 gene variant determines an approximately 2-fold increase in risk of developing autism. These results provide further evidence of ITGB3 involvement in autism spectrum disorders. Further analyses are underway to assess ITGB3-SLC6A4 interactions in reference to affection status.

136.120 120 Importance of in Depth Genotyping for Chromosome 15q13.3 and CHRNA7 in Evaluation of AUTISM, Mental Retardation, Schizophrenia, Bipolar Disorder, and Epilepsy.

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Background: Deletions of chromosome 15q13.3 of 1.6 or 0.68 Mb are associated with autism, mental retardation, schizophrenia, bipolar disorder, and epilepsy with incomplete penetrance. Both deletions inactivate the *CHRNA7* nicotinic receptor gene, and haploinsufficiency for this gene likely contributes to these phenotypes. Approximately reciprocal duplications of 1.6 and 0.43-0.68 Mb also occur with the latter being quite common in some control populations. There are common polymorphisms of the region including inversions and variable copy number for a *CHRFAM7A* fusion gene with or without a 2-bp deletion in exon 6.

Objectives: In autism and other neurobehavioral phenotypes, to determine the molecular heterogeneity and pathogenic effects if any for the 1.6 and 0.43-0.68 Mb duplications, to search for functionally significant point mutations in *CHRNA7*, and to evaluate the clinical significance of inversions within 15q13.3 and of any variation in the *CHRFAM7A* fusion genotype,

Methods: Array comparative genomic hybridization (CGH), MLPA, FISH and DNA sequencing are being used to compare samples from individuals with autism and other phenotypic abnormalities to controls.

Results: The deletions and duplications were observed at decreasing frequency from 0.43-0.68 Mb duplication, to 1.6 Mb deletion, 1.6 Mb duplication, and 0.68 Mb deletion in a series of ~10,000 pediatric samples submitted for clinically indicated array CGH studies. Phenotypes of mental retardation, developmental delay and/or autism were common in the deletion and duplication samples. Although the deletions are very likely pathogenic, any harmful effects of the duplications remain to be determined based in part on additional studies of control samples. MLPA provides reliable copy number information for exons 2 and 4 which are unique to *CHRNA7* and for exons 5 and 10 which are common to *CHRNA7* and the

CHRFAM7A fusion gene. PCR assays were developed to detect the presence or absence of the 2-bp deletion in exon 6 of the fusion gene or the functional gene. DNA sequencing using a first step of long range PCR to distinguish exons 5-10 of the *CHRNA7* gene detected two *de novo* missense mutations, many inherited missense mutations, and one nonsense mutation.

Conclusions: Loss-of-function mutations in *CHRNA7* likely account for most of the phenotypic consequences seen with deletions of 15q13.3. It remains unknown whether the *CHRFAM7A* gene produces a stable fusion protein with any function, although its structure would be impacted by the 2-bp deletion in exon 6. Similarly it is unknown whether the various duplication mutations result in over-expression of the normal *CHRNA7* protein or in some cases may produce transcripts subject to nonsense mediated decay and/or produce truncated proteins with dominant negative effects. In depth genotypying for 15q13.3 requires, array CGH or another general method for copy number assessment best supplemented with MLPA to determine copy number for *CHRNA7* and *CHRFAM7A*.Tiling arrays show some heterogeneity of the common 0.68 Mb duplications suggesting the possibility of functional heterogeneity in this class of duplication. In addition, sequencing of *CHRNA7* is important for detection of point mutations associated with autism and other neurobehavioral abnormalities.

136.121 121 Using Ingenuity Pathway Analysis to Study Gene Relationships Under Linkage Peaks of Interest in ASD. A. Hare*[1], M. Azaro[1], V. Vieland[2], J. Flax[1] and L. Brzustowicz[1], (1)*Rutgers University*, (2)*The Research Institute at Nationwide Children's Hospital*

Background: Over the past 10 years there has been compelling evidence supporting a genetic basis for autism using a combination of behavioral family studies and genetic linkage and association studies. Of particular interest for several research groups has been the attempt to define and then replicate significant linkage signals using language-based phenotypes in ASD probands with the outcome objective of finding genes that are associated with a language phenotype.

Objectives: While several linkage and association studies have used onset of first words and phrases as potential phenotypes, we suggest that there is a subset of individuals with and without ASD who have an expressive language impairment that is beyond the scope of tracking the onset of language. We have already identified strong linkage peaks based on two such behavioral phenotypes and are now defining the peaks and investigating genes of interest under each peak.

Methods: All individuals from the Autism Genetics Resource Exchange (AGRE) who received an ADI-R and had 550K genetic data available were included in our analyses regardless of their final ASD status. Variables used to develop two speech/language phenotypes were derived from specific items on the Autism Diagnostic Interview (1995, 2003).Linkage analyses were performed using the Posterior Probability of Linkage (PPL). A broad definition was used to define each linkage peak, including the entire contiguous region with PPL greater than the baseline of 2%. Genes under these regions were identified using the UCSC Genome Browser (NCBI Build 36.1). Ingenuity Pathway Analysis software (v. 7.0) was used to identify known relationships among the genes identified in the linkage regions. Relationships between these genes and other genes reported as Autism Susceptibility Genes (ASG) were also identified.

Results: Regions of linkage were identified for both phenotypes. NRXN3 was identified within the linkage region on Chromosome 14. IPA identified a direct binding relationship of NXRN3 to NLGN3, which was identified by IPA as an ASG. NXPH3 was identified within the linkage region on Chromosome 17 and IPA identified a direct binding relationship to NRXN1, an IPA identified ASG. Relationships between PTEN, another identified ASG, and 5 genes located within the linkage regions on Chromosomes 4, 5, 14, and 17 were identified with IPA.

Conclusions: Linkage analyses using the PPL algorithm has revealed several suggested regions of linkage for two unique language

phenotypes associated with ASD and other disorders with a language component. We have demonstrated that IPA software can be used as a useful method of prioritizing susceptibility loci by identifying relationships between specified molecules and thus allow us to narrow and refine further analyses.

136.122 122 Two Major Possible Mechanisms Emerge for Maternally Acting Gene Alleles That Contribute to Autism and Other Neurodevelopmental Disorders. W. G. Johnson*[1], S. Buyske[2] and E. S. Stenroos[1], (1)*UMDNJ - Robert Wood Johnson Medical School*, (2)*Rutgers University*

Background:

Multiple genes contribute to the clinical phenotype of autism and other neurodevelopmental disorders. The effects of these genes may be modified by environmental factors. Genes contributing to neurodevelopmental disorders are usually thought of as acting in the affected individual, i.e., the child or adult with the neurodevelopmental disorder. Here, an additional class of genes is considered, maternal genes that act in the mother to contribute to the phenotype of her affected offspring, i.e., maternally acting gene alleles. These alleles act in the mother most likely during pregnancy to alter development of the embryo or fetus, e.g., brain development in the affected children. These maternal genes may interact with fetal genes and with environmental factors. A number of maternally acting gene alleles have been identified in autism and other disorders, mostly neurodevelopmental disorders.

Objectives:

To determine whether maternally-acting genes fall into many unrelated categories or whether there are a smaller number of unifying mechanisms. Any unifying mechanisms identified could have relevance for the pathogenesis of autism and could be targets for developing treatment for autism.

Methods:

We identified reports of maternal genetic effects and excluded those that resulted from: maternal environmental effects on the fetus; maternal environmental effects interacting with a fetal genotype; mitochondrial genes, since they do not segregate; microchimerism; or genomic imprinting. We included maternally-acting gene alleles that affected the phenotype of the embryo or fetus. We determined possible mechanisms of action, understanding that genes may have more than one mechanism and considering the possibility of ascertainment bias.

Results:

Among 44 reports of maternally-acting gene alleles: 15 involved folate-related genes, 12 involved detoxification genes, 12 involved immune-related genes, 3 involved lipoprotein genes; 2 did not fit these categories. 5 reports involved maternally acting gene alleles in autism.

Conclusions:

Among 44 reports of maternally-acting gene alleles, nearly all involved neurodevelopmental disorders. 15 involved folate-related genes. 24 involved genes that could contribute to oxidative stress, raising the question of whether oxidative stress of maternal origin during gestation might be a significant contributor, along with folate-related mechanisms, to the phenotype of neurodevelopmental disorders, including autism.

We expected to find that the reports of maternally-acting alleles would implicate a large number of unrelated mechanisms, but to the contrary the results so far could potentially be grouped into two major mechanisms, both with implications for treatment.

All 5 reports so far of maternally acting gene alleles in autism have involved genes that can contribute to oxidative stress. No study of maternally acting folate-related gene alleles has yet been reported for autism – this area appears to be understudied.

Thus, since maternally acting gene alleles in oxidative stress pathways have been linked to autism, they may be targets for treatment of autism during gestation. If maternally

acting gene alleles in folate-related pathways could be linked to autism, these could also be targets for treatment of autism during gestation.

136.123 123 Molecular Analysis of Multiplex , Highly Inbred ASD Families in Saudi Arabia. M. Aldosari*, L. J. Al-Sharif, D. S. Khalil, J. M. Shinwari, A. Almuslamani, M. Nester, B. F. Meyer, H. Khalak and N. A. Al Tassan, *King Faisal Specialist Hospital and Research Center*

Background:

Autism Spectrum Disorders (ASD) represents a genetically complex developmental disorder. Several approaches have been used to find candidate genes linked to/ or associated with ASD. These include genome wide scans, linkage studies of multiplex families, cytogenetic studies and copy number variation [CNV]. These different approaches have yielded a number of associated and susceptible genes and high risk loci. Single base pair substitutions in *NLGN3*, *NLGN4*, *SHANK3* and *PTEN* genes were identified in rare cases of ASD with different degrees of severity. Whole genome screening in multiplex families shows that several genes (2-10 genes) may interact to generate the clinical phenotype.

Objectives:

Utilize whole genome scanning methods in highly inbred families with two or more affected members to map susceptibility loci for Autism Spectrum Disorders.

Methods: This is a report from an ongoing approved research project of studying multiplex ASD families in Saudi Arabia using Affymetrix GeneChip® Human Mapping Arrays. We have so far recruited 13 families with 2-4 affected individuals per family. The diagnosis of ASD was established by two independent evaluations by experienced clinicians utilizing DSM-IV criteria. In addition, many individuals underwent evaluations using Autism Diagnostic Observational Schedule (ADOS) module I and / or Autism Diagnostic Interview – Revised (ADI-R). Children were also evaluated by a multidisciplinary team specialized in evaluating children with ASD.

Results:

Analysis of 250K microarray data on both affected and unaffected individuals from each family independently revealed a number of loci in these families in which some may represent novel loci. Our data confirms the genetic heterogeneity and complexity of the disorder.

Conclusions:

The large number of loci and chromosomes associated with ASD fit the model for a complex genetic syndrome, in which more than one locus may contribute to high risk and increased susceptibility to a broad spectrum phenotype. The current and recent reported studies suggest that whole genome scanning methods in highly inbred families are of high yield and might lead to the discovery of new susceptibility genes for ASD which will help in clarifying the biological basis for ASD.

136.124 124 Molecular Investigation of An Autism Risk Region On Chromosome 12. H. N. Cukier*[1], I. Konidari[1], M. Y. Rayner-Evans[1], D. Ma[2], R. K. Abramson[3], H. H. Wright[3], J. Haines[4], M. L. Cuccaro[1], J. Gilbert[5] and M. A. Pericak-Vance[2], (1)*University of Miami*, (2)*Hussman Institute for Human Genomics*, (3)*University of South Carolina School of Medicine*, (4)*Vanderbilt University*, (5)*University of Miami Miller School of Medicine*

Background: There is a strong genetic component to autism, but studies to date have demonstrated that the underlying genetic architecture is complex, with numerous genes potentially involved. One strategy for uncovering these genes is the use of large, extended families with multiple, distantly related, affected individuals. Our previous genome-wide linkage study identified a 4 centimorgan region (75-79 cM) on chromosome 12 that demonstrated significant linkage (HLOD = 4.51) across eleven extended multiplex families with only male affected individuals.
Objectives: Our goal is to comprehensively evaluate the chromosome 12 candidate region in order to identify the genetic abnormalities that underlie the strong autism linkage peak. We anticipate that this genetic abnormality will confer a moderate autism risk due to its presence in these large, extended families.

Methods: We are currently using both traditional Sanger sequencing and next generation, deep re-sequencing to identify potential causative variants. Sanger sequencing is used to identify variants in known and well annotated genes, while the Illumina Genome Analyzer II will be utilized to identify all potential variants across the entire approximately 4 Mb candidate region. Sanger sequencing was performed on 12 autistic individuals in 8 distinct families that define the region, as well as 10 control Caucasian individuals for 20 of the annotated genes in the minimal shared region (60,710,030-64,239,801 bp).
Results: Preliminary sequencing results failed to show variations of interest in 8 genes while the remaining 12 genes demonstrate one or more alterations that warrant further investigation: *CAND1, CPSF6, FAM19A2, GNS, GRIP1, IRAK3, KIAA0984, MON2, RASSF3, TBK1, USP15,* and *XPOT*. Variations in the genes of interest included both synonymous and nonsynonymous changes and alterations identified only in affected individuals. For example, 26 variants were found in *MON2*, 16 of which fell in intronic regions, 3 within the UTR regions and, for those that fell in exons, 3 caused missense changes and 4 were silent alterations. Two of the intronic alterations were only found in affected individuals. Deep re-sequencing using the Illumina GA II next-generation sequencing system in combination with SureSelect sequence capture (Agilent) of the minimal candidate region to completely catalogue variation in these families is currently underway.
Conclusions: Studies are ongoing to determine if any identified single nucleotide or copy number variations within the chromosome 12 region of interest plays a role in the etiology of ASD.

Neurophysiology Program

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136.042 42 A Longitudinal Study Using ERPS to Predict Later Outcome in Toddlers with Autism. S. Coffey-Corina*[1], D. Padden[2] and P. Kuhl[2], (1)*University of California, Davis*, (2)*University of Washington*

Background: Language/communication deficits and social impairment are key components of Autism Spectrum Disorder (ASD). Event related brain potentials (ERPs) have been shown to be sensitive measures of differences in speech processing abilities of 3 year olds with typical development (TD) and ASD (Kuhl, et al., 2005). ERP measures of word processing have also been related to differences in language abilities in TD toddlers (Mills, et al., 1997).

Objectives: Our goals were to use ERP measures of word processing in a longitudinal study to (1) investigate differences in patterns of ERP response to words by TD children and children with ASD; (2) study the relationship between ERP measures and later outcomes in children with ASD (cognitive, language and social domains); and (3) examine the development of the ERP response over time in TD children and children with ASD.
Methods: Participants were children with ASD and age-matched TD controls. ERPs and behavioral measures of cognitive, language, and social function were collected at 18-30 months (T1) and again at 4 years (T2). ERPs were recorded using 22 channel electrocaps with standard 10/20 arrangement. Stimuli consisted of 3 word types: words known to the child, unknown words and backwards words (known words reversed). Parents of participants signed an informed, University IRB approved consent form prior to study participation.
Results: Significant differences in patterns of ERP latency and amplitude were observed at T1 and T2 between TD's and children with ASD, and between high functioning (HF) and low functioning (LF) children with ASD. In general TD children show a more focused response to known and unknown words, with a differential left temporal response to known and unknown words at T1. They exhibited a significantly smaller, less negative response to words at bilateral temporal (compared to frontal and parietal), at T2. Children with

ASD show a broadly distributed response across electrode sites for known and unknown words at both ages. HF children with autism exhibited a more localized response to words, similar to that of TD controls. LF children with ASD had more diffuse patterns of response. In addition, T1 ERP measures from children with ASD were significantly correlated with measures of language, IQ and severity of autism symptoms collected two years later at T2: mean amplitudes and peak latencies of known words at T1 predicted behavior scores at T2 (Coffey-Corina, et al., 2008).

Conclusions: In general, HF children with ASD exhibited more localized ERP response, similar to TD controls. LF children with ASD had more diffuse patterns of response. Significant predictive correlations were obtained between ERPs to known words and various measures of language, cognition/adaptation, and severity of autism symptoms obtained 2 years after ERP testing. Further research using brain measures of speech processing in children with ASD and TD controls is important to theory building and to understanding the nature of the relationship between the linguistic and social deficits which are characteristic of autism, and may have implications for diagnosis and treatment in children with developmental disabilities that involve language.

136.043 43 Atypical Pupillary Light Reflex in Children with Autism Spectrum Disorders. C. Daluwatte*[1], X. Fan[2], J. H. Miles[1], T. N. Takahashi[1] and G. Yao[2], (1)*University of Missouri*, (2)*Univeristy of Missouri*

Background: Pupillary light reflex (PLR) refers to the involuntary pupillary responses induced by a transient light stimulus. No comprehensive study has previously been conducted to assess PLR in children with autism spectrum disorders (ASDs).
Objectives: To compare PLR responses in children with an ASD with those in typically developing children.
Methods: A computerized binocular pupillography was used to measure transient PLR in 29 children with autism spectrum disorders (age 12.2 ± 4.4 years, 2 females and 27 males), including 12 with autistic disorder, 12 with Asperger's syndrome and 5 with PDD-NOS. The same tests were also conducted in a control group of 44 typically developing children (age 10.4 ± 2.7 years, 23 females and 21 males). The PLR was induced using a 100 ms light stimulation under both light- and dark-adapted conditions. Five basic PLR parameters, the resting pupil diameter, the latency (delay from stimulus onset to the beginning of constriction), relative constriction amplitude (ratio of pupil constriction to resting pupil size), constriction velocity and redilation velocity were calculated from the PLR profiles for quantitative analysis.
Results: We found that participants with an ASD showed significantly longer PLR latency ($p < 0.0001$), smaller relative constriction amplitude ($p < 0.05$), lower constriction velocity ($p < 0.05$) and lower redilation velocity ($p < 0.05$) than children with typical development. In addition, the variance in resting pupil diameters of children with an ASD was significantly larger ($p < 0.0001$). A discriminant analysis with cross-validation indicated that 90.3% of the participants were correctly classified by using PLR latencies alone. The cross-validated classification rate was further improved to 94.4% by using both resting pupil diameter and PLR latency. Further detailed analysis suggested that the observed group differences were not affected by gender, age and IQ.
Conclusions: We found that children with an ASD showed significantly different PLR responses from those with typical development. Further investigations are necessary to understand the implications of these findings and to explore the originations of the observed differences.

136.044 44 Auditory Evoked Fields Abnormalities in Children with Sensory Processing Differences Using Magnetocephalographic Imaging (MEG-I). S. S. Hill*[1], A. M. Findlay[2], S. Honma[2], A. Bernard[3], L. B. N. Hinkley[2], S. Nagarajan[2] and E. Marco[1], (1)*UC San Francisco*, (2)*University of California, San Francisco*, (3)*University of Denver*

Auditory Evoked Fields Abnormalities in Children with Sensory Processing Differences Using Magnetocephalographic Imaging (MEG-I)

Susanna Hill, Anne Findlay, Susanne Honma, Anne Bernard, Leighton Hinkley, Srikantan Nagarajan, Elysa Marco, MD

Background: Atypical sensory processing in the auditory domain are ubiquitous in children with and without autism. These sensory difficulties likely contribute to communication and social deficits. We have recently found that children with sensory processing differences show atypical connectivity during rest in brain areas specialized for higher order integration. We used magnetoencephalographic imaging (MEG-I), a functional imaging tool with millisecond temporal resolution and millimeter spatial localization, to measure auditory evoked fields (AEFs) in children with sensory processing difficulties and matched controls. Examination of AEFs may contribute to understanding how latency and amplitude differences in sound awareness and can serve as a diagnostic tool and measure of intervention response in affected children.

Objectives: We hypothesized that children with sensory processing differences (SP) would have atypical sensory responses to simple auditory stimuli manifesting in differences in latency, amplitude, or both relative to matched healthy controls (HC).

Methods: Brain responses to a monaurally presented -45dB auditory tone were recorded for the SP group (n=10, mean age=10.6 years) and the HC group (n=10, mean age=10.0 years) using a 275-channel whole-head MEG at a sampling rate of 1200Hz. Epochs of 900ms (400ms pre-stimulus) were collected in each subject. For evoked field analysis, MEG sensor data was bandpass filtered (2-40Hz) and averaged in each subject. This study examined latency and amplitude (root mean squared; RMS) of the M50, M100, and M200 peaks. Comparisons between groups were made using unpaired two-tailed t-tests. Receiver Operator Characteristic (ROC) curves were plotted using the RMS values to evaluate the applicability of this measure for predicting sensory behavior.

Results: Robust auditory evoked field peaks were identified in the HC and the SP groups. The SP group showed significantly reduced M100 amplitude in the left hemisphere and reduced M200 amplitude bilaterally ($p<0.05$). The ROC analysis showed that the M200 left hemisphere RMS values were the best predictor of sensory behavior (area under the curve (AUC)=0.89), followed by the M200 right hemisphere (AUC=0.86), and then the M100 left hemisphere (AUC=0.8).

Conclusions: Our results suggest that children with sensory processing difficulties have measurable and reduced auditory-evoked responses in the left hemisphere at M100 and in both hemispheres at M200 following simple auditory stimuli. Furthermore, these data were obtained via a non-invasive technique not requiring patient participation and may serve as good diagnostic predictors of atypical sensory processing.

136.045 45 Autistic-Like Behaviors, Social Personality Characteristics, and Neural Correlates of Face Perception in the General Population. E. Kilroy*[1], C. Cheung[2], D. Perszyk[1], L. Mayes[1] and J. McPartland[1], (1)*Yale Child Study Center*, (2)*Yale University*

Background: Anomalies in behavioral and neural aspects of face perception have been observed in individuals with autism spectrum disorder. Atypical face processing has also been detected in the broader autism phenotype, including undiagnosed parents and infant siblings of children with ASD. It is not yet understood to what extent neural markers of face perception reflect autistic-like traits in the general population. The current study measured autistic behaviors in college students and examined interrelationships among (a) subthreshold autistic symptomatology, (b) personality characteristics, and (c) neural correlates of face perception.

Objectives: To examine correlations among subthreshold autistic traits, personality characteristics, and electrophysiological indices of face perception.

Methods: Event-related potentials (ERPs; 128 channel Geodesic Sensor Net) were recorded from medically and neuropsychiatrically healthy university students during passive viewing of upright and inverted face stimuli. Peak amplitude and latency were extracted

for a negative component at approximately 170 milliseconds over lateral posterior scalp (N170). Autistic traits were measured via self-report with the Autism-Spectrum Quotient (AQ), and personality characteristics were measures with the Eysenck Personality Questionnaire (EPQ).

Results: Overall AQ score was correlated with EPQ extroversion score, such that higher levels of autistic behavior were associated with reduced extroversion ($r(15) = -.692$ $p < .01$). Perusal of AQ subscales indicated that extroversion was related specifically to the Social Skills domain ($r(15) = -.800$ $p < .01$). Preliminary analyses reveal significant correlations among N170 latency and AQ subscales.

Conclusions: Results concord with the theory that autistic-like traits represent a normal distribution, encompassing both typical and clinical levels of social ability and disability. Social personality characteristics and face processing differences were associated with autistic traits in typically-developing college students. Higher levels of autistic behavior and lower social skills were more common among individuals showing low levels of extroversion. Temporal processing of faces, as reflected in N170 latency, was associated with associated with degree of autistic-like behavior. Analyses in progress will investigate relationships among neural correlates of face perception and a broader range of behavioral traits and personality characteristics.

136.046 46 EEG Coherence and Social Behavior in Children with Autism Spectrum Disorders. 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 result from disturbance in a ventromedial "social brain" circuit and the frontal lobe. As social processing requires the integration of various brain areas, understanding how these regions interact is imperative. EEG coherence, or connectivity, is a marker of interaction between brain regions, providing insight into how they communicate during social interactions. Also, connections between neural measures and behavioral symptoms are important for developing interventions for autism. Objectives: This research explores EEG coherence between brain regions in children with autism during baseline, familiar person, and unfamiliar person video conditions. Coherence is related to parent report of behavioral symptoms of autism. Methods: Eighteen children with high-functioning autism (ASD), ages 8-12 (mean age 10.06; 17 males), viewed a baseline condition, a video of an unfamiliar person and a familiar person reading a story. Thirteen typically developing children (TYP) (mean age 9.92; 10 males) were tested for comparison. Brain activity in the frontal and parietal-temporal lobes was measured utilizing EEG. A 64-channel electrode cap collected data, which was analyzed using the Scan 4.3 program. Coherence was computed between electrodes in the frontal and right parietal-temporal lobes, frontal and left parietal-temporal lobes, and right and left frontal lobes using Compumedics-Neuroscan and Mathworks MATLAB programs. Caregivers completed the Social Skills Rating System (SSRS) and Social Responsiveness Scale (SRS). Coherence was entered into three repeated-measures ANOVAs. Diagnosis served as the between groups factor and video condition served as a three-level within groups factor. Coherence values were correlated with the SRS and SSRS. Results: A significant interaction between diagnosis and condition was found: the TYP group had higher coherence between the left and right frontal lobe than ASD during all conditions, Wilks Lambda=.59, F(2, 23)=8.14, p=.02, partial _2=.42. No significant interaction existed between diagnosis and video condition between the left parietal-temporal lobe and frontal lobe, Wilks Lambda=.91, F(2, 21)=1.08, p=.36, partial _2=.09), or between the right parietal-temporal lobe and frontal lobe, Wilks Lambda=.996, F(2, 23)=.04, p=.96, partial _2=.004. A main effect for video condition was found, Huynh-Feldt=.04, F(1.28, 23)=4.54, p=.03, partial _2=.16; ASD showed decreased coherence at baseline compared to TYP. No main effect for diagnosis was found, F(1, 23)=1.26, p=.27. Correlations for complete sample indicate higher intra-frontal coherence values during baseline were related to increased social

skills (SSRS Social Skills scale; r=.44, p<.05), and social motivation (SRS Social Motivation scale; r=-.46, p<.05). Within the ASD sample, higher levels of social motivation (SRS Social Motivation Scale) were correlated with higher intra-frontal coherence values during baseline (r=-.52, p<.05), familiar condition (r=-.53, p<.05), and unfamiliar condition (r=-.64, p<.05). Higher coherence values between the frontal lobe and left parietal-temporal lobe during baseline were related to lower levels of social awareness (SRS Social Awareness Scale; r=.57, p<.05), social cognition (SRS Social Cognition Scale; r=.79, p<.01), and social communication (SRS Social Communication Scale; r=.56, p<.05). Conclusions: Conclusions will discuss the overconnectivity hypothesis in the frontal lobe in ASD, as well as possible lateralization of the brain in ASD.

136.047 47 Effects of Repetitive Transcranial Magnetic Stimulation On Behavior and Functional Cortical Connectivity Outcomes in Autism. E. M. Sokhadze*, J. M. Baruth, A. S. El-Baz, T. Horrell, A. Tasman, G. Mathai, L. L. Sears and M. Casanova, *University of Louisville*

Background: Our prior neuropathological studies indicate that minicolumns in the brains of autistic patients are narrower, with an altered internal organization resulting in a disruption of the normal balance between excitation and inhibition. Networks of inhibitory interneurons acting as GABA gated pacemakers are critically involved in electroencephalographic (EEG) gamma oscillations. Abnormalities in these mechanisms in autism have been associated with binding problems, i.e., the co-activation and synchronization of neural assemblies. The concept of autism as a functional disconnection syndrome featured by reduced transfer of information due to local over-connectivity and long-range under-connectivity is broadly compatible with evidence derived from our minicolumnar neuropathology studies.

Objectives: The goal of our study was to test this theoretical construct of autism and institute a potential therapeutic intervention using low frequency repetitive stimulation (rTMS) known to exert inhibitory effects on the cortex. One aim of our study was to test whether temporal binding of perceptual items in a coherent Gestalt as indexed by induced gamma oscillation coherence and event-related potentials (ERP) is abnormal in autism. This aim used an oddball task with Kanizsa illusory figures known to readily induce gamma oscillations. We proposed that patients with autism will show reduced coherence of gamma activity between areas processing local features and reduced coherence between primary sensory and associative cortical areas. Another aim was to examine effects of rTMS on behavioral, EEG, and ERP outcomes in autism.

Methods: We used rTMS over the dorsolateral prefrontal cortex on a weekly basis for 12 weeks in a group of high-functioning individuals with autism. Twenty five autistic patients and 19 age-matched controls participated in the study. Six patients with autism formed a waiting-list group and were tested twice on Kanizsa oddball task within 2-3 months to rule out repeated test effects. We used oddball task with target and non-target Kanizsa figures, and non-Kanizsa standards at pre-, mid-treatment (6 rTMS) and post-12 rTMS treatment stages. Follow-up test was conducted after 3 months following the rTMS course completion.

Results: Outcome measures based on ERP, induced gamma EEG activity and behavioral measures pre- and post-TMS showed significant improvement which was maintained at the follow-up stage. During baseline test autistic subjects as compared to controls had higher magnitude of ERPs to non-target rather than target stimuli. Autistic patients showed also higher gamma local coherence and lower distal (e.g., frontal vs. parietal) coherence to all stimuli. TMS resulted in a decrease of the amplitude in the frontal and parietal ERPs to non-target stimuli. TMS positively affected the coherence of gamma in response on the ipsilateral frontal and parietal sites. 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. Irritability as measured by Aberrant Behavior Checklist also was significantly reduced.

Conclusions: Selected electrocortical outcome measures were shown as sensitive markers of functional connectivity changes and improved excitatory /inhibitory balance after rTMS trial. The outcomes of extended trial and follow-up suggest that that rTMS offers a potential innovative therapeutic intervention.

136.048 48 Oxidative Stress in Asperger Syndrome and Healthy Adolescents. M. Parellada*, C. Llorente, M. Giraldez, C. Moreno and C. Arango, *Hospital General Universitario Gregorio Marañón.*

Background: An adequate equilibrium between the production of reactive oxygen species (ROS) and the antioxidant capacity of the cell plays an important role in cerebral development and differentiation (Fantel and Person 2002; Gorman et al. 2000). In Autistic children, an increase in ROS and decrease in plasmatic antioxidant activity has been shown in comparison with healthy controls (Sogut, 2003, Zoroglu 2003, Zoroglu 2004, James 2004, Chauhan 2004; Chauhan 2006 for a review). Objectives: We aim to study the oxidative stress status in a subgroup of ASD adolescents without mental retardation, all with Asperger syndrome, and compare it with a group of healthy controls.We hypothesized that an excessive oxidative stress will be present in Asperger syndrome patients in comparison with control subjects.

Methods: 27 children and adolescents (7 to 17 years old) with Asperger syndrome, and 30 healthy controls, matched for sex and age, were recruited for this study. Diagnosis of Asperger Syndrome was made by DSM-IV criteria, Gillberg criteria and ADOS evaluation when needed. We selected healthy controls from publicly-funded schools with characteristics similar to those attended by patients in the community. Plasma Total Antioxidant Status (TAOS), which provides information on overall systemic antioxidant function was measured in .two consecutive analyses (separated by 8 weeks), and the mean between both determinations was compared between the two groups. Catalase, superoxido dysmutase ; gluthation peroxidase enzymes and plasma gluthation were also determined. All determinations were made by spectrophotometry.Results: Mean total antioxidant status was lower in adolescents with and Asperger syndrome than in controls (1.158 vs 1.272, p=0.047). No differences in any of the antioxidant enzymes or the glutathion was found.

Conclusions: Oxidative metabolism disequilibrium may be an intermediate pathophysiological pathway not only in severe, regressive or retarded autistic individuals, but also in Asperger individuals. This finding supports the altered detoxifying system theories of ASD.

136.049 49 Patterns of Hemisphere Asymmetry in EEG Activity in Infants at High Risk for Autism. L. Gabard-Durnam*[1], A. L. Tierney[2], C. A. Nelson[3] and H. Tager-Flusberg[4], (1)*Harvard College and Children's Hospital Boston*, (2)*Harvard Graduate School of Education and Children's Hospital Boston*, (3)*Children's Hospital Boston*, (4)*Boston University*

Background: A current direction of research in autism examines the correlations between early biomarkers and the development of the disorder's phenotype. One biomarker that has returned promising results is the brain's electrical activity. Frontal EEG asymmetry has been related to behavioral measures of temperament (Fox et al., 2001). In particular, asymmetry patterns in the alpha band have been shown to correlate strongly with temperament classification, and individuals with autism demonstrate a trend opposite to the expected correlation for this bandwidth (Fox et al., 2003; Sutton et al., 2005). This work has largely been done in older children with autism, and questions remain about the extent to which early asymmetry patterns in EEG activity, for all frequency ranges, serve as early risk factors of autism and how well they predict later behavioral phenotypes.

Objectives: This study examines developmental patterns of asymmetry in EEG activity in infants who are at high risk for developing autism and compares them to the patterns of low risk infants. EEG asymmetry is also examined in relation to temperament in this sample.

Methods: As part of a larger comprehensive study of infant siblings of children with autism, infants are being studied at 6, 9, 12, and 18 months. At each of these time points, EEG data are collected under an eyes-open

condition while the researcher blows bubbles to keep the infant quiet and alert. Additionally, at each of these visits, parents complete the Infant Behavior Questionnaire (IBQ). We calculate power spectra for frequency bands that collectively span the 1-50 Hz range and compare them between infants at high risk for autism (by virtue of having an affected sibling) and infants at low risk (having only typically developing siblings). Data are first examined for developmental patterns in asymmetry levels in various frequencies bands across all time points. Subsequently, in order to examine relations between early brain activity and later behavior measures, patterns of asymmetry at 6 months are compared with the IBQ temperament scores recorded at 12 months for a subset of infants.

Results: We have obtained usable data from 65 infants: 27 low risk and 38 high risk. Preliminary analysis indicates that the alpha bandwidth EEG asymmetry scores for the high risk infant group differ significantly from those of the low risk group across all time points. Infants displaying early clinical symptoms of autism represent outliers following a different asymmetry trend. For the high risk group, six-month EEG asymmetries appear to predict twelve-month temperament scores in accordance with low risk trends.

Conclusions: This analysis indicates that infants at high risk for autism demonstrate developmental patterns of EEG asymmetry that are distinct from those with low risk but also from those with clinical symptoms of autism. These early EEG patterns predict later temperament measures and may predict future scores on autism diagnostic measures.

136.050 50 "Native and Non-Native Speech-Evoked Responses in High-Risk Infant Siblings". C. R. Percaccio*[1], D. Padden[2] and P. Kuhl[2], (1)*Institute for Learning and Brain Sciences, University of Washington*, (2)*University of Washington*

Background: Studies of infants who have older siblings with autism indicate that 30-50% exhibit abnormal sensory behaviors, language and/or social delays as early as 12-months of age (Zwaigenbaum et al., 2005; Landa & Garrett-Mayer, 2006; Mitchell et al., 2006). Although children with autism are a densely heterogeneous population, communication and/or language delays are part of the fundamental triad of impairments contributing to a diagnosis of autism. Previous research has established that young infants can discriminate phonemes used in all languages (Werker & Tees, 1984; Best & McRoberts, 2003), but that between 10 and 12 months of age, native-language phonetic perception ability increases, while the detection of unfamiliar patterns in non-native languages declines (Cheour et al., 1998; Kuhl et al., 2006). Our lab has also demonstrated a predictive relationship between measures of native-language speech perception recorded at 7 months of age and the number of words produced in early childhood. Individual children who had better discrimination of an English syllable in infancy produced more words at 18 and 24 months of age (Kuhl et al., 2008).

Objectives: The goal of our research is to investigate if an abnormal pattern of speech perception is a risk marker that can be used to facilitate an earlier diagnosis of language delay or an autism spectrum disorder. We will also investigate the presence of a predictive relationship between early measures of speech discrimination and subsequent behavior in high-risk infants.

Methods: EEG data was recorded from high-risk infant siblings and from no-risk infants at 7 months of age. After data collection, high-risk infants were randomly assigned to either the early intervention group or the no treatment group. All infants were re-assessed at 12 months of age. At both ages, English and Chinese syllable contrasts were each presented in an oddball paradigm to test discrimination.

Results: Preliminary results indicate that before 8-months of age, at-risk infants have different physiological responses to English speech syllables compared to no-risk infants. The mismatch negativity is significantly different between groups at electrode FZ. Compared to typically developing infants, high-risk infants continue to process English syllables differently at one year of age; however, both groups of infants continue to process Chinese syllables similarly. As a

group, participation in a relationship-based form of early intervention did not normalize speech-evoked responses to English syllables at one year of age.

Conclusions: Taken together, these results may indicate that some infants who will develop autism have an auditory processing disorder that hinders the acquisition of critical language skills.

136.051 51 Altered Brain Phosholipids and Acylcarnitines in a Propionic Acid Induced Rodent Model for Autism Spectrum Disorder. R. H. Thomas*, K. A. Foley, J. Mepham, L. J. Tichenoff and D. F. MacFabe, *University of Western Ontario*

Background: Phospholipids are major structural components of cell membranes and are critical in modulating membrane fluidity, cell signaling and mitochondrial function throughout neurodevelopment. Altered phospholipid and acylcarnitine profiles, suggestive of impaired peroxisomal and mitochondrial fatty acid metabolism, have been found in many patients with autism spectrum disorders (ASD). Propionic acid (PPA) a dietary short chain fatty acid, a metabolic intermediate of fatty acid metabolism, an end product of enteric bacterial fermentation, and a common food preservative have been implicated as a potential environmental trigger in ASD. PPA and other enteric short chain fatty acids (butyrate and acetate), affect diverse physiological processes such as cell signaling, immune function, gene expression, mitochondrial function and lipid metabolism, making these compounds plausible environmental triggers for the disorder. Intraventricular infusions of PPA can produce brain and behavioural changes similar to those seen in humans suffering from ASD

Objectives: We used the PPA rodent model to investigate if there are any evidence for abnormal brain lipid metabolism associated with the occurrence of autistic-like behavioral changes following intraventricular infusions of phosphate buffer saline (PBS), propionic (PPA) and butyric acids (BUT).

Methods: Infusions (0.26M, 4μL animal^{-1}) was done twice daily for 7 days after which animals were sacrificed and brains lipids analyzed using thin layer chromatography (TLC) and gas chromatography-mass spectrometry and flame ionization detection (GC-MS/FID).Brain phospholipids were separated into SM, CL, PS+PI, PC and PE following TLC analysis.

Results: Hydrolysis of the separated phospholipid components revealed significant quantitative changes in fatty acid components after treatments with PPA and BUT compared to the controls (PBS), with PPA generally more extensive than BUT in altering the lipid composition. PPA infusion resulted in decreased levels of total monounsaturates, total _6 fatty acids and elevated levels of total saturates in all the separated phospholipid species. In addition, a decline in total plasmalogen PE and the ratio of _6: _3 was also present. Conversely, there was a consistent significant (P = 0.02) increase in total acylcarnitines, total long chain (C12 to C24) acylcarnitines, total short chain (C2 to C9) acylcarnitines, and the ratio of free to bound carnitine following infusions with PPA and BUT. Increases in the accumulation of the following acylcarnitines: C2:0, C14:1, C15:0, C16:0, C16:1, C18:0, C18:1, C22:0, C22:1 and C24:0 accounted for the increase levels of total acylcarnitines observed following infusions with PPA and BUT.

Conclusions: These results provide evidence of a relationship between changes in brain lipid profiles and the occurrence of behavioral changes associated with autism spectrum disorder using the autism rodent model.

136.052 52 Developmental Changes in Brain Bases of Face Perception in Autism as Revealed by ERPs. D. Perszyk*[1], E. Kilroy[1], P. Molfese[1], L. Mayes[1], A. Klin[2] and J. McPartland[1], (1)*Yale Child Study Center*, (2)*Yale University School of Medicine*

Background: Individuals with autism spectrum disorder (ASD) tend to exhibit behavioral and neural anomalies in face perception, which has been posited to reflect immature expertise resulting from reduced social motivation and consequent inattention to faces during development. Event-related potential (ERP) studies in typically developing children and adults have shown that face-sensitive ERP components (P1 and N170)

change in amplitude, latency, and morphology with age. Functional magnetic resonance imaging studies reveal corresponding developmental shifts in cortical loci for both face and object recognition. Collectively, these studies demonstrate the importance of understanding developmental changes in face processing. Previous work in a large sample of children with ASD and typically developing counterparts identified preserved specialization for a non-social cognitive process, letter perception, subserved by distributed cortical regions. The current study uses source localization within the same population in order to investigate the neural sources underlying face-sensitive ERP components associated with developmental maturation between middle childhood and adulthood.

Objectives: To chart changes in neural sources of face-related electrophysiological brain response associated with chronological development in individuals with ASD.

Methods: ERPs were recorded from high-functioning children with ASD and typically developing peers using a 256 electrode Geodesic Sensor Net. Participants viewed social and non-social stimuli from highly familiar and unfamiliar categories (human faces vs. houses, Roman letters versus pseudoletters). Peak amplitude and latency were extracted for components at 100 ms (P1), 170 ms (N170), and 250 ms (N250) over occipitotemporal scalp regions. Geosource software (EGI) was used to calculate a minimum-norm inverse solution to derive sources for each time window. Individualized sensor registration was performed using a Geodesic Photogrammetry System, and analyses in progress will compute source estimates based on individual-specific three-dimensional head models to improve the accuracy of derived source localizations for each subject.

Results: Source analysis revealed distinct patterns of face and letter processing in typically developing individuals and those with ASD. Estimations of neural sources showed developmental changes in both groups across a network of brain regions including the fusiform gyrus, superior temporal sulcus, visual cortex, and orbitofrontal cortex. Preliminary results using standard head models show that levels of activation across all brain regions in the network decreased with age in both groups. Analyses in progress are refining these findings using individual-specific head models.

Conclusions: This is the first study to employ dense array EEG and individualized head models to estimate neural sources associated with temporally distinct processing stages for face perception. Results reveal distinct profiles of developmental maturation between individuals with ASD and typical counterparts.

136.053 53 Developmental Pathways in EEG Activity in Infants at High Risk for Autism. A. L. Tierney*[1], L. Gabard-Durnam[2], C. A. Nelson[3] and H. Tager-Flusberg[4], (1)*Harvard Graduate School of Education and Children's Hospital Boston*, (2)*Harvard College and Children's Hospital Boston*, (3)*Children's Hospital Boston*, (4)*Boston University*

Background: A current goal of research in autism is to examine the link between early markers and the later onset of the disorder. Increasing attention is being paid to biomarkers of autism, including the brain's electrical activity. Brain activity, as indexed by EEG, has been related to certain cognitive processes (Basar, 1999). Activity in the gamma band in particular is hypothesized to relate to weak coherence in perceptual processing, both of which are impaired in individuals with autism (Brock et al., 2002; Happe and Frith, 2006). This work has largely been done in older children and adults, but questions remain about the extent to which early differences in EEG activity, gamma as well as other frequency ranges, serve as early risk factors of autism and how well they predict later autism outcomes.

Objectives: This study represents a first step in examining the relationship between patterns of brain activity and behaviors associated with autism. We examine developmental trajectories in EEG activity in infants who are at high risk for developing autism and compare them to those of infants who are at low risk.

Methods: EEG is collected in the infants under an eyes open condition while a researcher blows bubbles to keep the infant still and quiet. We calculate power spectra for frequency bands that collectively span the 1-50 Hz range in infants at high risk for autism (by virtue of having at least one affected sibling) and compare them to infants at low risk (by virtue of having a typically developing sibling). Infants are being studied at 6, 9, 12, and 18 months and this analysis is part of a larger, comprehensive infant-sibling project. Data are examined for patterns in developmental trajectories in various frequencies bands, each of which has a different functional relationship to cognitive processing.

Results: To date we have obtained usable data from 65 infants: 27 low risk and 38 high risk. Preliminary analysis indicates that high-risk infants exhibit lower power across all frequency bands at 6 months and that the subsequent development follows different paths. In particular, power in alpha activity at 18 months in high-risk infants is at the level of the 6 month alpha power in the low risk group suggesting that infants in the high-risk group may show a neurodevelopmental lag in alpha activity. For gamma activity, low risk controls show change over time in their power values while that of high-risk infants does not.

Conclusions: This analysis indicates that infants at high risk for autism demonstrate lower power in their EEG activity in each frequency range at six months of age. Additionally, the patterns of development in these neural measures show different patterns. Future studies will examine whether these developmental trajectories of power changes are associated with later autism behaviors.

136.054 54 Electrodermal Activity Versus Sensory Behaviors: A Pilot Study in Children with Autism. M. Chang*[1], D. Parham[2], E. Blanche[1] and A. Schell[3], (1)*University of Southern California*, (2)*University of New Mexico*, (3)*Occidental College*

Background:

The measurement of electrodermal activity (EDA) provides a window into sympathetic nervous system activation via detection of change in sweat gland activity. Using EDA measures, the innovative Sensory Challenge Protocol (SCP) enables researchers to study sympathetic reactivity to sensory stimuli in a controlled laboratory environment. The SCP is specifically designed for studies of children with developmental and behavioral conditions involving impaired sensory modulation (Miller et al., 1999; Miller et al., 2001). It is a painless and non-intrusive psychophysiological assessment in which a series of sensory stimuli are administered in a child-friendly laboratory.

Objectives:

The purpose was to provide empirical evidence regarding differences in reactivity to sensory stimulation of children with and without autism. This study uses the SCP, which includes 3 phases (baseline, "sensory challenge", and recovery), to measure sympathetic reactivity via EDA data at rest and in response to stimuli. Six types of stimulation were included in the "sensory challenge": auditory (tone and siren), visual (strobe light), tactile (feather), olfactory (wintergreen-scented oil), and vestibular (automated back-tilted chair) stimulations. Each stimulus lasts 3 seconds, and 8 trials were given for each type of sensory stimuli.

Methods:

Twenty-two children diagnosed with autism (AD) and 18 typically-developing children (TD) ages 5-12 were recruited from neighborhood clinics and communities. No age differences between the 2 groups were found. The Social Communication Questionnaire was used to confirm the diagnosis of autism, and the Sensory Processing Measure Home Form (SPM) was used to measure children's behavioral responses to sensory stimuli in natural environments, via parental report. Data from the TD group were included in the final analysis only if both of their sub-scores and total scores (in the SPM) were in the typical range.

Results:

Independent t-tests were used to evaluate differences between the AD and TD groups. For the parental reports on the SPM, the two groups are significantly different in all subscores and the total scores. For the EDA, at the two resting periods (baseline and recovery), the AD group demonstrated significantly higher levels of skin conductance (baseline: $p=0.01$; recovery: $p=0.04$). The AD group also showed significantly higher mean magnitude of the skin conductance orienting response (SCOR) to the visual ($p<0.01$), siren ($p=0.03$), olfactory ($p=0.02$), and vestibular ($p<0.01$) input than the TD group.

Conclusions:

Results suggest that children with autism tend to have higher arousal levels and are more physiologically reactive to sensory input than the typically-developing children. Additional analysis of amplitude revealed that a small number of children in the TD and AD groups were non-responders in different sensory input. Moreover, a preliminary analysis indicates that children's responses to different types of sensory inputs in the laboratory were correlated with the parental observation in the natural environment reported in the SPM Home Form. These issues will be further investigated in future studies.

136.055 55 Event-Related Potentials During Affective Face Processing and Social-Communicative Development in Infants at Low and High Risk for Autism Spectrum Disorders.

C. Damiano*[1], W. L. Stone[2], D. S. Messinger[3], E. H. Catania[1] and A. P. F. Key[2], (1)*Vanderbilt University*, (2)*Vanderbilt Kennedy Center*, (3)*University of Miami*

Background: Despite the high heritability and pervasive nature of autism spectrum disorders (ASD), recent research suggests that a behaviorally-based diagnosis of ASD may not be accurate until 30 months of age (Turner & Stone, 2007). To identify individuals with ASD at younger ages, prospective studies have examined both behavioral and neural markers in infants from high-risk populations, such as infant siblings of children with ASD (sibs-ASD). In addition to being at increased risk of developing ASD, sibs-ASD often show atypical patterns of social-communicative development regardless of diagnostic outcome. The current study examines the extent to which neural correlates of affective face processing may be related to later measures of social-communicative development.

Objectives: The specific aims of the current study are: 1) To determine whether 6-month-old infants are able to discriminate different degrees of positive affective expression from a neutral expression and to determine if this ability is evident in face-specific (N290 and P400) and non-face-specific novelty (Nc) event-related potential (ERP) components; and 2) To investigate whether individual differences in ERP amplitudes during face processing at 6 months are associated with social-communicative measures at 9 months in sibs-ASD and infant siblings of typically developing children (sibs-TD).

Methods: This study included 10 infants (1 sib-ASD and 9 sibs-TD) recruited from a larger longitudinal study of social emotional development. At 6 months of age, ERP responses were recorded during the presentation of neutral faces and faces with different degrees of positive affect (small and large smiles). At 9 months of age, parents completed the MacArthur-Bates Communicative Development Inventory (CDI) Words and Gestures form. Relations between the amplitudes of ERP components and the CDI Phrases Understood and Early Gestures subscores were examined using Pearson r correlation coefficients.

Results: Infants were able to discriminate both small and large smiles from a neutral expression, as evidenced by larger amplitudes of the P400 and Nc components in response to the positive expressions compared to the neutral. Furthermore, amplitudes of the face-specific N290 and the novelty Nc components at 6 months were related to the infant's inventory of communicative gestures at 9 months. Specifically, a larger inventory of gestures was correlated with a smaller (less negative) N290 amplitude during the neutral face condition ($r= .88$, $p = .02$). Greater use of gestures was also correlated with smaller

(less negative) Nc amplitudes during both the big smile (r = .95, p = .003) and neutral conditions (r= .85, p = .03).

Conclusions: These findings suggest that 6-month-olds are capable of discriminating between neutral expressions and expressions of positive affect. Furthermore, neural responses during the processing of positive affective expressions may be useful in predicting later social-communicative development. Future research will examine the potential of these ERP responses at 6 months to predict social-communicative development beyond the first year of life as well as explore the possibility that differences in these ERP responses may help to identify individuals who will later be diagnosed with ASD.

136.056 56 Performance-Monitoring and Evaluative Control in High Functioning Autism. A. Clawson*[1], E. Krauskopf[1], O. Johnston[1], M. J. Crowley[2], M. South[1] and M. J. Larson[1], (1)*Brigham Young University*, (2)*Yale University*

Background: Decision making difficulties in autism may arise in part from impaired awareness of feedback, including negative feedback. The error-related negativity (ERN) and post-error positivity (Pe) are event-related potential (ERP) components generated following the commission of errors. Current theories suggest the ERN reflects automatic performance- and error-monitoring while the Pe reflects error-processing and awareness. As reflections of the response monitoring system, these components have direct behavioral implications in self-monitoring and decision-making in social-emotional processes (Crowley et al., 2009). Findings from such paradigms may be especially helpful for elucidating individual differences across the autism spectrum (Henderson et al., 2006). Objectives: In light of somewhat disparate findings in the few previous studies of the ERN in autism, we included measures of anxiety, personality, and cognitive functioning to provide further information on factors that influence response monitoring. In response to suggestions by Henderson et al. (2006) we also included more trials in order to generate more errors; and we had a somewhat larger and balanced sample size (25 in each group). Methods: ASD was characterized using both the ADOS-G (total social communication score >7) and the SCQ (total score >15). High-density ERPs were acquired while 25 ASD participants and 25 matched controls performed a modified version of the Ereksen Flanker task over 400 trials. Response-locked ERPs were separately averaged for correct and error trials. Results: Behaviorally, both groups demonstrated robust response-time and error-rate interference. Similar to Groen et al. (2008), we did not find a significant group x accuracy interaction for either the ERN, nor for the Pe. However, visual inspection showed that the response to error trials but not correct trials was attenuated in the ASD group; t-test analysis confirmed this difference was significant. Unlike Henderson et al. (2006) we did not find an association between Verbal IQ and the ERN in autism; this association was significant for the control group, however. Behavioral inhibition, as reported by parent questionnaire, was significantly associated with the difference score between correct and incorrect trials in the Pe, driven by a significant positive correlation between the Pe and behavioral inhibition.
Conclusions: The ERN offers the potential for rich insight into response monitoring in ASD, but task-specific and sample-specific differences across studies have thus far preclude a clear understanding of the phenomenon. We encourage further studies that give explicit attention to important factors of diagnostic severity, cognitive function, anxiety and personality to help identify possible subtypes of autism that could be characterized by reliable physiological measures such as the ERN.

136.057 57 Resting-State Neural Abnormalities in Autism Spectrum Disorders. L. A. Cornew*, T. P. L. Roberts and J. C. Edgar, *Children's Hospital of Philadelphia*

Background: Previous research suggests neural abnormalities in individuals with Autism Spectrum Disorders (ASD), including aberrant activation in medial prefrontal cortex, posterior cingulate cortex, and the precuneus. These brain areas are implicated in social processing as well as in the "default mode network" that is active when participants are at rest. Although the default mode network is typically examined using

fMRI, an investigation of resting-state neural oscillations may provide greater insight into the neural abnormalities in ASD. Whereas resting-state neural oscillations are aberrant in several neurological conditions and often associated with neurocognitive dysfunction, it is unclear whether similar associations manifest in ASD.

Objectives: The present study probed neural oscillatory activity in nodes within the resting-state network in children with ASD. When differences between the ASD and control groups were observed, correlations between neural activity and clinical symptom severity were examined. It was hypothesized that children with ASD would show increased low-frequency activity, and that this increased activity would be associated with greater social and language impairments.

Methods: Participants were 18 children with ASD and 21 neurotypical control children who ranged in age from 6 to 14 years. All were medication-free. Whole-cortex MEG data were obtained while participants underwent a two-minute eyes-closed resting-state exam. Offline, a standard source model (15 regional sources) was used to transform each individual's raw MEG surface activity into brain space. At each localized brain area, a Fast Fourier Transform (FFT) was applied to artifact-free two-second epochs of the continuous data. Individual spectra were averaged, and oscillatory activity was examined in 6 standard frequency bands: delta (0-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta1 (12-20 Hz), beta2 (20-30 Hz), and gamma (30-50 Hz). Power in each frequency band (relative to total power) was compared between the ASD and control groups. When group differences were observed, correlations between relative power and scores on two clinical measures, the Social Responsiveness Scale (SRS) and the Clinical Evaluation of Language Fundamentals (CELF), were examined.

Results: The ASD and control groups did not differ on total power (0-50 Hz). The ASD group, however, exhibited elevated relative frontal midline delta power (p = .02), as well as elevated relative alpha power at midline and right parietal sources (ps = .01 and .03, respectively). Frontal midline delta activity correlated with SRS (r = .32, p = .03) and CELF (r = -.31, p = .03) scores. Parietal alpha power correlated with SRS scores (rs = .36 and .31; ps = .01 and .03, for the midline and right hemisphere, respectively).

Conclusions: Results indicate abnormal resting-state brain activity in ASD. In particular, children with ASD exhibited greater frontal delta and parietal alpha power. Abnormalities in these regions appear to have clinical significance, as increased activity was associated with greater social and language impairments. These results provide converging evidence for atypical default mode network function in ASD, as the midline prefrontal and parietal regions investigated here correspond to nodes in the fMRI-identified default network.

136.058 58 Social - Communicative Skills in Young Children with An Autism Spectrum Disorder: The Role of the Mirror Neuron System. L. Ruysschaert*[1], P. Warreyn[2], J. R. Wiersema[1], G. Pattyn[1], A. Handl[3] and H. Roeyers[2], (1)*Developmental Disorders, Ghent University, Ghent, Belgium*, (2)*Ghent University*, (3)*Max Planck Institute for Human Cognitive and Brain Sciences*

Background:

In children with autism imitation problems have consistently been found (Williams et al., 2004). Combining the research on imitation in autism with the discovery of mirror neurons led to the hypothesis of a dysfunctional mirror neuron system (MNS) in individuals with ASD (Williams, Whiten, Suddendorf, & Perrett, 2001). Since imitation appears very early in development, infancy seems to be an ideal period to study the relation between imitation in development and mirror neuron functioning. However, until now, research into the MNS with infants remains scarce.

Objectives:

The aim of this study is to investigate mirror neuron functioning during hand movement, action observation and action imitation in very young children with a diagnosis of ASD and in siblings (age 18-30 months). 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 of ASD and siblings (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 with 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:

Until now, more than 40 infants participated in the study. According to preliminary results, there seems to be mu suppression during action imitation and action observation, but not during hand movement in the ASD group. In the sibling group we found the same results as in the normally developing children group which is mu suppression during action imitation. This means that despite the shared genetic material with their brother or sister with ASD, the siblings show less impairments in the functioning of their mirror neuron system than the ASD group.

Given the small number of infants in each group, the results should be interpreted with caution.

Conclusions:

These preliminary results suggest that we developed a useful paradigm for studying mirror neuron functioning in young children. We can conclude that there is mirror neuron activity in siblings, but the mirror neuron activity seems to be less pronounced in infants with ASD in comparison with typically developing children.

Full results and conclusions will be presented at the IMFAR meeting.

136.059 59 Spectral Power and Coherence Correlations During Flash VEP for Typical and Autistic Children. K. M. Martien*[1], K. Singh[1], H. Bharadwaj[1], J. Isler[2] and M. R. Herbert[3], (1)*Massachusetts General Hospital-Harvard Medical School*, (2)*Columbia College of Physicians and Surgeons*, (3)*Massachusetts General Hospital*

Background: Children with autism have long been recognized to have atypical sensory perception with hypersensitivity to many external stimuli. They have also been shown to have decreased functional connectivity, which has been hypothesized to underlie the predominant perceptual-cognitive style termed weak "central coherence". We previously showed that children with autism spectrum disorders (ASD) had increased occipital spectral power compared to age-matched controls on flash-induced visual evoked potentials (VEP), which appears to be a biological measure for a hypersensitive visual system. This increase in power during activation was associated with a simultaneous decrease in inter-hemispheric synchrony (coherence). We supposed that this increased power/activation might be correlated with the decrease in inter-hemispheric coherence. Such a correlation would suggest a basic neurophysiologic tenet or rule: that power and coherence are driven by related underlying neural mechanisms, and possibly that poorly gated sensory processing undermines inter-hemispheric synchrony. Objectives: This investigation was undertaken to test the hypothesis that cortical activation as measured by spectral power in response to flash VEP would be inversely correlated with functional connectivity as measured by inter-hemispheric occipital synchrony (coherence)

in both autistics and controls. Methods: Flash VEPs were previously recorded from children (ages 5 to 8 yr) with ASD (n = 6) and from age-matched controls (n = 8) using high-density EEG recording. VEP power spectra (per channel) and coherence (per pair of channels) were computed for 1s epochs (100ms pre-stimulus). Regional analysis focused on primary visual areas showed increased power and decreased coherence ($p<0.05$) across the frequency spectrum in ASD compared to controls, most significant in the alpha band ($p<0.01$). Correlation analysis (Pearson) was performed for average power (right and left hemisphere combined) and coherence in the alpha band. Results: We found an inverse correlation between power and coherence in typicals such that increased VEP alpha power predicted decreased alpha coherence (r value: -0.79, p = 0.02). The correlation coefficient for the autistics as a group was poor (r value: -0.18, p = 0.73). However, the distribution of autistics suggested three subgroups: those whom when included with typicals strengthen the correlation between power and coherence, (n=3, r value: -0.88, p = 0.0004), and those above (n = 1) and below (n = 2) the regression line. Conclusions: Our results support the hypothesis that spectral power and coherence are highly inversely correlated in the typical brain and in a substantial subset of children with ASD. Some ASD children appear to follow a different set of "neurophysiologic rules" with either better or worse than expected power : coherence relationships. This finding, if it holds up in a larger data set, may help parse autistics as 1) operating within a typical neurophysiologic model or 2) operating outside typical models. The potential future significance of these observations lies in the value of parsing individual neurophysiologic profiles for intervention and treatment trials.

136.060 60 Atypical Object Processing in Children with Autism and Its Relationship to Research Diagnosis. J. P. McCleery*[1], V. Vogel-Farley[2] and C. A. Nelson[2], (1)*University of Birmingham (UK)*, (2)*Children's Hospital Boston*

Background: Previous studies have utilised event-related potentials (ERPs) to document atypicalities in early-stage facial emotion processing, as well as in both face and object processing, in children diagnosed with autism spectrum disorders. Among the atypicalities that have been observed are reduced differentiation of fearful and neutral faces in the N170 component (Dawson, Webb, Carver, Panagiotides, & McPartland, 2004), and reduced amplitude N170 responses to objects (Webb, Dawson, Bernier, & Panagiotides, 2006).

Objectives: In the current study, we assessed fearful versus happy face emotion processing and face versus object processing in children with autism spectrum disorders and control children in a single experiment. The goal of this research is to examine the processing of a new facial emotion contrast (fear vs happy), as well as the processing of face versus objects, in a single group of children.

Methods: ERPs were recorded while 3- to 5-year old high-functioning children (IQ > 80) diagnosed with autism spectrum disorders (ASD) and typically developing (TYP) control children viewed pictures of faces posed in emotional expressions (happy, fearful) and objects (drums, guitars). Faces and objects were presented separately in several short (~6 minute) blocks of trials, with face/object block order counterbalanced both within and across participant groups. Then, both the amplitudes and latencies of the N170 component were examined using Analyses of Variance (ANOVAs) in order to test the hypotheses that a) fearful vs happy face processing, and b) face vs object processing, differed between participant groups.

Results: N170 component amplitudes and latencies did not differ for happy versus fearful faces in either group of children, and there were no differences in emotional face processing between children with and without autism. Alternatively, for face versus object processing, N170 responses were of significantly larger amplitude for faces than for objects in both groups of children, and there was a significant stimulus type (face, object) by subject group (ASD, TYP) interaction. This interaction was driven by significantly reduced (i.e., less negative) N170 amplitudes in response to objects in the children with autism relative to controls. Furthermore, the inclusion of a third group of children who had received a community

diagnosis of autism but who did not meet criteria for an ASD when tested using the Autism Diagnostic Observation Schedule (ADOS) in the laboratory resulted in a further statistical interaction between stimulus type and the subject groups. In this interaction, the degree of object processing atypicality was systematically related to diagnostic grouping (ASD ADOS+: 6.9mV; ASD ADOS-: 4.6mV; TYP: -1.3mV).

Conclusions: In the context of previous research, these results suggest that early-stage object processing atypicalities are robust in young children diagnosed with autism, and further suggest that object processing atypicalities may be meaningfully related to concurrent social and communication functioning in children who have received a clinical diagnosis of autism.

136.061 61 Children with Sensory Processing Differences Show Atypical Resting Connectiviy Using Magenetoencephalographic Imaging (MEG-I). E. Marco*[1], S. S. Hill[1], A. Bernard[2], A. M. Findlay[3], S. Honma[3], L. B. N. Hinkley[3] and S. Nagarajan[3], (1)*UC San Francisco*, (2)*University of Denver*, (3)*University of California, San Francisco*

Background: Children with and without autism experience sensory processing difficulties that may be at the core of their learning and behavioral deficits. We have previously found neural activity differences in primary somatosensory cortex as early as 50 ms after simple tactile stimulation. However, the neurophysiological underpinnings of sensory perception and integration in children with sensory behavioral deficits remain unclear. We used magnetoencephalography (MEG-I), a functional imaging tool with millisecond temporal resolution and millimeter spatial localization to measure resting state functional connectivity in children with sensory processing difficulties and matched controls. This study aims to understand how the functional connectivity of affected children differs during resting and whether these differences are regionally specific. Objectives: We hypothesized that children with sensory processing differences (SP) would have decreased connectivity in regions of the brain known to process and integrate sensory information relative to matched healthy controls (HC). _ Methods: Resting activity (eyes closed) was recorded for the SP group (N=9, mean age=10.6) and the HC group (N=9, mean age=10.1) using a 275-channel whole-head MEG. Oscillations in the alpha range (8-12Hz) across a 60 second window were isolated from 4 minutes of continuous MEG recording. Neural sources were estimated using an adaptive spatial filtering technique and functional connectivity was computed using global imaginary coherence. Connectivity volumes were compared between the SP and HC groups. Voxelwise correlations between global connectivity and measures of sensory processing behaviors and autism behaviors were also performed. These behaviors were measured using parent-report questionnaires: the Sensory Profile (SP) and the Social Communication Questionnaire (SCQ). Results: Robust resting alpha activity was identified in the HC and SP groups. The SP group showed significantly less connectivity in two discrete hubs: left temporal-parietal (TP) and right dorsolateral pre-frontal cortex (DLPFC), both with a p-value < 0.1 (FDR corrected). Decreased connectivity in the L-TP region correlated exclusively with sensory processing deficits as measured by the SP ($p<0.1$, FDR corrected), while decreased connectivity in the left dorsal premotor cortex (L-dPMC) region correlated exclusively with autism specific traits as measured by the SCQ ($p<0.1$, FDR corrected). Decreased connectivity in the R-DLPFC region correlated with both autism specific traits and sensory processing deficits ($p<0.1$, FDR corrected). Conclusions: Our results suggest that children with sensory processing deficits have measurable and reduced alpha range resting-state functional connectivity. Furthermore, the coherence of cortical regions known to participate in sensory integration may be independently predictive of success with sensory modulation, whereas connections of higher-order prefrontal cortical fields associated with top-down modulation and cognitive control appear to be more broadly predictive of both autism and sensory processing traits. This data will contribute to our knowledge of basic sensory processing in children with and without autism. Furthermore, this is an exciting new direction for early diagnosis

using a non-invasive technique that does not require patient participation.

136.062 62 Contingency Sensitivity and Reward Prediction in High-Functioning Autism. E. Krauskopf*[1], A. Clawson[1], O. Johnston[1], M. J. Crowley[2], M. J. Larson[1] and M. South[1], (1)*Brigham Young University*, (2)*Yale University*

Background: Children and adolescents with High-Functioning Autism often demonstrate impulsive behaviors, possibly due to impaired sensitivity to stimulus-response contingencies and the ability to predict reward. The neurobiological mechanisms underlying these deficits have not been thoroughly explored, but can be examined using the 'feedback-related negativity' (FRN)—an event-related potential (ERP) component evoked following performance or response feedback (e.g., whether a monetary reward is obtained), with greater-amplitude FRN following unfavorable than favorable outcomes and following unexpected, relative to predicted, unfavorable outcomes.
Objectives: We know of no published study that has directly measured the FRN in autism. Because EEG is generally well-tolerated by individuals with higher-functioning ASD, we designed a study using a child-friendly task (choosing balloons of different colors) that has previously shown deficits in emotion regulation in adolescents with early life cocaine exposure (Crowley et al., 2009), to examine the possibility of similar deficits in ASD.
Methods: We examined ERPs elicited by favorable (monetary gain; 'reward') and unfavorable (no monetary gain; 'non-reward') feedback during a guessing task where expectation of reward outcome was manipulated (75% or 25% probability of reward counterbalanced across two blocks of 200 trials) in 25 children and adolescents diagnosed with ASD and 25 age- and IQ-matched healthy participants.
Results: Replicating previous work, controls showed larger amplitude FRN to 'non-reward' feedback and largest amplitude FRN following 'non-reward' when 'reward' feedback was expected (i.e., when reward probability was greatest). The same was true for the ASD group. However, inspection of correlation matrices observed a strong association between Verbal IQ and measures of the FRN. Regression analyses that included VIQ in the model consistently showed that VIQ explained a significant amount of the variance in FRN in both ASD and comparison groups, in fact washing out the significance of the difference between reward and non-reward trials.
Conclusions: We discuss the implications for understanding of decision making, learning, and motivation in ASD in the context of no significant differences in Feedback-related negativity compared to controls. More importantly in our view, we know of no previous studies that have reported the influence of IQ on the FRN even in healthy development, perhaps because it has never been measured. Although it is a serendipitous finding, this has important potential applications for understanding how we measure the reward system in both typical and atypical development.

136.063 63 Do Children with Low-Functioning Autism Disorder Have A More Extensive Declarative Memory Impairment Than Children with High Functioning Autism Spectrum Disorder? Implications for the Medial Temporal Lobe. S. Anns*[1], S. Bigham[2] and J. Boucher[3], (1)*City University London*, (2)*Bournemouth University*, (3)*City University*

Background: We have hypothesized that the language and learning impairments that distinguish autistic disorder (AD) from Asperger syndrome (AS) and other forms of high-functioning autism (HFA) most commonly result from an impairment of semantic memory additional to the impairment of episodic memory known to occur in all forms of autistic spectrum disorder. More specifically, we hypothesise that whereas relational memory (critically dependent on hippocampally mediated recollection) is impaired across the spectrum, single item memory (critically dependent on a sense of familiarity mediated by perirhinal and/or entorhinal medial temporal lobe cortex) is impaired only in individuals with AD.

Objectives: The objective of the research to be reported is to test this hypothesis.

Methods: *Study 1* tested single item recognition in adolescents with AD using shape and pattern recognition tasks, and assessed the relation between performance on these tasks and lexical-semantic

knowledge as assessed by the Pyramids and Palm Trees test and by the Similarities and Vocabulary subtests from the Wechsler scales.

Study 2 tested single item and relational memory in children with AS or HFA using a shape recognition task and an action recall source memory task.

Study 3 (ongoing) tests single item and relational memory in adolescents with AD and young children with AS or HFA using the shape recognition and action recall tasks used in Study 2, plus forced choice recognition tests developed by Migo, Mayes et al. specifically to discriminate between the process of familiarity that is critical for single item memory and the process of recollection that is critical for relational memory. Two comparison groups are included: a young typically developing (TD) group and a group of intellectually disabled adolescents without autism, equated with the AD group for age and ability.

Results: *Study 1* showed that single item recognition was impaired in the AD group relative to an ability-matched TD comparison group but not to an age and ability-matched intellectually disabled comparison group. However correlation between recognition and lexical-semantic ability was specific to the AD group.

Study 2 confirmed the prediction that single item recognition would be unimpaired in an AS/HFA group relative to an age and ability matched TD group (reflecting unimpaired single item memory), but that source memory would be impaired relative to the TD group (reflecting an impairment of relational memory).

Results of *Study 3* are not yet available.

Conclusions: Findings from Studies 1 and 2 provide preliminary support for the hypothesis. However, the results of Study 1 leave open the possibility that impaired single item memory may not be specific to AD, and Study 2 (designed to assess novel methods of measuring single item and relational memory separately) did not include an AD group. The results of Study 3 should resolve both these limitations.

136.064 64 Ferritin and Iron Levels in Children with Autistic Disorder. S. Herguner*[1], M. Copur[2], C. Tanidir[3] and F. Kelesoglu[4], (1)*Bakırköy State Hospital for Mental Health and Neurological Disorders*, (2)*Bakirköy State Hospital for Psychiatry and Neurology*, (3)*Okmeydanı State Hospital*, (4)*Istanbul Faculty of Medicine*

Background:

Iron is a component of many enzymes involved in neurotransmitter synthesis including tryptophan hydroxylase (serotonin) and tyrosine hydroxylase (noradrenalin and dopamine). Brain monoamine neurotransmitter systems may be affected by iron deficiency due to decreased activity of associated enzymes.

Low ferritin levels are a sign of iron deficiency and an early precursor of iron-deficiency anemia. Recent studies showed low ferritin levels in subjects with restless legs syndrome, attention deficit hyperactivity disorder and Tourette's syndrome. It was speculated that iron deficiency might contribute to the pathophysiology of RLS, ADHD and TS via its impact on the metabolism of dopamine and other catecholamines which have been involved in the pathophysiology these disorders.

Objectives:

High prevalence of low serum ferritin has been reported in children with autism spectrum disorder before. The aim of this study was to investigate and compare the iron status of children with autistic disorder (AD) in different age groups.

Methods:

The study group consisted of 112 children and adolescents (age 3–17; mean ± SD = 9.9 ± 2.8 years) who met DSM-IV diagnostic criteria for AD by clinical assessment. All patients were recruited from Bakırköy State Hospital for Mental Health and Neurological Disorders, Child Psychiatry Clinic during May 2008 – October 2009. The clinical evaluation of all subjects was made by two experienced child psychiatrists independently. Parents and children were interviewed about children's'

medical history; children with any diagnosed genetic, metabolic, or neurological disorders were excluded from the study. Children with dietary restrictions also were excluded.

Results:

The mean serum ferritin level was 26.2 ± 4.7 ng/ml. Children in preschooler group had significantly lower ferritin levels than school-age and adolescent groups, 20.7, 28.3, 34.9, respectively. The mean iron level was 73.2 ± 5.1. Children in preschool group had lower iron levels than other two groups, but this was not significant. Iron deficiency was detected in 19.5 % of the total sample; this was 26 % in preschoolers, 18 % and 12 % in school aged and adolescent groups.

Conclusions:

This current study confirmed the high prevalence of low ferritin levels in autism, in parallel with previous reports. The reason for lower ferritin levels in children with autistic disorder is unclear. Autism and iron deficiency could be linked by a common underlying genetic mechanism that has not been identified yet. Alternatively, because iron is involved in brain monoamine systems, iron may influence autism through its effects on monoamine-dependent neurotransmission. As intestinal dysfunction was described in autism, impaired absorption might be a possible cause of iron deficiency. However no subjects in our study group had evidence of intestinal malabsorption. Finally, as it is the case for most iron-deficient children in the general population, iron deficiency in autism may be a result of reduced dietary iron intake.

136.065 65 Magnocellular Processing Differences for Peripheral Stimulation Among Children with Autism Spectrum Disorders: Evidence From High-Density EEG. N. Russo*[1], H. P. Frey[1], E. C. Lalor[2], S. Molholm[1] and J. J. Foxe[1], (1)*City College of New York & Albert Einstein School of Medicine*, (2)*Neural Engineering Group*

Background: Individuals with autism spectrum disorders (ASD) frequently show self stimulatory behaviors. Some of these have a visual origin, and involve gazing at objects or fingers in the visual periphery. These behaviors, termed 'lateral glancing' are thought to reflect an attempt to filter visual stimulation (Mottron et al., 2007). The origin of lateral glancing is considered to be related to differences in the functioning of magno- and parvo- cellular visual pathways among persons with ASD. Behavioral studies have shown comparable visual performance for centrally presented stimuli (Bertone, Mottron, Jelenic & Faubert, 2005) but atypical processing for peripherally presented stimuli (McCleery, Allman, Carver, & Dobkins, 2007) in relation to TD individuals.

Objectives:

Our goal was to use a series of electrophysiological metrics to assess the integrity of both magno- and parvo-cellular pathways among children with an ASD at both central and peripheral locations in relation to a group of typically developing children (TD).

Methods:

We used two techniques, a standard visual evoked potentials (VEP) which contain information from both magno- and parvo-cellular pathways and the novel event-related potentials technique known as the VESPA (Visual Evoked spread Spectral Analysis). The VESPA allows us to bias stimulation towards either magno- or parvo-cellular pathways via the use of low and high contrast flickering stimuli respectively. Participants were asked to detect an infrequent target presented in the center of the screen to ensure that they were fixating, while checkerboards flickered at the appropriate contrast (VEP, magno and parvo VESPA). Stimulation was presented in both central and peripheral locations (at 6.3° visual angle). We synchronously recorded eye movements using high speed video eye tracker.

Results:

Both groups showed comparable evoked responses for centrally presented stimuli. At peripheral locations, parvo- VESPA were similar between groups, but the magnitude of the VEPs and magno- VESPA were much larger in the children with ASD than in the group of TD children.

Conclusions:

Visual responses of children with ASD appear to be typical when stimuli are presented centrally. However, in the visual periphery, children with ASD showed a relatively typical parvo- and an atypical magno-cellular system response.

136.066 66 Measuring Sleep in Autism Trials: Relationship of Socioeconomic Status to Data Collection. K. Adkins*[1], K. L. Surdyka[1], S. E. Goldman[1], D. Wofford[1], C. A. Molloy[2] and B. A. Malow[1], (1)*Vanderbilt University*, (2)*Cincinnati Children's Hospital Medical Center*

Background: Precise measurement of sleep patterns in children with autism spectrum disorders (ASD) is critical to developing effective treatments for insomnia. Appropriate parent education related to the collection of sleep measures within treatment trials may contribute to the success of these trials.
Objectives: To compare the impact of parent education, aimed at teaching parents to accurately complete sleep diaries and properly use actigraphs, on outcome data in two sleep treatment trials. Actigraphy uses measurements of inactivity/activity as surrogate measures of sleep/wake patterns.
Methods: Families were participating in two ongoing studies of sleep in children ages 2-10 years. Study #1 involves the use of supplemental melatonin to improve sleep in ASD children. Study #2 involves the use of behavioral interventions to improve sleep in ASD children within two sites of the Autism Treatment Network. All children met DSM-IV criteria for an ASD with confirmation on the Autism Diagnostic Observation Schedule and the Autism Diagnostic Interview-Revised. In Study #1 (n = 13), parents were given actigraphy watches for their children to wear, and sleep-wake diary to complete, along with brief verbal instructions. In Study #2 (n = 11), research coordinators spent between 30 minutes and 1 hour individually with each parent (separately from their children) reviewing the actigraphy and diary procedures. Study #2 also incorporated scenarios for completing the data collection tools and a quiz to measure parent comprehension of the tools.
The proportion of scorable nights of data in Study #1 (minimal parent education on actigraphy/sleep diary procedures) was compared with Study #2 (intensive parent education on actigraphy/sleep diary procedures). Mann-Whitney non-parametric tests were performed to compare the two study groups on proportion of scorable nights and socioeconomic status (SES—defined by averaging the four-factor Hollingshead Index of Social Status for each parent). Spearman rank product correlation coefficients were also performed to examine the association of SES with the proportion of scorable nights within the two studies.
Results: Mean (± standard deviation) child age in Study #1 was 6.5 ± 2.3 and in Study #2 was 5.7 ± 2.6 ($p = 0.46$). Based on the first three weeks of actigraphy data, the proportion of scorable nights was higher: 0.86 +/- 0.25 in Study #2 compared to 0.71 +/- 0.25 in Study #1, although significance was not reached potentially due to the small sample size ($p = 0.19$). In Study #2, SES was highly correlated with the proportion of scorable nights ($r = 0.95$; $p < 0.0001$). In Study #1, SES was not correlated with the proportion of scorable nights ($r = 0.27$; $p = 0.37$). SES did not differ for parents enrolled in Study #1 and Study #2 ($p = 0.26$).
Conclusions: Socioeconomic status may influence data collection during trials in children with ASD, especially in the setting of intensive parent education. Although our findings require confirmation in larger samples, we are refining our actigraphy education to ensure that education provided is successful for families regardless of socioeconomic status. Our findings are generalizable to other ASD trials involving parental data collection.

136.067 67 Melatonin for SLEEP IN AUTISM: A DOSE-RESPONSE STUDY. K. L. Surdyka*, S. E. Goldman, K. Adkins, D. Wofford, L. Wang and B. A. Malow, *Vanderbilt University*

Background:
Retrospective and small open label studies have shown that supplemental melatonin promotes sleep in children with autism spectrum disorders (ASD). However, information on effective dose, and time required to reach it, has not been fully explored.
Objectives:
In preparation for a large multicenter randomized controlled trial, we are carrying out a pilot study of supplemental melatonin

in children with ASD. A major objective is to define the relation of sleep latency (SL; minutes to fall asleep) to melatonin dose over time.
Methods:
Children were ages 4-10 years, with a clinical diagnosis of ASD based on DSM-IV criteria. Diagnosis was confirmed on the Autism Diagnostic Observation Schedule and the Autism Diagnostic Interview-Revised. All children had sleep delay, defined as inability to fall asleep within 30 minutes at least 3 nights a week. Medical causes of insomnia and primary sleep disorders were addressed prior to enrollment. Children on medications which affect melatonin pharmacokinetics were excluded. Objective measures of sleep were measured over 17 weeks with actigraphy in conjunction with sleep diaries. All children received one week of baseline actigraphy followed by two weeks of an inert flavored liquid 30 minutes before bedtime, to acclimate them taking a liquid medication at bedtime. At week 3, children began 1 mg of supplemental melatonin (Natrol ®). The child's response to melatonin was reevaluated every three weeks based on mean SL. Dose was increased every three weeks (from 1 mg, to 3 mg, to 6 mg, to 9 mg) until the child reached a satisfactory response, defined as SL within 30 minutes on 5 or more nights in the week. Once a satisfactory response was achieved, the child remained on that melatonin dose for the remainder of the 17 weeks.
Results:
Fifteen children were included, with mean age of 6.5 years [standard deviation (SD) = 2.2]. Mean sleep latency was 44.5 minutes (SD = 23.8) at baseline and 23.7 minutes (SD = 8) at the end of study; p = 0.05, Wilcoxon-signed rank test. All children achieved a satisfactory response. The percentage of children achieving a satisfactory response (SL within 30 minutes on 5 or more nights a week) was 47% in week 4 (corresponding to the first week of the 1 mg dose) and 67% by week 7 (corresponding to the first week of the 3 mg dose). Of the five other children, three reached a satisfactory response by the end of 3 mg dosing period and two reached a satisfactory response at 6 mg. No children required 9 mg dosing. In the overall sample, there was no significant decrease in sleep latency in the 2nd and 3rd weeks, as compared to the first week, of each dosing period.
Conclusions:
In this pilot work, we documented that supplemental melatonin decreases sleep latency, as documented by actigraphy. Low dose melatonin (3 mg or below) appears effective in reducing SL in the majority of children, with a relatively rapid dose response. Randomized clinical trials of supplemental melatonin appear warranted.

136.068 68 Non-Neuronal Targets of Antipsychotics. C. Gottfried*[1], A. Quincozes-Santos[1], L. D. Bobermin[1], M. C. Leite[1], R. T. Abib[1], V. Bambini-Junior[1], F. Zeidán-Chuliá[1], R. Riesgo[2] and C. A. Goncalves[1], (1)*UFRGS*, (2)*Universidade Federal do Rio Grande do Sul - UFRGS*

Background: Although classical and atypical antipsychotics may have different neurotoxical effects, their underlying mechanisms remain to be elucidated, especially regarding to neuroglial function. It still remained unclear which and to what extent is the specific effect exerted on glial cells upon neuroleptic treatment.

Objectives: In the present study, we compared the atypical antipsychotic risperidone (0.01-10 _M) with the typical antipsychotic haloperidol (0.01-10 _M) regarding to different aspects such as glutamate uptake, glutamine synthetase (GS) activity, glutathione (GSH) content and intracellular reactive oxygen species (ROS) production in C6 astroglial cells.

Methods: C6 glial cells were cultured in DMEM (pH 7.4) supplemented with 5% serum at 37°C/5% CO_2. Experiments were performed in absence or presence of risperidone in a range from 10 to 40 μM. Glutamate uptake was measured by addition of L-[2,3-^{3}H] glutamate. Glutamine synthetase (GS) activity was measured by colorimetric assay, glutathione (GSH) levels were measured by fluorimetric assay. Glial marker S100B was measured by ELISA. Cell death was performed by propidium iodide uptake assay. Data were analyzed statistically by ANOVA followed by Tukey´s test. $P < 0.05$ was considered significant.

Results: Risperidone was able to induce a significantly increase on glutamate uptake

(32%); GS activity (15%); GSH levels (58%) and S100B secretion (80%). In the presence of high doses of risperidone, C6 cells become stellate, with process-bearing cells and partial retraction of the cell body followed by detachment from the adhesion surface with no cell death. Lysophosphatidic acid, a specific positive regulator of the GTPase RhoA, prevented the effects of risperidone on cell morphology.

Conclusions: These data contribute to the available knowledge regarding to neural responses after antipsychotic-induced stimulus and it could give rise to important insights about how to promote brain rewiring in autism spectrum.

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136.125 125 Training Community-Based Mental Health Providers to Use a Research-Based Intervention. L. I. Brookman-Frazee* and A. Drahota, *University of California, San Diego*

Background: Children with autism spectrum disorders are served in community-based mental health (CMH) settings for behavioral and psychiatric problems commonly associated with ASD. Previous research suggests that many CMH providers have limited training in ASD and that discrepancies exist between community care and research-based practices. Training providers to use research-based intervention strategies is a critical component of improving CMH services.

Objectives: To examine the initial feasibility and acceptability of training community MH providers to implement a research-based intervention protocol aimed to decrease behavior problems in children with ASD. The specific goals of this study were to examine changes in therapists' perceptions of their knowledge and confidence related to treating children with ASD and their observed adherence to the intervention protocol.

Methods: Participants included 14 therapist/ family dyads. Therapists were recruited from three community-based mental health clinics and represented multiple mental health disciplines: 36% MFT, 36% Psychology, 21% Social Work, and 7% Psychiatry. Child age ranged from 5 to 12 years (M=9.71; SD=2.13). Family race/ ethnicity included, 64% White, 14% Hispanic, and 21% Other/ Mixed. Therapists received comprehensive training (i.e., introductory workshop, self-study, bi-weekly consultation) for five months in an intervention protocol that was developed to integrate research-based behavioral and cognitive behavioral methods to address behavior problems in children with ASD ages 5 to 13 ("AIM HI: An Individualized Mental Health Intervention for Children with ASD"). AIM HI was developed based on data on the clinical characteristics of children served in CMH clinics and the training needs of CMH providers. Mixed qualitative and quantitative analytic methods were used to analyze therapist surveys, observational data on therapist behaviors, and observations of consultation/ training process.

Results: Following the introductory workshop, therapists reported significant improvements in their perceived knowledge related to working with children with ASD (i.e., characteristics of ASD, treatment planning, adapting psychotherapy for ASD, and ASD-specific behavioral and cognitive behavioral intervention strategies) (t=-8.0, p<.001). Likewise, therapists reported increased confidence applying their knowledge in their work with children with ASD (t=-7.3, p<.001). Further, initial data indicate that therapists do adhere to certain individual components of the protocol with ongoing consultation. Qualitative analyses of the consultation process indicate that there are a number of organizational and provider-level factors that impede (competing time demands, staff productivity requirements, attitudes, previous training) and facilitate (management/ leadership support, therapist attitudes) the implementation of this model. Parent and therapist perceptions of the utility of the intervention and changes in therapists' general attitudes towards research-based practices will also be reported.

Conclusions: Initial results from this pilot study suggest that it is feasible to train clinicians to implement a research-based intervention model for ASD in CMH clinics. Therapists actively participated in training, reported more positive attitudes serving children with ASD after initial training, and adhered to many aspects of the intervention. Despite these positive findings,

there are a number of challenges to training therapists in this setting, highlighting the importance of developing flexible models that can be adapted to "fit" the constraints of the settings and needs of the providers.

136.127 127 Socio-Demographic Factors Associated with Level of Parenting-Related Stress Reported by Parents of Toddlers with Autism Spectrum Disorders. L. E. Herlihy*[1], M. L. Barton[1], T. Dumont-Mathieu[1], S. Hodgson[1], J. Green[1], K. Knoch[1], E. Troyb[1], L. Berry[2] and D. A. Fein[1], (1)*University of Connecticut*, (2)*Children's Hospital of Philadelphia*

Background:

Parents of children with autism spectrum disorders (ASDs) are known to have higher levels of parenting-related stress than parents of children with other developmental delays. Within this group of parents, a small number of studies have produced conflicting evidence for the relationship between socio-demographic factors such as parental socioeconomic status (SES) and levels of parenting stress. Clarifying the relationship between these factors and parenting-related stress could lead to a better understanding of the needs of this population of parents and therefore enhance our ability to meet those needs as professionals.

Objectives:

The aim of the current study was to examine the extent to which socio-demographic factors such as yearly income are associated with parenting-related stress levels in parents of toddlers diagnosed with ASD.

Methods:

Participants were 62 parents of children receiving an initial diagnosis of ASD between ages 18-24 months. Parenting-related stress was measured by the Parenting Stress Index-Short Form (PSI-SF), which produces a Total Stress score and three subscale scores: Parental Distress (PD), Parent-Child Dysfunctional Interaction (P-CDI), and Difficult Child (DC). A Total Score of greater than 90 indicates clinically significant distress. Respondents to the PSI-SF included both mothers (N= 56, 90.3%) and fathers (N= 6, 9.7%). Parents self-reported yearly income data (a proxy for SES) along with other socio-demographic information such as race/ethnicity, educational attainment, and employment status. Yearly income ranged from <$10,000 to >$100,000 and was coded in $10,000 increments. Children were diagnosed with ASD for the first time as part of our larger Early Detection of Pervasive Developmental Disorders study. Child symptom severity was measured using the Childhood Autism Rating Scale (CARS) and adaptive behavior with the Vineland Adaptive Behavior Scales communication and socialization domain scores.

Results:

Child symptom severity as measured by the CARS was not correlated with total parenting stress as indicated by the PSI-SF total score. Similarly, child adaptive communication and social skills as measured by the Vineland were not correlated with total parenting stress. Preliminary results indicate a negative correlation between PSI-SF total score and yearly income ($r= -0.23$, $p= .038$) for parents of toddlers with an ASD. When examining the subscales of the PSI-SF separately, yearly income was negatively correlated with the PD subscale ($r= -.403$, $p=.002$), but was not significantly correlated with the P-CDI or DC subscales.

Conclusions:

In this preliminary study of parents of newly-diagnosed toddlers with ASD, parenting stress levels were not correlated with child symptom severity. Overall parenting-related stress tended to decrease with increasing yearly income in our sample. This effect appears to be driven by a significant negative correlation between Parental Distress subscale scores and yearly income. The PD subscale is thought to measure distress a parent experiences in his or her role as a parent as a function of personal factors related to parenting, such as sense of parenting competence and lack of social support. These preliminary results suggest that parents in lower yearly income brackets may be particularly susceptible to experiencing stress in the parenting role with very young children with ASD.

136.128 128 Reaction to ASD Diagnosis: Parental Depression, Family Support, and Service Access. J. L. Taylor*[1] and Z. Warren[2], (1)*Vanderbilt Kennedy Center*, (2)*Vanderbilt University*

Background: Given the numerous challenges involved in raising children with autism spectrum disorders (ASD), it is not surprising that parents of children with ASD report higher levels of parenting stress and psychiatric difficulties than parents of children with other developmental disabilities and parents of typically developing children.

While parenting stress has been one of the most frequently researched aspects of families of children with ASD, we have limited understanding of the clinical, child, and family characteristics associated with this stress in families of young, recently diagnosed children. Clarification of the factors impacting parenting stress, as well as identifying families at-risk for elevated distress at the time of ASD diagnosis, may better assist researchers and clinicians in targeting prevention and intervention efforts to enhance outcomes for children and families.

Objectives: In this study we explored relations between depressive symptoms in the week following diagnosis and current depressive symptoms, family support, and ability to access appropriate supports following the diagnosis of ASD.

Methods: All families coming through a university affiliated ASD clinic and receiving a diagnosis of ASD were asked to complete a survey regarding their reaction to diagnosis, family functioning, and parental well-being. A modified version of the CESD was created with parents providing a retrospective report of depressive symptoms in the week following diagnosis. Parents also completed the CESD regarding their current depressive symptoms, and likert-rating scales of perceptions of family support and accessing appropriate services.

Results: Seventy-four parents completed the study measures. Over 75% reported CESD scores above clinical threshold in the week following diagnosis. Of these parents, 39% reported CESD scores at clinical levels long after the diagnostic event. All parents who had clinically elevated CESD scores at this later time reported elevated scores during the week following diagnosis. Overall, 30% of the sample had elevated CESD scores both during the week following diagnosis and at the time of data collection. Clinically elevated CESD scores in the week following diagnosis were significantly related to decreased family support, t (72) = 2.15, p <. 05, but not to perceived service access.

Conclusions: The diagnostic assessment experience itself represents a pointed stressor for families of children with ASD. Many parents report clinically significant levels of depressive symptoms in the immediate aftermath of a diagnosis. Levels of depression are associated with perceived family support. These results point to the importance of pointed clinical attention to parental functioning following an ASD diagnosis.

136.129 129 Psychometric Analysis of the Parent Perception Measure for Parents of Children with Autism Spectrum Disorders. J. A. MacMullin*, M. C. Cappadocia and J. A. Weiss, *York University*

Background: Children with Autism Spectrum Disorders (ASD) are more likely to have poor student-teacher relationships and negative school experiences compared to typically developing peers (Hamre & Pianta, 2001). Positive student-teacher relationships and teacher-parent relationships are important factors in promoting successful academic, social, and behavioral outcomes for children with ASD (Birch & Ladd, 1997; Boyd et al. 2008, Kunce, 2003; Robertson, Chamberlain, & Kasari, 2003), and there are few parent report measures that assess these relationships. The Parent Perception Measure (PPM; Lauderdale & Blacher, 2008; Lauderdale, Howell, & Kaladjian, 2009) is a new measure that aims to understand the child-school experiences from the parent's perspective, by measuring the child's (a) School quality, (b) Socialization, (c) Teacher quality, and (d) Happiness. It also aims to assess parent-school experience by assessing (e) School Communication with the parent, and (f) Family involvement at school. Objectives: The purpose of the present study

is to investigate the internal consistency and construct validity of the PPM with parents of youth with ASD. Based on prior psychometric analyses of the PPM (Lauderdale & Blacher, 2008; Lauderdale, Howell, & Kaladjian, 2009), we expect that child-school variables would be positively correlated with measures of social skills and negatively correlated with measures of autism symptomatology and maladaptive behavior. We also expected that the parent-school experience would be positively correlated with parent empowerment. Methods: As part of a larger Canadian online survey of bullying in youth with ASD, 200 parents (92% mothers) of children and youth 6-18 years of age (M = 11.1 years, SD = 3.4) completed the PPM. Participants also completed measures of prosocial and maladaptive behavior (Nisonger Child Behavior Rating Form; NCBRF; Aman, Tassé, Rojahn, & Hammer, 1996), ASD symptomatology (Autism Spectrum Quotient; ASQ; Auyeung et al., 2007), and family empowerment (Family Empowerment Scale; FES; Koren et al., 1992). All children were still in school, and 85% were male. Diagnoses of the children were reported by parents as follows: 47% Asperger syndrome, 38% Autism, and 15% PDD-NOS. Results: Tests of internal consistency revealed good to excellent Cronbach's alpha coefficients for the PPM subscales (.70 to .96). Preliminary analyses indicated that PPM Socialization and Happiness scores were significantly correlated with NCBRF Positive Social Domain (r = .40 to .45), NCBRF Overall Maladaptive Behaviors scores (r = -.45 to -.46), and ASQ Total scores (r = -.36 to -.41). Scores on the FES were significantly related to PPM School Communication, Family involvement, and Teacher quality scores (r = .22 to .30). Conclusions: Evidence suggests that the PPM can inform educators and researchers about parent perceptions of their child's school with respect to their child with ASD and their family functioning.

136.130 130 Teacher, Caregiver, and Child Predictors of Educational Outcomes of Children with Autism. L. A. Ruble*[1] and J. H. McGrew[2], (1)*University of Kentucky*, (2)*Indiana University - Purdue University Indianapolis*

Background:

Public schools have reported a notable increase in the numbers of students with autism served. To help schools provide more efficacious services for students with autism, information is needed on predictors of educational outcomes. Although information is available on pre-treatment child predictors (i.e., intelligence, language, social abilities, and autism severity), little information is available on caregiver and teacher predictors of school-based educational outcomes.

Objectives:

To identify the child, caregiver and teacher pre-treatment characteristics predictive of educational outcomes of children with autism.

Methods:

Thirty-five special education teachers participated in a randomized controlled study of a consultation intervention. Teachers were responsible for the individual educational programs (IEPs) of students with autism ages 3 to 8 years old. Following teacher recruitment, a student with autism was randomly selected for participation and the caregiver was recruited. Prior to group assignment, each teacher, caregiver, and child triad completed a comprehensive baseline evaluation at the start of the school year (Time 1). The experimental group consisted of 18 teachers. Both groups received a Time 2 evaluation at the end of the school year. Observational rating of child goal attainment of IEP objectives using curriculum based assessment at Time 2 was used to assess outcomes. The difference in the goal attainment score from Time 1 and 2 was used as the dependent variable. A correlation analysis was conducted to identify potential predictor variables from four child (age; IQ; language; autism severity), six teacher (years teaching autism; number children taught; stress related to child; child problem behavior; knowledge of autism; instructional engagement), and six caregiver (race; income; maternal education level; stress related to child; child problem behavior; teacher alliance) characteristics possibly associated with the dependent variable. Separate analyses for teacher,

caregiver, and child variables were conducted using standard multiple regression.

Results:

Analysis of the correlation matrix indicated that of the 16 variables, no child, two teacher (stress; report of child problem behavior), and two caregiver (stress; report of child problem behavior) variables were significantly associated with educational outcome at $p < .05$. Two separate analyses were conducted for teacher and caregiver predictors separately (with a criterion of $p < .05$ to enter variables). Assumptions (multicollinearity, outliers, normality, linearity, homoscedasticity, and independence of residuals) were met for analysis. For teacher predictors, teacher report of child problem behavior was strongly negatively related to GAS improvement (Beta = -.551 for , p=.001); however, teacher stress did not remain significant in the regression (p = .085). For parent predictors, parent stress was strongly negatively related to GAS improvement (Beta = -.674, p = .007). Caregiver report of problem behavior was no longer significant once the impact of parent stress was regressed on the outcome (p = .808).

Conclusions:

Preliminary analysis of child, teacher, and caregiver pre-treatment predictors of educational outcomes suggest that teacher report of child problem behavior and parent report of stress related to the child were significant pre-treatment predictors of child educational outcome; surprisingly, pretreatment child variables found significant in other outcome research were not predictive in this outcome study.

136.131 131 Psychoeducational Group Interventions for Parents of Children with Autism: Where Are the Fathers?. M. Elfert* and P. Mirenda, *University of British Columbia*

Background: Various types of group interventions have been developed to address the psychological experiences (e.g., marital satisfaction, parenting stress, depression, self efficacy) of parents of children with autism (e.g., Brereton & Tonge, 2006). These interventions vary widely with respect to content, mode of delivery, and outcomes; however, a common factor to them is that the majority were designed for mothers of children with autism and rarely include fathers as participants. Although research has shown that fathers are in need of and benefit from psychoeducational interventions, no such treatments have been described in the research literature to date.

Objectives: To conduct a systematic review of the intervention literature for parents of children with autism and propose procedural modifications for future research and clinical applications, particularly for fathers.

Methods: A literature search was conducted to identify research studies that have examined the effectiveness of psychoeducational interventions designed for parents of children with autism. Studies were assigned quality ratings using previously-established criteria across 10 dimensions that included treatment fidelity, follow up data, and statistical controls for group differences (Singer, Ethridge, & Aldana, 2007).

Results:

Ten studies were located and examined with regard to group structure, composition, and content; research design; frequency and duration of sessions; participant demographics; dependent variables; and outcomes. A wide variety of group treatments were employed, ranging from educational/skill training interventions to psychological/therapeutic interventions. The treatments employed group instruction alone or in combination with individual sessions. None of the interventions was aimed exclusively at fathers and only 40% included fathers as participants. Only 30% of the studies involved randomized control trials. Outcomes were quite variable, primarily as a function of group type, content, sample size, and the dependent variables that were measured. One of the largest and most rigorous studies (Tonge et al., 2006) found no statistically significant differences between a skills training group and a counselling-based group intervention with regard to parental mental health, although both treatments were superior to a control group that received no intervention. Tonge et al.

also noted that the number of fathers who participated was "insufficient to provide empirical evidence of the benefit of these interventions for fathers" (p. 568)

Conclusions: Research is needed to examine the effectiveness of psychoeducational treatment groups specifically designed for fathers, to ascertain their psychological needs and how to help them become more effective parents and partners. Research is also needed to investigate the effectiveness of various types of psychoeducational group interventions using more rigorous research methodology, psychometrically sound measures, and evidence-based interventions, such as manualized treatments. Finally, research is required to compare specific types of psychoeducational group treatments, in order to determine which components (e.g., stress management, parenting skill training, social support, etc.) are most effective.

136.132 132 The US Recession and Changes in the Use of ASD Assessment Services. C. Klaiman*, J. Slay and L. Huffman, *Children's Health Council*

Background: In September 2008, the US economy drastically changed. Almost overnight, families were feeling the impact of the economic crisis. The Children's Health Council (CHC) is a non-profit organization in the San Francisco Bay Area of California. It specializes in comprehensive multidisciplinary assessments of academic, behavioral and developmental problems and sees hundreds of child clients each year, with a large proportion of services related to family concerns about autism.
Objectives: This CHC study assessed trends in assessment service use by parents of children with a suspected autistic spectrum disorder (ASD). We hypothesized that, due to financial concerns, parents sought and received more streamlined assessments during the year after September 2008 compared to the previous year.
Methods: Secondary data analysis of an extensive CHC clinical dataset was conducted. Current services data were collected 10/1/08 through 9/30/09 (after the estimated start of the economic crisis). Past services data were collected 10/1/07 through 9/30/08 (before the crisis). Analyses addressed demographic, services, and insurance data from all children who, following a diagnostic assessment, were diagnosed with an ASD (i.e., Autistic Disorder, Asperger Syndrome, Pervasive Developmental Disorder NOS).
Results: Across the selected 2 years, 420 children had an assessment resulting in an ASD diagnosis. 229 children started assessments in the 'past' year and 191 children started in the 'current' year. Preliminary analyses showed that, as in the past year, the current year clients were 86% male with 19% receiving public insurance. Across years, the majority of diagnostic assessments were conducted by a single-discipline (~56 %). However, there were significant year-based differences with regard to client age and number of assessment service hours utilized. In the current year, compared to past year, children were significantly younger at the time of assessment (8.4 yrs vs. 7.4 yrs, p=.00). In addition, there were fewer assessment service hours utilized (timeframe, the average length of diagnostic evaluation was 19.2 hrs vs. 12.5 hrs, p=.00).

	Past (10/1/07 - 9/30/08) (N=229)	Current (10/1/08 - 9/30/09) (N=191)	p-value
Child demographics			
Age (M, SD)	8.4 (4.9)	7.2 (4.3)	.00
Gender (% male)	196 (86%)	165 (86%)	.82
Family financial status			
Health Insurance (% public)	46 (20%)	34 (18%)	.55
Assessment services			
Service type (% single-discipline)	135 (59%)	99 (52%)	.16
# disciplines included (M, SD)	1.7 (1.0)	1.8 (0.9)	.42
# service hours (M, SD)	19.2 (22.3)	12.5 (13.9)	.00

Conclusions: It appears that, since the downturn in the economy, there are fewer assessment service hours spent evaluating children with possible ASD diagnoses. This shift is true for both publicly and privately insured families. It may be that while parents are seeking assessment services

that cost less, diagnostic clinicians are also offering shorter, more focused assessments to retain clientele. The current economic climate should thus encourage clinicians to revisit assessment protocols and identify tools that provide the most information with less cost.

136.133 133 Parental Experience of Caring for Young Adults with Asperger Syndrome. I. Fisher*[1], H. Omer[1], O. Golan[2] and H. Shilo[2], (1)*Tel-Aviv University*, (2)*Bar-Ilan University*

Background: Asperger Syndrome (AS) is a neuro-developmental condition that has profound effects on individuals' socio-emotional functioning and, as a consequence, on their ability to cope independently. Since the condition is lifelong, continuous care and support for individuals with AS may be needed, alas, support systems for adults with AS are not widely available. Hence, parents of young adults with AS often serve as mediators between their son/daughter and society. Parents may be burdened with great feelings of responsibility and invest heavily in their children's welfare, attempting to prepare them to adulthood and promote their independence. The constant parental care required may have grave emotional and practical effects on parents' quality of life. Previous attempts to study the effects of parenting a son/daughter with AS have focused on the parenting of children.
Objectives: This study aims to describe the experience of parents of adults with AS. We studied the emotional impact supporting an adult son/daughter with AS may have on the parents, as well as the price paid for a disrupted marital and family life. The study explored the acceptance of the situation by the parents, their struggles to bring up their adult son/daughter with AS and their worries and hopes for the future. The study sheds light on the parents' differing perspectives and their varied ways of coping with their situation. Additionally, this study aims to lay the foundation for an intervention intended to help parents of adults with AS.
Methods: Parents of 10 adults (7 males and 3 females), aged 20-30, who were diagnosed with AS, were interviewed by the first author. The interview was semi-structured and lasted about 90 minutes. After completing the interviews, transcripts were analyzed using a qualitative method, according to the principles of grounded based theory.
Results: Analysis of the interviews revealed several themes which were common to the parents' experience. Among the themes that were most prevalent: (1) The experience of harsh feelings such as frustration, anger, embarrassment, and anxiety. These were directed towards the adult son/daughter, towards the other parent, and towards support workers (2) Different styles of coping with the situation, both emotionally and practically. (3) Differences between fathers' and mothers' perspectives and coping styles and (4) varied attitudes relating to the adult son/daughter's dependence on the parents, as well as parents' ability to set demands and limits to their son/daughter.
Conclusions: AS has profound effects not only on the diagnosed individual but also on his/her parents and family. Parents report of difficulties in a wide range of aspects of life. The identification of the specific experience of parents of adults with AS can lay the foundation for an intervention, aimed to help the parents deal in a more effective manner with their son/daughter's condition.

136.134 134 Stress in Parents with Children at-Risk for ASD: Self-Referred Versus Pediatrician-Referred. C. Carrillo*, R. L. Koegel and L. K. Koegel, *University of California, Santa Barbara*

Background: There is a widespread body of literature suggesting parents of children with developmental disabilities experience significantly higher levels of parenting stress than parents of children without developmental disabilities. Although many studies have investigated parental stress after a child has received a diagnosis, little research has examined parental stress while parents are seeking a diagnosis. The current literature suggests that parents experience considerable stress during the process of obtaining a diagnosis. Moreover, different avenues of referral are possible, self-referred versus professional referred. In general, parents are spending 1.5years to 4 years trying to obtain an accurate diagnosis. This period of time may be filled with uncertainties, questions, and frustrations, thus proving to be a tremendously stressful experience for parents.

Objectives: The purpose of this study was to examine stress in parents whose children were at-risk for autism spectrum disorders at the time of a developmental screening. Specifically, we compared parents' stress levels based on referral type, *pediatrician-referred* or *self-referred*.

Methods: All participants in the current study were parents who had contacted our center because of a referral by a pediatrician or because they saw a brochure, poster, and/or website advertising a free developmental screening. All parents went to their pediatrician reporting concerns about their child's development, however, not all parents were referred by their pediatrician for a screening for autism. The Parental Stress Index-Short Form was administered to all twenty-four parents, *pediatrician-referred (n=14)* and *self-referred (n=10)*. A one-way multivariate analysis of variance (MANOVA) was conducted to determine the effect of referral type. A linear regression analysis was conducted to test the prediction of total stress score from the overall number of months parents are concerned about their child's development.

Results: The Hotelling's Trace multivariate test of overall differences between self-referred and pediatrician-referred groups was statistically significant (F (3, 20) = 8.61, p <.01), indicating that self-referred parents differ from pediatrician-referred parents. Self-referred parents exhibited significantly higher levels of Total Stress than pediatrician-referred parents. Univariate between-subjects test showed that the group effect (self- vs. pediatrician-referred) was significantly related to the Difficult Child subscale (F (1, 22) = 21.62, p <.01). There was no group effect (self- vs. pediatrician-referred) related to the Parental Stress subscale nor the Parent-Child Dysfunctional Relationship subscale. No relationship was found between length of concern and referral type.

Conclusions: Thus this study, in line with previous literature, highlights the importance of health care providers to listen to and acknowledge parental concerns regarding a child's development. The data suggests that for parents, who voice their concerns to their pediatrician, the action and referral made by the health-care provider may lead to lower stress levels than parents who voice their concern and no action is taken. Overall, these results are consistent with the previous qualitative research that documents parents' difficulties and experiences they face while searching for explanations of their child's behaviors.

136.135 135 The Effects of Inclusive Education On Neurotypical Students' Attitudes Toward Autism. M. H. Hodge* and E. R. Hahn, *Furman University*

Background: The Individuals with Disabilities Education Act mandates that schools educate children with exceptionalities in the "least restrictive environment" possible. The law resulted in an increase in inclusive educational practices in which students with exceptionalities are taught in settings with neurotypical peers. In recent years, the number of students with autism in inclusive classrooms has increased in response to the increasing prevalence of autism diagnoses. Research investigating the effects of inclusive education has focused primarily on the students who have exceptionalities. Comparatively less research has examined the effects of inclusion on neurotypical students.

Objectives: The current research investigates neurotypical students' attitudes toward peers displaying characteristics of autism and peers with physical exceptionalities as a function of the type of school that the neurotypical students are enrolled. We hypothesize that neurotypical students who attend inclusive educational programs will have more favorable attitudes toward peers with autism and peers with physical exceptionalities than the neurotypical students who attend schools that do not practice inclusion.

Methods: Neurotypical students in grades 4-8 from two schools were invited to participate. Students in one school (n = 15) were educated alongside one or two peers with autism for the majority of the school day. Students in the other school (n = 18) had no exposure to peers with autism while at school. Groups of children were tested at two sessions conducted in a classroom during

regular school hours. At the first session, the experimenter showed a 2-min video clip of a boy named Davie who exhibited autistic behaviors (e.g., repetitive behaviors, lack of eye contact). Immediately following the film-clip, students were asked to complete a modified version of the Chedoke-McMaster Attitudes toward Children with Handicaps scale (CATCH, Rosenbaum, Armstrong, & Kind, 1986). Items assessed children's self-reported attitudes toward Davie (e.g., I wouldn't worry if Davie sat next to me in class; I would not introduce Davie to my friends; I wouldn't know what to say to Davie). At the second session, students were shown pictures of six children, three of whom had obvious physical disabilities (e.g., wheelchair, arm crutches). After each picture, students were asked to circle words they would use to describe the child (e.g., happy, ashamed, smart).

Results: Preliminary data analyses indicate that children who do not have exposure to peers with autism in school rate a novel autistic child less positively than children who attend an inclusive school. Additionally, the results suggest that the positive attitudes toward autism that children develop in an inclusive setting generalize to children's impressions of physically-based exceptionalities.

Conclusions: Educational programs that integrate children with autism in classrooms with neurotypical peers appear to improve attitudes toward autism as well as other exceptionalities. As a non-randomized trial, the results are limited by the possibility that selection bias drove the results. Suggestions for future research are discussed to address this concern.

136.136 136 Using a Distance Learning Program to Introduce Naturalistic Behavioral Techniques to Parents of Young Children with Autism. A. L. Wainer* and B. Ingersoll, *Michigan State University*

Background: There is an increasing need for the adaptation of evidence-based interventions to non-traditional service delivery methods for families of children with autism. Internet-based instructional formats have been shown to be an effective means of dissemination of interventions for various populations. Additionally, self directed learning programs have been successfully used to teach intervention techniques to numerous groups, including parents of children with autism. Objectives: An internet-delivered, distance learning program (DLP) was created to introduce strategies for eliciting imitation during play from young children with autism. The self directed DLP was used to teach parents the intervention techniques involved in Reciprocal Imitation Training, a naturalistic behavioral intervention that has been shown to increase imitation on objects and gestures in young children with autism. Methods: A randomized switching replications design was used to assess the impact of a distance learning program on changes in behavior for parents and their children with autism. Parents were randomly assigned to two groups, immediate treatment and treatment delayed. Parents in the immediate treatment condition were immediately granted access to the web-based program, while parents in the treatment delayed condition were granted access to the program after two weeks. Parent knowledge was assessed at pre- and post-intervention. Changes in parent behavior were measured based on scores from videotaped play interactions. Additionally, data addressing the DLP's strengths and suggestions for improvement were collected.
Results: Preliminary results suggest that parents improved their knowledge and use of the intervention strategies in response to the DLP and rated the program positively. Conclusions: An internet-delivered, distance learning program may be an effective method for disseminating evidence-based practices to families of children with autism.

136.137 137 Predictors of Support Group Use in Parents of Children with ASD: Testing the Self-Regulatory Model. 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 coping style, perceived controllability of the disorder, mood, social support, and beliefs and attitudes about support groups have been an important predictors of use (Grande, Myers, & Sutton, 2006; Fontana, Fleischman, McCarton, Meltzer, & Ruff, 1988; Mickelson, 1997; Smith, Gabard, Dale, & Drucker, 1994).

The Self-Regulatory Model (Leventhal, Benyamini, Brownlee, Diefenbach, Leventhal, Patrick-Miller et al., 1997; Leventhal, Brissette, & Leventhal, 2003) asserts that representations of the illness, coping strategies used in dealing with the illness, and social input received from significant others (i.e., family, friends, professionals) contribute to decisions about seeking treatment or help. This model has been widely used in evaluating treatment use and adherence to treatment for individuals with a variety of medical illnesses (e.g., Bradley, Calvert, Pitts, & Redman, 2001; Hobro, Weinman, & Hankins, 2004; Whitmarsh, Koutantji, & Sidell, 2003) and has recently been proposed as a useful model for understanding treatment use for people with mental health problems (Lobban, Barrowclough, & Jones, 2003).

Objectives: This study will examine predictors of support group use for parents of children with ASD using the self-regulatory model (Leventhal et al., 1997; Leventhal et al., 2003). The following predictors will be examined; beliefs about controllability and cause of ASD, beliefs about support groups, mood, coping style, and social support.

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 expect that parents who are involved in support groups may be differentiated from those who are not participating in support groups, based on their coping styles, social support, mood, and beliefs about ASD and support groups. Specifically, we hypothesize that parents who are involved in support groups will report: 1) greater use of adaptive coping strategies (e.g., reframing and support-seeking), 2) fewer social supports, and 3) stronger beliefs that support groups can be helpful to parents with a child with ASD.

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.

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136.138 138 Training Needs for Those Who Support Children and Adults with Autism. V. Smith*, S. Patterson, A. Lever and A. Sung, *University of Alberta*

Background: Very little formal data exists regarding the state of personnel preparation and family service support training in autism. For example, according to a report from the National Research Council (NRC; 2001), not much is known about the number of autism specialists who are trained annually, how many autism personnel preparation programs operate, or which professional disciplines are involved in autism training either in the U.S. or Canada. Understanding the state of personnel preparation and service support training for individuals with autism and their families across the multiple disciplines who provide supports, is the first step in ensuring that the provision of service is adequate and that identified gaps in service are addressed. Objectives: The objective of this study was to conduct a needs assessment to identify the local service and training needs for families and individuals with autism. Three smaller goals were to document: 1) the scope of the problem; 2) the stakeholder perceived adequacy and availability of training programs; and 3) the needed training content and acceptable training methods. Methods: This assessment

included an online survey (i.e., Survey Monkey) of the nature of the unmet training needs of families and service providers and series of focus groups to identify the range of content and the acceptable delivery models by group. Participants: A representative sample of family, clinicians, educators, and community service providers of individuals with autism. Results: Two hundred and seven parents and 337 service providers completed the online survey. One third of the participants from rural settings and the remaining from urban locales described training needs for individuals with mild to severe autism across the lifespan. Parents indicated highest satisfaction with early intervention providers and lowest satisfaction with adult services, both diagnostic and intervention. Priority areas of training were identified across diagnosis, early intervention, and school age and adult services. Over the course of eight focus groups in six communities, 48 parents and service providers described a lack of accountability and standards in services. They emphasized the need for a central resource hub, preferably staffed, to obtain information and training. Two types of training were identified: knowledge of the 'basics' and in depth training and coaching in skills to facilitate learning and support. Conclusions: This study revealed that parents and service providers have multiple needs in regard to training to support individuals with autism. While they indicated that many workshops and short-courses were available, especially for service providers in early intervention, there is limited co-ordination among training agencies/institutions and few training opportunities to provide the knowledge and skills needed to feel competent in service provision. Further research is needed to enhance understanding of models of training that will meet the diverse service and family needs to support individuals with autism.

136.139 139 Young Adults with Autism: What Happens After High School?. P. Shattuck*, *Washington University in St. Louis*

Background: There is a dearth of nationally representative data on the prevalence and correlates of service use and functional outcomes among young adults with ASDs. Basic descriptive data on the prevalence and patterns of service use and related outcomes is necessary for planning by policy makers and administrators. Knowledge of the correlates of service use and related outcomes can help identify underserved populations and plan targeted services. If there are significant disparities, despite similar levels of need, then new strategies are needed for improving access. Estimates of service use and correlates will help clinicians, service providers, and family members be more informed and better prepared as they try to help teens with ASDs navigate the transition from adolescence to young adulthood.

Objectives: The aim of this study is to examine the prevalence and correlates of service engagement and functional outcomes during the first six years after exiting high school.

Methods: Data for this report came from the National Longitudinal Transition Study 2 (NLTS2), a 10-year prospective study being conducted by SRI International for the U.S. Department of Education that is following more than 11,000 youth enrolled in special education as they age into young adulthood. The study included 922 youth enrolled in the special education autism category at the start of data collection in 2001. Analyses for this paper are based on data from wave 4, collected in 2007 and 2008, which included 680 youth with an ASD. Of these, 406 had exited high school by wave 4. Weighted estimates generalize to the national population of youth who had been receiving special education services for a given age range and disability type. Use of these data is governed by a data use agreement with the U.S. Department of Education and was approved by the Washington University Institutional Review Board.

Results: Overall rates of service use during the prior 12 months were 22.6% for medical services, 32.5% for mental health, 39.5% for case management, and 8.9% for speech therapy. Almost half (43.2%) had not received any of these services during the prior 12 months. Lack of any services was more likely among households with income less than $25,000 as compared to those with incomes greater than $50,000. The adjusted

odds of not receiving any services were 2.73 times higher for females, and 3.09 times higher for African American compared to white youth. Fully 48% of youth had neither a competitive job nor engagement in any type of post-secondary education or job training. The likelihood of no job or education was higher among youth from poorer households. Approximately 40% of youth had no social contact with peers during the previous 12 months. Among youth capable of responding, 40% responded never, rarely, or sometimes when asked how often they felt hopeful about their own future.

Conclusions: There are significant disparities by race and socioeconomic status in post-high school service access and engagement in work and education among youth with autism.

136.140 140 Putting Recommendations Into Practice: Obtaining Services for Children Recently Diagnosed with ASD. M. A. McCarthy*[1], K. S. Branch[1], L. J. Lawer[1], L. A. Plummer[1] and D. S. Mandell[2], (1)*University of Pennsylvania*, (2)*University of Pennsylvania School of Medicine*

Background: Children with autism spectrum disorders (ASD) often require a variety of therapies and services to address the core deficits and ancillary problems. Guidelines suggest children with autism require intensive and specific therapies. It is not known to what extent physicians provide recommendations according to those guidelines, how well these recommendations are implemented, and the barriers parents face obtaining these services. The limited literature in this area suggests challenges to obtaining appropriate services.

Objectives: To examine physician recommendations to parents of children newly diagnosed with ASD, compare them with what children receive post diagnosis, and describe the difficulties and barriers parents report in attempting to obtain recommended services.

Methods: The sample consisted of 37 parents of children who were recently diagnosed with an ASD at one children's hospital in a large urban setting. Parents completed questionnaires and participated in a semi-structured interview eight weeks post-diagnosis. The diagnosing physician's recommendations were extracted through chart review. Transcripts from interviews were reviewed for parent report of service use, desire for additional services, and difficulty obtaining services.

Results: 27 charts have been reviewed to date. Preliminary findings suggest that the majority of families (76%) were receiving early intervention services prior to diagnosis. Diagnosing pediatricians recommended between 3 and 13 services and referrals, with an average of 7 per child. Speech therapy and occupational therapy were the most commonly recommended services for 82% and 75% of the children, respectively. Seventy-six percent of parents reported that their child received speech therapy, with 11% seeking additional hours based on the physician's recommendation. Occupational therapy was reported for 94% of children, with no one reporting an increase based on recommendations. Physicians recommended behavioral intervention for 78% of children; however only 29% reported receiving any behavioral intervention and 11% reported unsuccessfully seeking behavioral intervention based on physician recommendations. Physicians specifically recommended ABA-based therapies for 37% and Floortime for 33% of children; however, only 6% received each of these types of therapy, with an additional 6% unsuccessfully seeking these therapies. Of the sample, 35% noted that it was very difficult to obtain services, while 17% found it somewhat difficult.

Conclusions: Most children are receiving at least some physician-recommended services, especially speech and occupational therapies. However, more specific treatments, such as ABA and Floortime, were not specifically and regularly recommended. The lack of recommendations may be due to physicians' awareness of the challenges obtaining such services or the availability of trained professionals. Parent descriptions of the process of acquiring services for their child will be helpful in understanding the barriers to obtaining care.

136.141 141 Services Utilized by Adults with Autism Spectrum Disorders. L. A. Plummer*[1], M. A. McCarthy[1], K. S. Branch[1], L. J. Lawer[1] and D. S. Mandell[2], (1)*University of Pennsylvania*, (2)*University of Pennsylvania School of Medicine*

Background: Until recently, the focus of autism research has been primarily on children. A study recently published in the UK suggests that the prevalence of autism in adults mirrors the prevalence of autism in children at approximately 1 in 100. As with children, adults with autism require services and supports to address the disability associated with autism. Research suggests that quality of life for adults with autism is directly related to the services they receive rather than to the characteristics of their disability; however, little is known about the types and patterns of services these adults use. Objectives: to 1) describe the types and quantity of services used by adults with autism and their families, 2) evaluate the perceived effectiveness of these services, and 3) determine gaps in services identified by adults with autism and their families. Methods: The ASERT (Autism Services Education Research and Training) Needs Assessment survey was mailed to more than 30,000 individuals and families of children with autism spectrum disorder in the Commonwealth of Pennsylvania. The survey asked questions about services currently received by individuals with autism and their families. For the current study, we included surveys completed by adults (18 years of age and over) with autism, or a family member of an adult with autism. Results: Data collection is ongoing. To date, 69 adults with autism and 233 parents of adults with autism completed the survey. Individuals with autism about whom the survey was completed ranged in age from 18 to 67 years and encompassed individuals with Asperger's disorder, autistic disorder, and pervasive developmental disorder – not otherwise specified. Respondents reported numerous services that adults with autism are receiving, including college support, vocational support, behavior management, and mental health counseling. Seventy-eight percent of adults with autism who were currently enrolled in a post secondary education program described needing special support. All 78% were receiving one or more types of educational support services, the most common being test-taking assistance. Only 16% of respondents with autism reported being actively employed. Twenty-three percent of respondents reported receiving some type of vocational support, including vocational training, supported employment, and career counseling. Many families reported receiving services for their child's behavioral symptoms. The services most widely used included support for anxiety (50%) and aggressive behavior (30%). Forty-eight percent of people with autism used mental health counseling and 60% received case management services. The most common services reported as needed but not received were social skills training (42%), career counseling (30%), and vocational training and supported employment (both 28%). Conclusions: Survey results to date suggest a complex array of service needs among adults with autism and significant gaps in access to services. Of particular interest were the significant number of adults in higher education settings and the large number using services to address issues related to anxiety and aggression. Of particular concern were the low number in any type of employment and the high numbers without access to social skills and vocational supports.

136.142 142 The Effect of An Integrative Parent Education Program On Quality of Life for Families of Children with An Autism Spectrum Disorder. C. J. White*[1] and A. J. Lincoln[2], (1)*Center for Autism Research, Evaulation, and Service (CARES)*, (2)*Alliant International University*

Background: Families with children with Autistic Disorder (AD) exhibit decreases in cohesion and adaptability, increased social isolation (Higgins et al., 2005), higher levels of marital dissatisfaction (Hastings et al., 2005), and overall disruption to daily life (Bristol et al., 1988). Higher levels of stress, depression, and anxiety (Moes et al., 1992), and lower levels of parenting ability (Bristol et al., 1988) have been evidenced in mothers and fathers of children with AD. Siblings of AD children exhibit higher levels of psychological distress (Seligman & Darling, 2007), and maladjustment (Wolf, et al. 1998). Moreover, the sparse research on Quality of Life (QoL) specific to AD has suggested QoL is also compromised (Lindholm, 2007). Research

with families of children with AD has demonstrated the positive outcome of parent training (Ingersoll & Dvortcsak, 2006; Koegel et al., 1996). Specifically, these studies examined the effect of training parents to become treatment providers for their children. Few studies have taken parent training a step beyond assisting parents in providing treatment, making the curriculum more integrative. What is known is that the discussion of additional support components may increase parent's maintenance of skills in implementing intervention techniques (Stahmer & Gist, 2001).

Objectives: This aim of this study was to examine the effect of an Integrative Parent Education Program (IPEP) on knowledge gain, comfort in managing challenging behaviors, and QoL in caregivers of children diagnosed with an Autism Spectrum Disorder (ASD), utilizing a between-group, repeated-measure research design.

Methods: Participants to date are 43 primary caregivers of children diagnosed with an ASD. All participants received a standard score above 70 on the Gilliam Autism Rating Scale-Second Edition and also had previously received a formal diagnosis by a licensed psychologist. Caregivers all endorsed behaviors that were challenging to manage. Referrals were made by a state agency for behavior intervention and parent training. Participants were assigned to either the IPEP (n=23) or Treatment as Usual (TU) condition (n=20). Caregivers in the treatment condition attended a total of four IPEP modules. Course topics included general information on ASD diagnoses, typical child development, efficacious treatments, principles of ABA, behavior management, facilitation of social and communication skills, family stress, etc. Pre- and post-measures included multiple choice exams for each IPEP module, a Likert scale rating of comfort in managing behavior problems in their child, the Caregiver Evaluation of Quality of Life (CEQOL), and the Pediatric Quality of Life Inventory (PedsQL).

Results: Preliminary findings show that a small sample of caregivers who completed the IPEP program showed improved scores of parent knowledge (p=.011) and greater comfort with behavior management (p=.028) from pre- to post-test. Caregiver ratings of quality of life (QoL) appeared to remain more constant. However, pre-post test correlations for the QoL measures used appeared adequate.

Conclusions: The implementation of an Integrative Parent Education Program is effective in increasing caregiver's knowledge and comfort in managing challenging behaviors. However, changes in perceived QoL may remain constant. It is possible such improvement in QoL lags behind the increases in caregiver knowledge and comfort in managing behaviors.

136.143 143 Predictors of No Show and Patient Cancellation at An Outpatient Autism Clinic. C. Foster*, L. Kalb, C. Wolf, P. Law and D. Menon, *Kennedy Krieger Institute*

Background: Patient appointment absenteeism has a deleterious effect on the global functioning of healthcare facilities and ultimately, public health (Melnikow & Kiefe, 1994; Sharp & Hamilton, 2001). No Shows (NS) and Patient Cancellations (PC) can lead to longer waiting times, clinic fiscal instability, poor utilization of personnel, and an overall decline in the timeliness and quality of care (Satiani, 2009). This decrease in quality service delivery is alarming for specialized autism settings given the growing prevalence of Autism Spectrum Disorders (ASD) in the US, the scarcity of autism service providers and clinics, and the preexisting long wait times within these centers. Despite this hazard, there is a dearth of research that has examined the rates or predictors of NS and PC in community autism clinics.

Objectives: The aim of this study was to examine attendance rates at an outpatient autism center and explore what factors influence whether patients NS or PC for appointments.

Methods: Longitudinal data from eight hundred and twelve children ages five months to seventeen years (M=7y) were used for this study. Appointment data from 2003 to 2009 were gathered from the local scheduling information system and additional demographic information was collected from

a research registration form. A random effects logistic regression model was employed to examine predictors of patient absenteeism. This approach is most useful when making inferences about individuals rather than population averages, given the heterogeneity of our sample (overall r^2=.01). Time-dependent predictors included provider type, patient age, academic semester, wait time, and appointment time. Static demographic predictors included race/ethnicity, gender, distance from the clinic, and history of medical assistance, serving as a proxy for low family income. Separate models were developed to independently examine our dependent variables: NS and PC.

Results: A total of 14,714 appointments were analyzed (*M*=108, p50=40, Max=1062), of which 1,470 (12%) were NS and 991 (8%) were PC. Receiving medical assistance (OR 1.78), non-white families (OR 1.49), wait-time beyond 60 days (OR 1.25), winter school semester (OR 1.26), and having a non-evaluation appointment type (OR 2.36) increased the risk of NS. Having an appointment with an MD (OR .54), female children (OR .71), and a wait time less than 60 days (OR .73) decreased the likelihood of NS (all p<.05). Having a child older than 8 years of age (OR 1.32), living further than 10 miles from the clinic (OR 1.34), non-white families (OR1 .47), a wait time beyond 60 days (OR 1.59), an evening appointment time (OR 1.26), and an appointment with an OT (OR 1.46) increased the risk of PC. An appointment with an MD (OR .53) or psychologist (OR .57), and an appointment during the spring semester (OR .80) was protective (all p<.05).

Conclusions: To our knowledge, this is the first study to investigate rates and predictors of patient absenteeism at an outpatient autism center. This data identifies numerous child, family, and clinic factors associated with both NS and PC. These data hold important implications to the prospective design of interventions seeking to reduce this burden.

136.144 144 Quality Improvements in ASD Health Service Delivery. J. E. Farmer*, K. Dunne, M. J. Clark, W. A. Mayfield and J. S. Hawks, *University of Missouri*

Background: Children with autism spectrum disorders (ASD) are less likely to receive comprehensive, coordinated, and family-centered care compared to children with other special health care needs (Kogan et al, 2008). New models of care to address these concerns have been described (IACC, 2005), but strategies must be developed to implement quality improvements in clinical settings that serve children with ASD and their families.

Objectives: To determine the quality of family-centered care provided at a tertiary care center that offers health and behavioral services for individuals with autism and other developmental disorders (DDs). This study is part of a larger effort to create quality improvement (QI) processes that enhance ASD service delivery.

Methods: A randomized sample of 200 children with ASD and other DDs was selected from 1,133 individuals seen for diagnostic and medical services at a Midwest academic health center over a 6 month period. Parents were invited to complete the Quality of Care Survey by telephone (adapted from Family Voices, 2008). Ninety-eight parents (49%) completed demographic information and the 30-item survey, ranking each item on a Likert scale (0 = Never to 4 = Always; higher scores are better).

Results: The mean age of the sample was 10.92 (SD = 4.58); 47% were 3-11 years and 53% were 12-21; 79% were male; and 89% were Caucasian. Half reported an ASD diagnosis, and the remainder had either other developmental (48%) or physical health conditions (2%). The survey included four subscales that showed adequate internal consistency (>.75). Parents reported high levels of satisfaction on the Care & Support of the Child subscale (Md = 3.70, Range = 2-4) and Care Coordination subscale (Md = 3.50, Range = 0-4). Nearly all respondents (98%) reported that their providers listen to their concerns and 79% reported partnering with providers to make decisions for their child's care (i.e., most of the time or always). Respondents indicated lower satisfaction on the Care & Support of the Family subscale (Md = 2.75, Range = 0-4) and on the

Transition to Adulthood subscale (Md = 1.67, Range = 0-4; completed if child was 12 or older). The majority (78%) reported their providers rarely/never helped them write a plan for their youth's transition to adult services and supports. Nearly two-thirds (63%) reported their providers rarely/never helped them connect with other families who share similar life situations. Overall satisfaction with quality of care varied by child age (M = 3.30 for younger vs. 2.89 for older children, p=.006) and by level of child functioning (M = 3.31 if condition affects child "some" vs. 2.95 if condition affects child "a great deal", p=.033).

Conclusions: Survey results are consistent with national reports of unmet family needs and the vulnerability of youth in transition to adulthood (IACC, 2005; Kogan et al., 2008). These data provide a rich resource for QI initiatives in clinical settings and will guide development of best practices in health service delivery for those with ASD and their families.

136.145 145 What Do Pre-Service Teachers Believe and Feel about Teaching Students with Autism Spectrum Disorders (ASD)?. A. R. Ly*, L. S. Kao, L. E. Richland and W. A. Goldberg, *University of California, Irvine*

Background: Research on educating children with disabilities focuses on special education personnel. However, there has been an impressive rise in the number of children with ASD in general education (GE) classrooms. In 2004, there were 48,568 students with ASD in an inclusive setting. Research about in-service and pre-service teachers' inclusion attitudes toward children with special needs, broadly defined, has emerged from European and Australian education systems. Internationally, GE teachers feel unprepared and want training about ASD (Spears, Tollefson, & Simpson, 2001). Less is known about U.S. pre-service GE teachers' attitudes specific to ASD. The limited research focuses on practicing teachers with varying training and experience. Further examination of teacher preparation is important given the increase in included students with ASD.

Objectives: To determine factors associated with pre-service teachers' (1) ASD-specific teaching efficacy and (2) attitudes toward inclusion of students with ASD.

Methods: Participants were 94 GE pre-service teachers (73 female) at a large university in the western U.S. (K-6 program: n = 28; 7-12 program: n = 65). Announcements were made during classes or through course emails. Participants could complete a paper or online survey. Most participants were Caucasian (53%) or Asian-American (36%) with a median age of 24 years. Measures tapped general teaching efficacy (i.e., Teacher Self-Efficacy Scale [Bandura, 1977]) and ASD-specific teaching efficacy (i.e, modified Teacher Efficacy Scale-Short Form [Hoy & Woolfolk, 1993]), professional development (scale created for this study), and perceptions regarding inclusion of students with ASD (i.e., Impact of Inclusion Questionnaire [Hastings & Oakford, 2003]). All scales had good internal reliability (a > 0.80). Participants also provided information about whether or not they had experiences with ASD (personal, professional, and/or educational) and the number of months spent student teaching.

Results: (1) Pre-service teachers who felt more efficacious teaching children with ASD also expressed significantly greater positive attitudes toward inclusion (r =.535, p <.001), overall teaching efficacy (r =.469, p <.001), and had more experience with persons with ASD (r =.266, p =.010).

(2) Pre-service teachers who believed more strongly in inclusion also felt more efficacious teaching students with ASD (r =.535, p <.001) and reported higher likelihood of participating in future professional development (r =.210, p =.043). However, more time spent student teaching was associated with more negative attitudes toward inclusion (r = -.209, p =.048).

Conclusions: The finding of less favorable attitudes to inclusion of students with ASD with more teaching experience replicates findings about disabilities from a decade ago (Soodak et al., 1998; Wilczenski, 1991). However, unlike previous studies, participants in the current study were graduate level pre-service teachers. Perhaps these negative

views stemmed from pre-service teachers' observations of challenges faced by master teachers who lacked specialized training themselves and felt overwhelmed by the demands to meet the instructional needs of both typically developing students and those with ASD. The hopeful finding that teaching efficacy is positively associated with inclusive beliefs, suggests that credential programs should provide greater training to equip teachers with the skills and confidence required to effectively teach diverse classrooms.

136.146 146 Parental Reactions to Their Child's Autism Diagnosis Predict the Working Alliance Between Parent and Intervention Providers. K. K. Berry*[1], M. Siller[2], T. Hutman[3] and M. Sigman[3], (1)*Hunter College, City University of New York*, (2)*Hunter College of the City University of New York*, (3)*University of California, Los Angeles*

Background: It is generally assumed that a strong working alliance between parent and interventionist is crucial for successful parent education. A better understanding of parental characteristics that influence working alliance will help us to anticipate challenges and educate parents more effectively.

Objectives: This study investigated the relation between parental reactions to their child's diagnosis of autism and independent ratings of the working alliance between the parent and an interventionist.

Methods: Participants included 32 parents that participated in a clinical trial and were randomly assigned to one of two treatment conditions. Parents assigned to the experimental treatment were invited to participate in 12 in-home training sessions designed to encourage communication in children diagnosed with autism spectrum disorders. For each participant, we used an observational measure (Davis & Carter, 2003) to evaluate indicators of working alliance during two videotaped intervention sessions; data from both sessions were subsequently averaged to compute a single working alliance score. The modified working alliance scale consists of 7 individual rating scales and evaluates the parents' alignment with intervention goals and level of trust toward the interventionist. Good inter-rater reliability was established based on 20 intervention sessions (ICC = .72).

Parental reactions to their child's diagnosis of autism were assessed with the Reaction to Diagnosis Interview (RDI; Pianta & Marvin, 1992). The RDI is a structured interview asking parents to describe their diagnostic experience. Based on their responses, parents are classified as either 'resolved' or 'unresolved' with regards to the child's diagnosis. Resolution is characterized by the parent: 1) having a balance between positive and negative descriptions of the experience, 2) describing a change in his or her feelings about the diagnosis after the initial reaction, and 3) suspending the search for existential causes of the disability. A research assistant and the third author established an agreement rate of 100%, kappa = 1 during 14 interviews, approximately 20% of the sample.

Results: Thirty-two parents were classified as resolved (n = 13) or unresolved (n = 19) based on the Reaction to Diagnosis Interviews; four parents were not interviewed due to scheduling conflicts. Parents who were resolved (M = 2.11; SD = .39) received higher ratings of working alliance than parents who were unresolved (M = 1.76; SD = .23), $t(30) = -2.93$, $p < .01$. The relation between RDI classifications and working alliance levels could not be explained by child's ethnicity, chronological age, non-verbal IQ, or language abilities. They were also not explained by mother's age, years of education, or household income.

Conclusions: Findings from this study suggest that parental reactions to their child's autism diagnosis influence the parents' ability to develop a strong working alliance with their child's intervention providers. Helping parents to reach resolution concerning their child's diagnosis may be an important component of successful parent education programs.

136.147 147 The Influence of Rurality On Quality of Services for Children with Autism Spectrum Disorders. M. A. Murphy*, B. Rous and K. McCormick, *University of Kentucky*

Background: Access to quality mental health services for children with Autism Spectrum Disorders (ASD) is crucial to their later

outcomes and quality of life (American Academy of Pediatrics, 2001). Unfortunately, access to these important services is somewhat limited, especially for individuals living in rural areas (Chen, Liu, Su, Huang, & Kim, 2008). This is despite evidence that early identification and early intervention (American Academy of Pediatrics, 2001; Rickards, Walstab, Wright-Rossi, Simpson & Reddihough, 2009) have substantial impacts on the individual's acquisition of important skills, such as social skills, language, and communication methods.
Currently, research indicates disparities exist between the number of available mental health professionals in rural areas compared to their urban counterparts (Baldwin et al., 2006). Further, there is initial research findings demonstrate that individuals with ASD are often diagnosed at a later age than their urban counterparts (Chen et al., 2008; Mandell, Novak & Zubritsky, 2009). Current research suggests that for children with ASD living in rural areas, access to services may be limited due to shortages of professionals in these areas. Further, the quality of the services they receive may be limited by the nature of their ability to access these services.
Objectives: The purpose of this study is to compare the quality of preschool services received by children with ASD in early childhood (ages 3 to 4 years) in rural areas. Quality of services will be measured through information obtained through family interviews and teacher surveys, which will be used to assess the congruence of these services with best practices for this population. It is predicted that children with ASD living in rural areas will have access to lower quality of services than those living in urban areas.
Methods: This study will use existing data from a multi-state study conducted through the National Early Childhood Transition Center. While this data set includes children with a variety of disabilities (age 0 - 6 years), data analysis will be focused on children who have a diagnosis of Autism, Asperger's Syndrome and PDD-NOS who are exiting public preschool services. The independent variable in this study is the area or region in which the child with ASD lives in (i.e., rural versus urban). The dependent variable in this study is the quality of services the individual with ASD receives. Rurality of the area or community the individual lives in will be established from the zip code in which they report residing in. Rurality of a county will be determined using the Rural-Urban Continuum Codes (Butler & Beale, 1993).
Results: To address the predictions posed by the study, a Univariate One-Way Analysis of Covariance will be used. Socio-economic status will serve as a covariate.
Conclusions: The results from this study will provide information regarding the current environment and quality of services received by children with ASD in rural areas. Further, the findings may highlight the current disparities between rural and urban regions, and provide evidence for the need of the improvement of the services available to this population.

136.148 148 Stress in 1 Parent and 2 Parent Households with Children with Autism. A. D. Sherman*[1], S. Shin[2], C. M. Harker[1], E. M. Reisinger[2] and D. S. Mandell[1], (1)*University of Pennsylvania School of Medicine*, (2)*University of Pennsylvania*

Background: Parents of children on the autism spectrum experience greater stress than parents of children with other developmental disorders. Research suggests that stress in families with children with autism varies, depending on the amount of social support (formal and informal) and the child's functional level. Previous studies also suggest that single mothers of children with special needs experience higher levels of stress than parents in two- parent households. The role of these two factors – social support and marital status – has not been examined in the same study. If social support mediates the relationship between marital status and stress among parents of children with autism, it suggests a malleable mechanism to help these vulnerable families cope.

Objectives: To examine the association between marital status and stress among parents of children with autism and the mediating roles of social support, socio-economic status, and level of child impairment.
Methods: Data were collected as part of a behavioral intervention study in a large urban

school district. The sample comprised 127 students in 39 kindergarten-through-second-grade autism support classrooms. Students were assessed through direct observation, parent and teacher report at the beginning and end of the school year. The current study relied on direct observation measures (Autism Diagnostic Observation Scale) and parent measures (Parenting Stress Index (PSI), Adaptive Behavior Assessment System-II, Social Support Questionnaire, and socio-demographics).

Results: Analyses are ongoing. 44% of the sample was married, 43% never married, and 13% divorced or separated. Households with married parents experience more stress in the Parent- Child Dysfunctional Interaction (P-CDI) subscale of the PSI than households with a single parent ($p<.05$). No statistically significant differences were found between the two groups in levels of stress in the Difficult Child and Parental Distress subscales of the PSI. There was no statistically significant association between marital status and social support. Of the sample 18% scored $\geq 85^{th}$ percentile in all three subscales of the parenting stress index. Analysis of associations with types of social support, severity of diagnosis and functioning is ongoing.
Conclusions: Preliminary results are contrary to previous reports of the association between marital status and parental stress. Married families experience higher levels of stress in the P-CDI subscale of the PSI than single parents which suggest that single parents are more reinforced by the interactions that they experience with their children. Results from an analysis of social support, severity of diagnosis and functioning will be used to determine possible explanations for the differences in level of parent interactions based on marital status.

136.149 149 Personal Growth Aspects in the Experience of Parenting a Child On the Autistic Spectrum. M. Yehonatan* and O. Golan, *Bar-Ilan University*

Background:

Parenting is considered to be one of the most meaningful and complex human experiences, shaping the parent's sense of self. Parenting a child with an Autism Spectrum Condition (ASC) has a unique effect on various aspects of the parent's experience, including the relationships with the diagnosed child, as with the other family members, use of support systems, negotiation with educational and welfare agents, views and hopes for the future. Autism research has documented parenting difficulties and negative emotional outcomes for parents of children with ASC, but has not examined possible positive outcomes of this experience. Personal growth literature emphasizes positive benefits perceived by individuals as emerging from difficult and even traumatic life experiences.

Objectives:

This study aims to examine the possibility that parenting a child with ASC can lead to perceived positive aspects and personal growth by the parent. Using a qualitative approach, it explores the ways in which these positive experiences manifest themselves and documents parents' authentic, self-defined experiences, relating to their unique interactions with their child with ASC. The assumption is that these interactions may contain positive, growth promoting elements, which until now have been largely over-looked.

Methods: Nineteen parents of children with ASC were interviewed using semi-structured interviews. Interviews were designed to help parents reflect upon their parental experience and its effects on their lives and sense of self. Parents varied in background, level of functioning of their child with ASC, and time from diagnosis. This wide sampling has enabled the uncovering of varied narratives. Interviews were transcribed and content analysis was performed.

Results:

Parents reflect upon various positive aspects that the encounter with ASC had brought to their lives. A recurring central theme in parents' narratives was the sense of personal growth, including a sense of empowerment and personal strength, a new existential perspective or a spiritual-emotional experience, altered interpersonal realm

(including aspects of family life, marriage, relationships outside the family and encounter with diversity) and increased expertise, professional or political involvement. In parallel, parents have reflected on the pain and hardship in their parental experience. The interrelations between enriching, positive factors and hardship or distress in parents' experiences, as well as factors associated with positive experiences and parents' personal growth will be discussed.

Conclusions: This work suggests a different perspective on parenting a child with ASC, demonstrating positive aspects of parental experience and even meaningful personal growth. This altered perspective can be harnessed by professionals when working with parents of children with ASC.

Invited Educational Symposium Program
137 Relationship Between Epilepsy and Autism

Moderator: S. Spence *NIH*

This symposium is designed to explore the relationship between epilepsy and ASD. While higher rates of epilepsy have long been reported in ASD, prevalence estimates vary from 5% to as much as 46%. While variation likely reflects differences in study samples, several factors appear to truly increase epilepsy risk such as lower IQ, co-morbid syndromes (e.g. non-idiopathic autism) and gender. However, the rate of epilepsy in idiopathic ASD with normal IQ is still significantly above population risk, suggesting autism itself is associated with an increased epilepsy risk. The recent appreciation that epileptiform EEG abnormalities occur with rates as high as 60%, even in the absence of epilepsy, has lead investigators to propose they may play a causal role. We posit that epilepsy and epileptiform EEGs represent biomarkers of cortical dysfunction in ASD and believe relationships should be vigorously explored. This symposium will review clinical and electrophysiological data and describe the breadth of association with ASD. Next we will describe a genetic disease model known to overlap with ASD and epilepsy: Tuberous Sclerosis Complex (TSC), whose pathways provide researchers a window into this relationship as well as novel therapeutic targets. Finally, we discuss pathophysiological data that characterizes ASD as an imbalance between neuronal excitation and inhibition, which in turn suggests possible directions for future research.

137.001 EPILEPSY, EPILEPTIFORM EEG AND AUTISM: Who has it and what might it mean?. M. Chez*, *Sutter Neuroscience Institute*

137.002 Magnetoencephalography in ASD: How can new electrophysiological imaging techniques help explore the relationship?. J. D. Lewine*, *Alexian Brothers Medical Center*

137.003 Tuberous Sclerosis Complex: What can the knowledge of signaling pathway abnormalities teach us about ASD?. M. Sahin*, *Director of Multi-disciplinary Tuberous Sclerosis Program*

137.004 Excitatation/Inhibition Imbalance in ASD: Is this a pathophysiological model of cerebral dysfunction in ASD?. T. Hensch*, *Center for Brain Science, Harvard University*

Clinical Phenotype Program
138 Clinical Phenotype 2

138.001 Pragmatic Language and Social Cognitive Overlap in Children with Autism and Fragile X Syndrome. G. E. Martin*, M. Losh, J. Klusek and A. Harris, *University of North Carolina at Chapel Hill*

Background: Impairments in pragmatic language and social cognition are core features of autism. Fragile X syndrome (FXS) is the leading single-gene disorder associated with a diagnosis of autism; recent estimates suggest that up to ~50% of males with FXS meet diagnostic criteria for autism on gold standard instruments (Hall et al., 2008). Moreover, many of the pragmatic difficulties attributed to FXS are also observed in autism (Roberts et al., 2007).
Objectives: This study compared the pragmatic language and social cognitive skills of boys with autism and boys with FXS in order to identify precise autism phenotypes that could be linked with the Fragile X Mental Retardation-1 gene (*FMR1*).
Methods: Pragmatic language and social cognition were examined in boys with autism (n=19) and FXS (n=54), ranging in chronological age from 3-15 years, as well as a typically developing (TD) control group (n=22), ranging in age from 2-6. We administered the Pragmatic Judgment subtest of the Comprehensive Assessment of Spoken Language (CASL) (Carrow-Woolfolk, 1999), a standardized assessment of pragmatic language. Conversational discourse in a more naturalistic context was elicited using the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 1989), and examined for the degree to which the child's turn was contingent, or topically related to the preceding turn. We examined

social cognitive performance using standard theory of mind (ToM) tasks for children (perspective taking, diverse desires and beliefs, and false belief understanding). For some analyses, we divided boys with FXS into two groups based on autism status (FXS-A and FXS-O).

Results: Data were analyzed using a series of ANCOVAs controlling for nonverbal mental age and receptive and expressive language skills. On the CASL, controls scored significantly higher than children with FXS ($p<.005$) and autism ($p<.0001$), and the FXS group scored significantly higher than the autism group ($p<.01$). During conversation, both groups of boys with autism (autism-only and FXS-A) used significantly more noncontingent (off-topic) language than boys with FXS-O ($p<.01$; $p<.0001$, respectively) and controls (p values $< .0001$). Moreover, boys with autism without FXS used significantly more noncontingent language than even the boys with FXS-A ($p<.01$). Boys with autism-only and FXS-A showed significantly more impairment in ToM than boys with FXS-O and TD (p values $< .05$). ToM skills were significantly associated with boys' pragmatic skills measured through the CASL for boys with autism-only ($r=.82$, $p<.001$), FXS-A ($r=.65$, $p<.05$), FXS-O ($r=.54$, $p<.05$), and TD ($r=.72$, $p<.01$).

Conclusions: These findings suggest substantially overlapping phenotypes among children with autism and FXS. Moreover, the similarity in performance compared with controls of the autism-only and FXS-A groups and the lack of discourse and ToM impairments found in the FXS-O group are together striking findings which point to a specific role of autism in the discourse and social cognitive impairments in FXS. Results also suggest that ToM ability, impaired in autism-only and FXS-A, may be a key underpinning of pragmatic language deficits.

138.002 Clinical and Neuropsychological Overlap in the Broad Autism Phenotype and the FMR1 Premutation. M. Losh*, G. E. Martin and J. Klusek, *University of North Carolina at Chapel Hill*

Background: Fragile X syndrome (FXS) is associated with an increased risk of autism, with conservative prevalence rates ranging from ~25-50%, suggesting that mutations in *FMR1* (the gene causing FXS) is a highly important risk for autism. While efforts to uncover the etiologic mechanisms in autism are often confounded by multiple unknown etiologies, genetically defined syndromes such as FXS provide an uncommon opportunity to examine gene-brain-behavior associations in a more etiologically homogeneous condition.

Objectives: This study investigated the role of *FMR1* in autism symptomatology through the study of 1st degree relatives who are at increased genetic liability (and in the case of FXS, who are carriers of the *FMR1* premutation), along measures of the broad autism phenotype (BAP) and neuropsychological characteristics shown to co-segregate with autism and the BAP.

Methods: To address the hypothesis that *FMR1* may play a role in the BAP, we administered the Broad Autism Phenotype Questionnaire (BAP-Q; Hurley et al., 2007) to a group of 53 FXS mothers, 24 autism mothers, and 17 control mothers. The BAP-Q is a sensitive and specific self- and informant-report questionnaire, developed for detection of the BAP. We also examined group differences on a battery of social cognitive tests previously shown to distinguish autism parents with the BAP from controls (i.e., the Reading the Mind in the Eyes Test, the Trustworthiness of Faces Task, and the Movie Stills Task; Losh et al., 2009). Parent-child correlations were also assessed for evidence of familiality which could further implicate genetic influence.

Results: Significantly higher rates of the BAP were detected in both FXS and autism parent groups, relative to controls (x^2 (2) = 8.64, $p < .05$). FXS and autism parents also performed significantly worse than controls on each of the social cognitive measures (p values $< .01$). Significant parent-child correlations were also detected among FXS families (child data was not available for the autism or control families). The presence of BAP characteristics in parents was significantly associated with children's vocabulary measured through the PPVT ($r=-.66$, $p<.05$). We found similar relationships between parental social cognitive performance on the Movie Stills and Trustworthiness of Faces Tasks, where impaired performance on these

measures was correlated with greater delays in children's vocabulary (r=-.81, p<.05; r = -.73, p< .05, respectively) and more severe impairments in children's pragmatic language ability (r=-.71, p<.05); r= -0.60, p = .10, respectively). Finally, analyses revealed that parental activation ratio (an index of cells producing FMRP) positively correlated with children's expressive and receptive vocabulary skills (r=.55911, p<.05; r=.61169, p=.0602, respectively), so that mothers with more normal X activation (i.e., higher activation ratio) tended to have children with more advanced lexical abilities
Conclusions: Findings demonstrate substantially overlapping phenotypes among autism parents and FXS parents who are carriers of *FMR1* in its premutation state. Results support a role of *FMR1* in the BAP, and in the social cognitive profiles associated with the BAP. Parent-child correlations in phenotypes and genetic characteristics provide further support for genetic influence and overlap of FXS and autism.

138.003 Variants in the Social-Emotional Phenotype of Children with Autism and Children with Fragile X Syndrome. N. M. Russo*, E. Berry-Kravis, C. McKown and M. Lipton, *Rush University Medical Center*

Background: Autism spectrum disorders (ASD) and Fragile X Syndrome (FXS) have elements of shared neurobiology. Individuals living with either condition suffer from severe language and social impairments. These impairments often manifest in distinctly different ways and may arise from different underlying origins.

Objectives: This study aimed to identify similarities and differences in the ways children with ASD and FXS encode, interpret, and reason about social and emotional information. Our central objective was to compare social-emotional learning (SEL) skill in children with ASD and children with FXS and to determine diagnosis-specificity of patterns of deficits.

Methods: SEL skill is a constellation of cognitive, affective, and regulatory processes that govern social behavior. We compared the SEL phenotype of children with ASD to girls with FXS. Autism diagnoses and severity were confirmed via the Social Communication Questionnaire and the Autism Diagnostic Observation Schedule. Six children (ages 7-12 years) with autism (5 males, 1 female) were individually age-matched and compared to six full-mutation girls with FXS. Three of the children with FXS also met criteria for autism spectrum disorders.

We administered an assessment battery that measured the child's: (1) ability to label the emotion of faces and voices, (2) pragmatic language skills, (3) perspective-taking and theory of mind abilities, and (4) social problem-solving skills.

Results: Results indicate that, with the exception of performances on a measure of pragmatic language and one aspect of social problem solving, children with ASD tend to perform at a higher level than children with children with FXS. Although not reaching significance, children with ASD were more accurate at labeling emotion from nonverbal cues than girls with FXS. Children with ASD also performed significantly better than girls with FXS on the perspective-taking assessment. Finally, although children with ASD were consistently better at identifying social problems, the children with FXS were more likely to identify a competent solution at first prompting. Exploratory regression analyses showed that although the differences were partially mediated by IQ, they were not shown to be mediated by autism severity.

Conclusions: Although a small sample, these data suggest that children with ASD differ from girls with FXS with respect to SEL skill. These data further suggest that the social phenotype characterizing ASD is qualitatively different than that which characterizes FXS. Importantly, this is one of the few studies documenting SEL deficits in girls with FXS. A larger sample is needed to confirm and extend the findings of this preliminary study. Once the nature of SEL deficits are defined in these populations, future work may address the neurobiology of these differences and the development of interventions specific to each child's struggles.

138.004 A Comparison of Sleep Patterns and Behaviour in Children with Autism, Other Developmental Disabilities, and Typically Developing Children. A. L. Richdale*[1] and S. Cotton[2], (1)*La Trobe University*, (2)*University of Melbourne*

Background: Sleep problems are common in developmental disabilities including autism, and Down (DS), Prader-Willi (PWS), and fragile-X syndromes and children with familial intellectual disability (FID). However, few researchers compare the sleep of children with autism with specific developmental disorders, instead using mixed comparison groups. Additionally while disruptive behaviour has been shown to be related to reported sleep problems the impact of both daytime and nighttime behaviour on sleep patterns is generally not considered. Objectives: 1) To examine 24-hour sleep patterns of children with autism DS, PWS and FID, and typically developing (TD) children; (2) To elucidate how 24-hour sleep patterns related to behaviour patterns across this period. Methods: Participants represented 115 (75%) children between 3 and 16 years of age (M=7.9, SD=3.0 years) previously reported in Cotton and Richdale (2006) and were all from three earlier studies conducted by one or both authors. 34 children had autism, 12 had DS, 12 had PWS, 24 had FID, and 33 children were TD. The groups did not differ on age and all groups had more males than females with a 3:1 ratio in the autism group. Fourteen-day sleep diary data covering daytime and nightime sleep and behaviour were examined. Parents also provided qualitative information in the diaries. Given the uneven and sometimes small group sizes non-parametric analyses were conducted: Kruskal-Wallis H statistic for group comparisons ($p < .05$), Mann-Whitney-U for multiple pair-wise comparisons ($p < .05$) and Spearman's Rho for all correlations ($p \leq .01$). Results: Group comparisons showed significant differences for daytime behaviours with children with autism showing the most difficult daytime and bedtime behaviour, more energetic and excited daytime behaviour and less daytime and bedtime sleepiness. Multiple pairwise comparisons variously showed significant differences with the DS, FID and TD groups, with the autism group being significantly less sleepy at bedtime than all other groups. Children with autism napped less than the PWS and DS groups. They fell asleep later, spent longer awake if they woke, slept less at night and over 24 hours, and had poorer sleep quality than all other groups. With the exception of night sleep, multiple pairwise comparisons variously showed significant differences between the autism and the PWS, FID and TD groups. Children with autism were more likely to be woken in the morning than all the other groups and the PWS comparison was significant. There were a large number of significant associations between behaviours and sleep patterns in the autism group compared to the other groups. In particular these associations suggested that higher levels of daytime activity and poor behaviour were associated with poor sleep quality in children with autism as opposed to the other groups. Conclusions: Comparison of sleep and behaviour patterns in autism, DS, PWS, FID and TD children indicates that there are some sleep characteristics that differentiate these disorders. In autism sleep patterns are generally more problematic, sleep quality is poorer and unlike the other disorders, poor sleep quality is related to over-active behaviours and disturbed sleep. Implications will be discussed.

138.005 Effects of Social and Non-Social Cues On Saccadic Eye Movements in ASD and ADHD. B. Azadi*[1], U. Ettinger[2], P. Asherson[3], K. L. Ashwood[1], S. Cartwright[1], G. Childs[1] and P. Bolton[1], (1)*Institute of Psychiatry, King's College London*, (2)*Department of Psychiatry, Ludwig-Maximilians-University Munich*, (3)*Institute of Psychiatry*

Background: Information gained from another person's eyes plays a crucial role in social communication. People with autism have difficulty following gaze in naturalistic and semi-naturalistic situations. Children with ADHD also exhibit behavioral difficulties with social interaction, although it is unclear whether their problems arise from substrates similar to those with ASD. It has been suggested that poor social behaviors in ASD are related to deficits in social perception, while in ADHD they are associated with inattention and impulsivity. Recently, the attentional mechanism corresponding to reflexive orienting towards the direction of others' eye gaze was assessed using the Posner-style spatial cueing paradigm. Evidence that people with autism can

reflexively orient their attention in response to eye gaze cues is contradictory. Although some studies have demonstrated apparently normal effects of social cueing, the results of other experiments suggest that people with autism respond to social cues such as eye gaze in much the same way as they do to non-social cues such as arrows, whereas in non-autistic people, a greater salience to social cues has been reported.
Objectives: Studies comparing the ASD group with other neuropsychiatric disorders are lacking. This study uses an eye-tracker to investigate social attention comparing pure ASD and ADHD groups for the first time with a group of co-morbid ADHD&ASD.
Subjects & Methods: Boys aged 7 to 16, with diagnosis of pure ADHD, pure ASD or comorbid ASD+ADHD (FSIQ>70) were tested on a cueing paradigm. Participants were instructed to shift their gaze to the peripheral target that appeared on either side of a visual fixation point. Before the target appeared, a centrally presented stimulus (eye gaze or arrow) cued the participant to the correct or incorrect side. The cue was predictive (i.e. congruent) only in 50% of trials.
Results: Results of 13 ADHD, 7 ASD & 8 co-morbid subjects (age and FSIQ matched) are reported with data collection still in progress. Saccadic reaction times were analysed using repeated measures analysis of variance with group as between-subject factor and cue (arrows versus eyes) and congruency (congruent versus incongruent) as within-participant factors.
There were no group effects, and no significant group by cue interaction. The group by congruency interaction approached significance ($p=0.054$). In the ASD group the SRT for incongruent condition was significantly faster than the congruent condition ($p=0.01$) whilst both ADHD and comorbid groups were significantly slower in incongruent than congruent conditions ($p=0.04$ and $p=0.007$; respectively). The congruency by cue interaction was also significant ($p=.047$) suggesting longer reaction times with congruent than incongruent cues in the arrow but not the face condition.
Conclusions: Reaction time facilitation for the congruent conditions was seen in the ADHD and co-morbid groups but not in the ASD. This pattern points to a dissociation of the clinical groups at the level of attentional cue processing and it seems as if the ASD participants didn't acknowledge the salience of cue. The comparison of the data with a control group will enable us to better explain the different patterns of social attention in theses clinical groups.

138.006 Personal Space and Interpersonal Distance in Autism: Insights From the SRS. D. P. Kennedy*[1], J. N. Constantino[2] and R. Adolphs[1], (1)*Caltech*, (2)*Washington University School of Medicine*

Background: Research on social behavior in autism has focused considerably on face processing and mentalizing abilities. Relatively ignored have been other equally important real-world social behaviors that can be more difficult to quantify in laboratory experiments, and about which less is known neurobiologically. One such behavior is the regulation of interpersonal distance (the physical distance between individuals). Distance regulation is critical for successful social interaction, and its impairment can result in violations of personal space. This topic is ripe for investigation in part because we recently showed that the amygdala plays a key role in it, and because anecdotal observations suggest it is impaired in autism. Objectives: Given the lack of research on interpersonal distance in autism together with its patent importance in social interaction, we began by analyzing questionnaire-based data from a large sample of individuals with autism. We were interested both in quantifying possible impairments in general, as well as in identifying individual differences that might carve out potential subtypes of autism. Methods: One item on the Social Responsiveness Scale (SRS), a 65-item parent- or teacher-report questionnaire that quantifies severity of autistic impairment, deals explicitly with personal space and interpersonal distance (Question 55: "knows when he or she is too close to someone or is invading someone's space"). The question is rated on a 4-point scale with higher scores reflecting more common interpersonal distance violations. We examined differences in this parent-report measure between autistic probands and their siblings, by using

a large sample of phenotypic data from the Simons Simplex Collection and the Autism Genetic Resource Exchange (representing 766 autism-sibling pairs in total), as well as our own sample of identical and fraternal twins (J.C.). Results: Autistic probands had significantly higher levels of parent-reported interpersonal distance violations than their siblings (proband mean = 2.22, sibling mean = 0.70, p <.0000001). There were no differences in mean ratings across the various autism spectrum diagnostic categories (autism mean = 2.20; Asperger's mean = 2.22; PDD-NOS mean = 2.17). Results of additional analyses, including an analysis of the heritability of interpersonal distancing, will also be presented. Conclusions: Individuals with autism have impaired interpersonal distance regulation. This deficit is pervasive, in that it affects the majority of individuals with an autism spectrum diagnosis, and in that it is observed to a similar degree across the various diagnostic categories (i.e., autism, Asperger's, and PDD-NOS). Given recent findings of the role of the amygdala in interpersonal distance regulation and in one's sense of personal space (Kennedy et al., 2009), it is of particular interest to determine whether such abnormalities in autism might reflect an endophenotype of amygdala dysfunction. The present results should lead to a greater understanding (and perhaps acceptance) of personal space violations made by individuals with autism, and might also prove helpful in resolving situations arising from such violations.

138.007 Sex Differences in Autistic Traits: Is High Verbal IQ Protective against Social Impairments in Girls but Not Boys?. K. Dworzynski*[1], A. Ronald[2], R. A. Hoekstra[3], F. Rijsdijk[1] and F. Happé[1], (1)*Institute of Psychiatry, King's College London*, (2)*Birkbeck College, University of London*, (3)*University of Cambridge*

Background:

The increase in male to female ratio in autism spectrum conditions (ASCs) with increasing IQ may be an important clue to the aetiology of these disorders. Recent research (Skuse et al., 2009) suggests verbal IQ (VIQ) at the high extreme is protective against social communication impairments in girls only.

Objectives: The aim is to extend this finding to both verbal (VIQ) and nonverbal (NIQ) effects on the whole triad of autistic-like traits and to more clearly analyse the shape of the relationship between autistic traits and IQ for boys and girls separately.
Methods: IQ data at age 7 and parental ratings of autistic traits at age 8 came from 8250 twin pairs from the Twins Early Development Study (TEDS). The analyses are phenotypic and treat twins as individuals accounting for family membership and zygosity. Total autistic-trait scores (as measured by the Childhood Autism Spectrum Test, CAST - Scott, Baron-Cohen, Bolton & Bayne, 2002) with subscales for social, communication and repetitive, restricted behaviors and interests (RRBIs) were related to VIQ and NIQ using categorical (autistic traits in distinct IQ groups along the entire range of abilities) and continuous (structural equation modelling) approaches.
Results: Boys had higher mean autistic-like traits in all IQ groups. A continuous analysis revealed both linear and curvilinear effects of IQ on autistic-like traits with smallest effects of IQ on RRBIs. In VIQ sex differences occurred only in curvilinear effects on communication impairments in boys but not girls. This indicated that girls' communication impairments decreased with increasing VIQ in a linear pattern whereas boys showed an upturn in communication impairments at the high end of VIQ (i.e. a significant curvilinear shape for boys only). Effects of NIQ were smaller throughout with significantly curvier slopes in girls for the total CAST score which is the opposite pattern to the expected protective effects. Linear effects of NIQ originated entirely from the communication subscale. NIQ did not play a significant mediating role on RRBIs.
Conclusions: This study replicates recent findings that high VIQ is a protective factor for communication difficulties in girls only. The novel structural equation modeling approach used in this study allows more precise predictions about the number of autistic traits given a specific IQ. A sex difference in the slope between VIQ and communication traits indicates that with increasing VIQ girls show fewer autistic traits whereas boys have proportionally more autistic traits at the high end of VIQ. RRBIs

appear to be least affected by level of IQ. When interpreting sex ratios in autistic traits at the high end of IQ abilities, our findings indicate that it is important to take into consideration the particular type of high IQ as well as which part of the triad is measured. The central role of communication traits, which are differently mediated by IQ according to sex, and the interpretation of possible protective effects of high VIQ are discussed.

138.008 Head Circumference Developmental Course in the First 14 Months of Life in Children with ASD. A. Narzisi*, T. Filippi, F. Apicella, E. Santocchi, S. Calderoni, S. Calugi, R. Tancredi and F. Muratori, *University of Pisa – Stella Maris Scientific Institute*

Background: Several retrospective, prospective and postmortem studies have reported increased incidences of macrocephaly (head circumference > 97th centile). On the basis of this findings, it has been suggested that macrocephaly could represent a clinical marker for grouping individuals with autism.

Objectives: The present study aims to describe head circumference developmental course in the first 14 months of life in a large group of children with ASD.

Methods: 50 patients with ASD were recruited at Centre for Autism at the Stella Maris Scientific Institute in Pisa. All patients were full term at birth and parents were in possession of the pediatric records reporting head circumference (HC), height (H) and weight (W) measurements at four age periods: birth (T0); 1-to-2 months (T1); 3-to-5 months (T2) and 6-to-14 months (T3). HC, height and weight data from 100 healthy children, from healthy pediatric population followed by several italian pediatrician in the metropolitan area of Pisa were made available to us for comparison with the ASD sample.
t-Test and analysis of variance for repeated measures, with Bonferroni post-hoc test, was performed to compare differences in HC, weight and height at the considered periods between ASD and healthy infants.
Results: At T2 and at T3 HC was significantly greater in ASD group compared to healthy infants.
At T1, T2 and T3 weight was significantly smaller in ASD group compared to healthy infants.
With respect to height there are no significant differences between AS D group compared to healthy infants in all four considered periods (T0,T1,T2 and T3).
Analysis of variance for repeated measures showed that, over time, the rate of HC was growth in both groups, but the growth was greater in ASD subjects compared with healthy infants.
ASD group showed a smaller weight than control group at all time points, but no differences were found in the rate of weight growth between the two groups. With respect to rate of height growth, there were no significant differences between the two groups. In order to assess the differences between the rate of HC between the two groups, regardless of body size, we performed a new analysis of variance for repeated measures, controlling for weight and height. After controlling for both height and weight, the rate of HC growth was different between groups, in particular, change in HC growth continued to be significantly greater in the ASD group compared with the control group.

Conclusions: This study confirmed the existence of an abnormal rate of growth of HC in the first two years of life in children affected by PDD, characterised by a sudden and excessive increase in head size between 3-5 and 6-14 months. Moreover, it confirmed the association between ASD and macrocephaly at 6-14 months of life. Finally, it outlines the importance to measure the HC in the first months of life of children because an its abnormal rate of growth, in association with other clinical signs, may serve as an early warning signal of risk for autism.

Developmental Stages, Imitation, and Play Program

139 Developmental Stages, Imitation, and Play

139.001 Evidence That Anomalous Patterns of Imitation-Dependent Visuomotor Sequence Learning Is Specific to Autism. L. R. Dowell*[1] and S. H. Mostofsky[2], (1)*Kennedy Krieger Institute*, (2)*Kennedy Krieger Institute, Johns Hopkins University School of Medicine*

Background: There is increasing evidence that autism is associated with anomalous motor development (Gidley Larson and Mostofsky, 2006), including impaired imitation and execution of goal-directed skills ("dyspraxia"). Development of these skilled gestures, including those involving social communication as well as tools use, likely depends on intact visuomotor learning (Haswell et al., 2009), in particular learning that involves imitating others' actions. However, children with autism spectrum disorder (ASD) commonly demonstrate impaired action imitation (Williams, Whiten, and Singh, 2004); as such, they may demonstrate a pattern of imitation-dependent visuomotor sequence learning that is anomalous and specific to ASD.

Objectives: To examine whether children with ASD show anomalous patterns of imitation-dependent visuomotor learning as compared with typically developing (TD) children and to determine the specificity of the findings through comparison with a separate Attention Deficit/Hyperactivity Disorder (ADHD) control group.

Methods: Seventeen children with ASD (3 female), 16 children with ADHD (8 female), and 34 typically developing (TD) children (11 female), completed an imitation-dependent version of a serial reaction time task (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 task included seven blocks of 80 trials. Blocks 2-5 and 7 consisted of an implicit 10-item repeated sequence; blocks 1 and 6 were random. Visuomotor sequence learning was assessed using repeated measures ANOVAs (RM-ANOVA) to examine a change in the mean reaction times (RT) over the repeated sequenced blocks 2 through 5.

Results: Initial analyses revealed that the groups were matched on gender, race, handedness, age, socioeconomic status, and performance IQ. RM-ANOVA of all three groups revealed a significant main effect of block ($F = 11.170$, $p < .001$), and a trend-level interaction effect of block by diagnosis ($F = 1.987$, $p = .069$). Follow-up two-group RM-ANOVA examining TD and ADHD children revealed no significant interaction effect of block by diagnosis ($F = 1.012$, $p = .389$), whereas RM-ANOVA examining TD and ASD children did ($F = 2.790$, $p = .043$). RM-ANOVA within groups showed that TD and ADHD children displayed significant decrease in RT over blocks 2-5 (TD: $F = 13.382$, $p < .001$; ADHD: $F = 6.727$, $p = .001$). However, the RT of children with ASD did not change significantly ($F = .197$, $p = .898$).

Conclusions: Children with ASD show a different pattern of learning than both children with ADHD and TD children. In contrast, differences in learning were not seen between ADHD and TD children. The findings suggest that ASD is associated with differences in mechanisms underlying imitation-dependent visuomotor sequence learning, consistent with previous findings (Gidley Larson and Mostofsky, 2009; Mostofsky et al, 2000). Furthermore, the similarity of the patterns of learning between children with ADHD and TD children suggests that these differences in motor learning may be specific to autism.

139.002 Spontaneous Mimicry and Imitation in Children with Autism. E. Moody*[1], D. McIntosh[2] and S. Hepburn[3], (1)*University of Colorado Denver, Anschutz Medical Campus*, (2)*University of Denver*, (3)*University of Colorado Denver School of Medicine*

Background: Within 1000ms of seeing an emotional facial expression, typical adults rapidly mimic the expression. Deficits in such rapid mimicry have been found in adults, adolescents and children with Autism Spectrum Disorder (ASD) (McIntosh et al., 2006; Beall, et al., 2008). Such deficits are theorized to influence social functioning and development (Moody & McIntosh, 2007) and may represent deficits in the mirror system (Oberman, et al., 2009). Objectives: To explore what types of movements and expressions children with autism mimic; and to use that information to infer whether mimicry deficits are related to emotional processes, general mimicry processes, or attentional deficits. Methods: 40 children (31 children with autism, 9 typically developing siblings) were shows a series of 48 videos of actors displaying several face and body while electromyographic (EMG) readings were taken

to assess the degree of mimicry. Actions were varied on emotional content and body part being moved (happy and angry facial expressions, puckering and stuttering mouth movements, waving and arm wrestling). Participants first saw the series of video clips and were asked to "just watch" to get a baseline level of spontaneous mimicry. Next participants were asked to "copy what you see on the screen" to assess their ability to imitate these actions. Participants wore EMG electrodes over the muscles corresponding to each action displayed in the stimuli (zygomaticus major for smiling, corrugator supercilli for scowling, orbicularis oris for stuttering and puckering, and the forearm flexor for arm wrestling and waving). Results: Preliminary results indicate that children from both groups spontaneously imitated the actions in the "just watch" condition (i.e., made overt actions congruent with observed actions). This was despite repeated reminders to "just watch". This degree of spontaneous imitation has not been reported in previous EMG studies that have used static images for stimuli. However, the children with autism generally showed more disorganized and incongruent imitation (e.g., laughing at anger expressions). Further analyses will be conducted to evaluate the degree of rapid mimicry in these groups. Conclusions: These data suggest that although children with autism have a deficit in rapidly mimicking static faces, they still spontaneously imitate observed dynamic actions. Combined with work showing a delay (not absence) in matching during emotion decoding tasks (Oberman et al., 2009), this finding indicates that task demands and stimulus characteristics affect mimicry. Moreover, that the imitation was generally less natural and consistent with the stimuli further suggests that this ability may not function typically or that other processes may interfere with it. Continued examination of what factors facilitate imitation and mimicry and what the limits are on them when they are observed will identify which processes are preserved and which are disrupted in children with autism. This work will support work identifying social and emotional outcomes affected by these deficits, and focus attention on possible ways to enhance social-emotional functioning.

139.003 Phonological Errors in the Signing of Deaf Autistic Children: More Evidence for a Self-Other Mapping Deficit. A. Shield* and R. P. Meier, *University of Texas at Austin*

Background: Poor imitation of other people's bodily movements (gestures and/or actions) is one characteristic of people with autism (Smith & Bryson, 1994; Williams et al., 2004). However, researchers have failed to reach a consensus about the exact nature of this imitation deficit. Some researchers (e.g., Rogers et al., 1996; Green et al., 2002) have argued that the addition of meaning facilitates gesture imitation, but this assertion has been contradicted by other studies (Mostofsky et al, 2006). In evaluating six different proposals from the literature, Williams et al. (2004) concluded that a deficit in "self-other mapping ability" is the most likely explanation for the imitation deficit in autism. Self-other mapping (Rogers & Pennington, 1991) is the ability to relate one's own movements to the movements observed in others. The most striking evidence derives from studies in which autistic subjects produced "reversal errors" during imitation; e.g., they reproduced gestures with palm reversed or reversed direction of movement, seeming to indicate an inability to adopt the perspective of the person being imitated (Ohta, 1987; Brown, 1996; Hobson & Lee, 1999; Whiten & Brown, 1999). Objectives: The signing and imitation skills of deaf autistic children have never been systematically examined. Sign-learning children must imitate the body movements of others in order to learn lexical items. Thus, sign depends crucially on skills that may be impaired in autism. If autism entails a deficit in self-other mapping, then the signing of deaf autistic children could show evidence of this at the phonological (articulatory) level. Though phonology is a relative strength of hearing autistic children learning speech (Minshew et al., 1995), self-other mappings are needed to learn the phonological forms of some basic signs, such as those specified for inward/outward palm orientation, like the American Sign Language (ASL) signs WEDNESDAY and BATHROOM. Our objective in this research is to investigate whether there is evidence of a self-other mapping deficit in the lexical phonology of deaf autistic children. Methods: We tested a group of 10

deaf children of deaf parents (DoD) diagnosed with autism (age range: 4;7 to 16;3; M=9;6) and a control group of 13 typically-developing (TD) DoD children (age range: 3;7 to 6;9; M=4;9) on a sign elicitation task, an imitation task of nonsense signs, and a fingerspelling task. Items were coded for reversals on the palm orientation parameter, and the Freeman-Halton extension of the Fisher exact probability test was performed to detect group differences. Results: The autistic group made significantly more palm orientation errors than the TD group ($p < .005$). Age was a significant factor, with younger autistic children (under 10) making more reversals than older autistic children and TD children. Conclusions: These results are consistent with the hypothesis that the imitation deficit in autism reflects an impairment in self-other mapping. Further, they do not support the hypothesis that the addition of meaning facilitates gesture imitation in autism. This study shows that, unlike speech, an impairment in self-other mapping has consequences for basic phonological development in sign.

139.004 Early Developmental Trajectories of Autism Symptoms in a High-Risk Infant Cohort. L. Zwaigenbaum*[1], S. E. Bryson[2], J. Brian[3], I. M. Smith[4], W. Roberts[5], P. Szatmari[6], T. Vaillancourt[7] and C. Roncadin[8], (1)*University of Alberta*, (2)*Dalhousie University/IWK Health Centre*, (3)*Hospital for Sick Children & Bloorview Kids Rehab*, (4)*Dalhousie University & IWK Health Centre*, (5)*University of Toronto*, (6)*McMaster University*, (7)*University of Ottawa*, (8)*Peel Children's Centre*

Background: Previous studies suggest that the initial symptoms of autism spectrum disorders (ASD) are often detected by parents by the age of 2, but that there is considerable variability in onset and developmental course. Prospective studies of high-risk infants have provided new insights about early ASD symptoms, but mainly focus on cross-sectional comparisons, with limited attention to changes over time. Objectives: To assess whether there are distinct symptom trajectories among a longitudinal cohort of infant siblings of children with ASD (hereafter, 'high-risk infants') and low-risk comparison infants, and whether trajectory membership is associated with diagnostic outcomes.

Methods: Developmental trajectories of ASD symptoms from ages 6 to 18 months, indexed by the total score on the Autism Observational Scale for Infants (AOSI; higher scores indicate greater symptomatology), were identified by semi-parametric group-based modeling using SAS (PROC TRAJ) in a combined sample of high- and low-risk infants (n = 401 and 160, respectively). We then examined whether trajectory membership was associated with diagnostic outcomes among the 225 high-risk and 91 low-risk infants followed to age 3 years. ASD diagnoses were based on the ADI-R, ADOS and expert clinical judgment using DSM-IV, blind to prior study data.

Results: A 3-group solution provided optimal fit to variation in ASD symptom trajectories. One group, which included all but one of the low-risk infants and 68% of the high-risk infants, had minimal ASD symptoms from ages 6 to 18 months. A second group, who scored higher on the AOSI than the first group but had a similarly flat trajectory, included 24% of the high-risk sample: 6 of 22 diagnosed with autistic disorder (27%), 13 of 30 with other ASDs (43%) and 36 of 173 (21%) who were not diagnosed with ASD (21 with clinical concerns such as language delay, and 15 who were typically developing). One of 91 infants in the low-risk group belonged to this trajectory (the only low-risk child diagnosed with ASD). Thus, membership in this second group (moderate but stable levels of early symptoms) was associated with increased risk of ASD ($\chi^2 = 5.36$, $p=.021$), but was non-specific and had relatively limited positive predictive value. A third group had similar levels of 6-month symptoms as the second group, but a markedly inclining trajectory. This included 12 of 52 children with ASD (10 of 22 or 46% with autistic disorder; and 2 of 30 or 7% with other ASDs), compared to 4 of 173 siblings who were not diagnosed with ASD (2.3%), 3 of whom had other clinical concerns such as language delay at age 3 ($\chi^2 = 65.2$, $p<.001$). Overall, 12 of 16 high-risk infants (75%) in the third group were diagnosed with ASD.

Conclusions: The presence of increasing ASD symptoms between 6 and 18 months was highly predictive of autistic disorder at age 3.

However, 27% of high-risk infants later diagnosed with autistic disorder and 43% of those diagnosed with other ASDs had stable moderate-level symptom trajectories to age 18 months shared by some high-risk infants not diagnosed with ASD.

139.005 Incremental Validity of a Second Screen at 24 Months and Stability of Diagnosis Made at 18 Vs. 24 Months of Age. S. Hardy*[1], D. A. Fein[1], D. L. Robins[2] and C. Chlebowski[1], (1)*University of Connecticut*, (2)*Georgia State University*

Background:

The American Academy of Pediatrics has recommended autism screening for all children at 18 and 24 months, but empirical data are lacking to determine the added value of screening at two time points. Furthermore, diagnostic stability has been shown to be good past the second birthday, but limited data bears on the stability of diagnosis made during the second year of life.

Objectives:

To investigate the incremental validity of a second screen at 24 months, and to establish the stability of diagnosis made at 18 vs. 24 months of age.

Methods:

Seven thousand and sixteen 18-month olds were screened using the MCHAT (mean age = 18 months 15 days.). Of those, 122 failed both screener and follow-up interview and agreed to a developmental-diagnostic evaluation. Three thousand eighty four 2-year-olds were screened (mean age = 26 months 14 days); of these, 243 failed both screener and follow-up interview and agreed to an evaluation. Further, a subset (n = 612) of the 18-month olds who passed the screen at 18 months received a second screen with the MCHAT at 24 months; of these, 26 failed the screener, but only 2 failed the follow up interview, both of whom received a developmental and diagnostic evaluation. Forty-six children who were evaluated at 18 months were re-evaluated at 4 years old while 141 children evaluated at 24 months received a re-evaluation.

Results:

65.6% (n = 80) of 18-month olds who were evaluated were diagnosed with an ASD and 34.4% (n = 42) were diagnosed as non-ASD. 70% (n = 170) of 24-month olds were diagnosed with an ASD and 30% (n = 73) were diagnosed as non-ASD. Only 1 of the 2 children who were evaluated after passing the screen at 18 months but failing at 24 months received an ASD diagnosis. Thirty-two (69.6%) of the ASD and non-ASD diagnoses made at 18 months remained stable at the 4-year old re-evaluation. Sixty seven (47.5%) of the diagnoses made at 24 months remained stable at the 4-year old re-evaluation.

Conclusions:

69.6% of 18-month olds maintained the same ASD vs. non-ASD diagnosis at a second evaluation while 47.5% of the 24-month olds maintained their diagnoses ($p<.05$). Thus, diagnoses made during the second year appear to be as stable, or more so, as those made at 24 months. In this small data set, a second screening at age 24 months picked up very few additional cases.

139.006 Early Attention to Facial Expressions and Eye Gaze Direction in Infant Siblings of Children with Autism. M. S. Davies*[1], M. Del Rosario[1], L. Gomez[2], S. L. Marshall[1] and M. Sigman[2], (1)*UCLA*, (2)*University of California, Los Angeles*

Background: Social referencing behaviors typically develop between 9 and 12 months of age, and first instances of responding to joint attention (RJA) and initiating joint attention (IJA) begin emerging atop a foundation of referencing and gaze-following abilities shortly around this time. While it is known that the downstream cascade of gaze-related development is interrupted in children with autism, the earliest signs of this altered development in infancy are still poorly understood. Such understanding may be critical for early screening and treatment efforts. Objectives: To characterize visual fixation patterns to emotional faces with direct or averted gaze direction in infant

siblings of children with autism (I-Sibs) across their first year. Methods: While undergoing infrared eye tracking, 25 I-Sibs at 6 and 12 months of age were presented a pseudo-randomized series of photographed faces depicting happy and angry expressions with either direct or averted gazes. Results: Overall attention to these faces at 6 months of age was disproportionately focused on the upper / eye regions, which was significantly more pronounced for direct-gaze happy faces. At 12 months of age, I-Sibs overall still preferred happy faces and direct gaze over angry faces and averted gaze. By this age, however, fixation of infants with higher developmental scores in expressive language and overall intelligence (as measured by the Mullen) was modulated by gaze direction and emotion type of the depicted face. Lower-performing infants preferred direct gaze in angry faces, whereas higher-performing infants preferred averted gaze in angry faces, and direct gaze in happy faces. Diagnostic outcome data will also be discussed, where available. Conclusions: Findings suggest that by 12 months of age, I-Sibs with higher language and cognitive abilities may discriminate differences in gaze and facial emotion to a greater degree than I-Sibs with lower language and cognitive abilities, and may adjust their visual attention accordingly. This is consistent with the literature of studies on early typically-developing infant looking preferences. We would expect I-Sibs who will go on to develop autism to achieve poorer early language and intelligence scores, and these individuals may also show coinciding impairments in the discrimination of and response to emotion and gaze cues early in infancy. Abnormally interpreting or responding to gaze and emotion cues as measured by visual fixation may offer easily-identified early risk factors for those infants within the first year of age who will subsequently be diagnosed with autism. Research supported by NIH/NIMH Autism Center for Excellence (ACE) center grant P50 HD055784.

139.007 Parental Well-Being Is Associated with Child Behavior Among Toddlers with Early Autism Symptomatology. A. S. Nahmias*[1], A. H. Brown[1], P. Yoder[1], A. S. Carter[2], D. S. Messinger[3] and W. L. Stone[4], (1)*Vanderbilt University*, (2)*University of Massachusetts Boston*, (3)*University of Miami*, (4)*Vanderbilt Kennedy Center*

Background:

Parents of children with autism often report elevated levels of depression and parenting-related stress relative to parents of children with typical development or those with other developmental disorders (Carter et al., 2009; Davis & Carter, 2008; Estes et al., 2009). Additionally, higher levels of depression have been shown to be related to lower perceived parenting efficacy (Kuhn & Carter, 2006).

Objectives:

This study examines the relation of parental well-being (i.e., stress, depression, and perceived parenting efficacy) and child behaviors within parent-child dyads involving young children exhibiting early symptoms of autism.

Methods:

Parental well-being and child characteristics were assessed in families of 55 toddlers (mean CA = 21.2 mo., range = 15.5 – 25.0 mo.) as part of the initial assessment of a multi-site clinical randomized trial of the Hanen More than Words intervention. Children had met a predetermined cutoff on the Screening Tool for Autism in Two-Year-Olds (STAT) and had a clinical presentation consistent with an ASD. Parental well-being was evaluated using the Center for Epidemiologic Studies Depression Inventory (CES-D), Parenting Stress Index-Short Form (PSI), and Maternal Efficacy Scale (MES). Child behaviors were measured using the Parent Interview for Autism-Clinical Version (PIA-CV), Brief Infant-Toddler Social and Emotional Assessment (BITSEA), Infant-Toddler Social and Emotional Assessment (ITSEA) and Vineland Adaptive Behavior Scales- Second Edition (VABS II).

A multi-step process was used to select predictors for the exploratory multiple regression model that: (a) created same-construct groupings of bivariate correlates with parental well-being and (b) selected the child characteristic most strongly related to parental well-being.

Results:

High levels of depression and parenting stress were reported, with 25.5% of parents obtaining clinically elevated CES-D scores and 30.9% exceeding the clinical cutoff for PSI Total Stress. Significant associations between all three measures of parental well-being were found, with correlations ranging from |.34| to |.56| (*p*s < .05). Parent-reported measures of child characteristics and measures of parental well-being were also significantly correlated (*r* values ranged from |.32| to |.71|, *p*s < .05). Regression analyses revealed two unique predictors for each parental measure of well-being. For the CES-D, 20.9% of the variance was accounted for by the ITSEA Maladaptive and PIA-CV Language Understanding subscales, with each subscale uniquely accounting for about 7% of the variance. For the PSI, 49.7% of the variance was accounted for by the BITSEA Problem and PIA-CV Language Understanding subscales, with BITSEA Problem and PIA-CV Language Understanding subscales uniquely accounting for 21.5% and 7.3% of the variance, respectively. For the MES, 60% of the variance was accounted for by the BITSEA Competence and BITSEA Problem subscales, with each subscale uniquely accounting for about 18% of the variance.

Conclusions:

Parents of young children with early autism symptoms demonstrated elevated levels of depression and parenting stress. Both child competence and problem behaviors contributed to the variance in parental stress, depression, and efficacy, with particularly strong predictions found for parental efficacy. The emergence of language understanding as a significant predictor of parental well-being highlights the importance of helping parents learn strategies for communicating effectively with their children.

139.008 Sex Differences in Siblings of Children with ASD at 3 Years. W. Roberts*[1], L. Zwaigenbaum[2], J. Brian[3], C. Roncadin[4], I. M. Smith[5], P. Szatmari[6], T. Vaillancourt[7] and S. E. Bryson[8], (1)*University of Toronto*, (2)*University of Alberta*, (3)*Hospital for Sick Children & Bloorview Kids Rehab*, (4)*Peel Children's Centre*, (5)*Dalhousie University & IWK Health Centre*, (6)*McMaster University*, (7)*University of Ottawa*, (8)*Dalhousie University/IWK Health Centre*

Background: Most epidemiological studies have shown a preponderance of males among children with autism spectrum disorder (ASD), with male-to-female ratios ranging from 3.5:1 to 4:1. However, some authors have proposed that milder social and behavioural impairments may impede identification of ASD in girls. Objectives: 1)To compare rates of ASD in boys and girls in a high-risk cohort of infant siblings of children with ASD (hereafter, 'high-risk infants'), and 2) by looking at the entire cohort, to understand the sex differences in light of their respective developmental trajectories of ASD symptoms and cognitive function.

Methods: ASD diagnoses at age 3 years were based on ADI-R, ADOS and DSM-IV criteria applied by expert clinicians blind to prior study data. Early ASD symptoms were assessed from ages 6 to 18 months using total scores from the Autism Observational Scale for Infants (AOSI). Cognitive development was assessed from ages 6 months to 3 years using the Mullen Scales of Early Learning, Early Learning Composite scores (Mullen-ELC). Developmental trajectories of ASD symptoms and cognitive function were identified independently by semi-parametric group-based modeling using SAS (PROC TRAJ) in our total sample of 401 high-risk and 160 low-risk infants. Sex differences in trajectory membership were then assessed among the 225 high-risk and 91 low-risk infants followed to age 3 years.

Results: ASD rates at age 3 years were similar in boys and girls. Seventeen of 112 boys (15.2%) and 12 of 99 girls (12.1%) received a diagnosis of ASD at 36-42 months. Relative odds of ASD in boys compared to girls was 1.25 (95% CI = 0.63-2.49), robust to age of recruitment and sex of the older affected sibling (in whom the sex ratio was 4:1). Between 6 and 18 months, boys and girls had similar distributions in AOSI symptom trajectories. However, significant sex differences were found between 6 months and 3 years in Mullen-ELC trajectory membership. Three distinct trajectories were identified: two stable trajectories characterized by average and above average scores respectively, and a third (10.2 % of the total sample including

13.4% of the high-risk group), characterized by marked decline from average to intellectually disabled by age 3. High-risk boys were over-represented in the third trajectory (15.7% vs. 5%; _2 = 21.5, p<.001), as well as among those diagnosed with ASD (52.6% boys vs. 27.8% girls, p = .07). Findings were similar for verbal and non-verbal cognitive trajectories when examined separately.

Conclusions: In our high-risk cohort, preliminary evidence suggests that 1) there are similar rates of ASD in boys and girls at age 3; and 2) girls with ASD tend to show more stable cognitive trajectories than boys. The lack of clear early sex differences in rates and cognitive levels raises interesting questions about whether trajectories diverge after age 3, with some girls no longer meeting ASD criteria as they get older.

Mandell Program
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140.001 A Play and Joint Attention Intervention for Teachers of Young Children with Autism. C. Wong*[1], S. Booth[2], B. Gapinski[2] and P. Maas[2], (1)*University of North Carolina at Chapel Hill*, (2)*Cleveland State University*

Background:

Extensive research has shown that both symbolic play and joint attention are delayed or deficient in young children with autism, and predictive of their later language and social development. Recent studies have shown that these skills can be taught by trained interventionists with a few studies emerging that demonstrate the success of caregiver-mediated interventions in facilitating some of these behaviors. However, little focus has been given to teachers of young children with autism in the preschool special education classroom.

Objectives:

The aims of this study were to develop and then pilot test a classroom-based intervention focused on facilitating play and joint attention for young children with autism. Specifically, we aimed to assess changes in the child's engagement, play, and joint attention during and following the intervention.

Methods:

Thirty-three children diagnosed with autism (confirmed with the CARS), ages three to six years (mental ages ranging from 15 to 58 months), participated in the study with their classroom teachers (n=13). The thirteen preschool special education teachers were randomly assigned to one of three groups:

1) Symbolic play intervention (4 weeks) then joint attention intervention (4 weeks)

2) Joint attention intervention (4 weeks) then symbolic play intervention (4 weeks)

3) Wait period (4 weeks) then further randomized to either group 1 or 2 (8 weeks)

In the intervention, teachers participated in eight weekly individualized 1-hour sessions with a researcher that emphasized embedding strategies targeting symbolic play and joint attention into their everyday classroom routines and activities. The main child outcome variables of interest were collected through one-hour classroom observations over three-day periods. Using a PDA, children's engagement levels were tracked and then calculated to determine percent time spent in a joint engagement state where the child and another individual (teacher or peer) were actively involved with the same object or event. Additionally, the frequency of play (functional and symbolic) and joint attention (responses and initiations) behaviors were also recorded.

Results:

Results show that before intervention, children with autism were spending about 21 percent of the classroom observation time in a joint engagement state. An ANCOVA (with CARS scores as a covariate) indicated that in the classrooms where the teacher first received either the symbolic play or joint attention training sessions, the children increased their joint engagement time to 44 percent of the observation time as compared to the children with teachers in the wait-list control group who remained at approximately

20 percent. Finally, analyses of the target behaviors throughout the intervention of all children showed an increase of symbolic play and joint attention initiations with children having CARS scores in the mild/moderate range (<37) displaying greater increases.

Conclusions:

Findings indicate that teachers can implement an intervention to improve joint engagement, symbolic play, and joint attention of young children with autism in their classrooms, especially with children who were classified more as having mild/moderate autism. These pilot data emphasize the need for further research and implementation of classroom-based interventions targeting play and joint attention skills for young children with autism.

140.002 Increasing Parent Verbal Responsiveness: A Pilot Intervention Study. C. Erickson*[1], A. McDuffie[2], S. Ellis Weismer[1], L. Abbeduto[1], A. Stern[1], E. Haebig[1] and M. Leonard[1], (1)*University of Wisconsin-Madison*, (2)*University of Wisconsin*

Background:

Correlational studies suggest that verbal input from responsive parents can make a positive contribution to language development for young children with ASD (Siller & Sigman, 2002; McDuffie & Yoder, in press). These types of parent utterances follow into the child's current focus of attention and are contingent upon what the child is looking at, touching, or playing with just prior to the parent's verbal response. Early language learning requires that children make a mapping between the verbal language that they hear and the objects and events to which this language refers. This process often is challenging for young children with ASD who may find it difficult to respond to attention-directing cues from conversational partners. Teaching parents to talk about their child's current focus of attention should increase the efficiency with which young children with ASD learn language.

Objectives:

To examine whether participation in a clinician-implemented parent education program: a) increased the frequency with which parents used verbal utterances that described the child's focus of attention; and, b) decreased the frequency with which parents redirected their child's focus of attention.

Methods:

Child participants (N=14) ranged in age from 28- to 68-months (*M* = 41.14 mos, *SD* = 10.39) and had a community diagnosis of an ASD. Diagnoses were confirmed through administration of the *MCHAT (M* = 9.14*, Range* 3-17*)* and *ADOS* (*M* = 20.6, *Range* 11-28). Parent-child dyads were randomly assigned to a treatment or delayed treatment group. The intervention lasted eight weeks and consisted of five 2-hour parent education sessions, twice weekly 1-hour small group parent-child play sessions (14 total), and two 45-minute individual parent-child coaching sessions. The content of the parent sessions was adapted from *More Than Words – The Hanen Program for Parents of Children with ASD* (Sussman, Honeyman, & Lowry, 2007) and was implemented by a Hanen certified speech-language pathologist. Small-group parent-child sessions were implemented by graduate student clinicians enrolled in a masters program in Communication Disorders. Individual coaching sessions were implemented by the Hanen certified SLP. During group and individual parent-child play sessions, parents were coached in using the strategies presented during the parent education sessions Parent-child dyads participated in an unstructured play session with a standard toy set at the pre- and post-treatment periods and an interval-based coding system was used to derive the variables of interest.

Results:

Parents in the treatment group significantly increased their use of utterances that followed into and described their child's focus of attention during play, $t(6)=2.56$, $p<.02$, one-tailed, and significantly decreased their use of utterances that redirected their child's focus of attention, $t(6) = 2.15$, $p<.04$, one-

tailed). These parent behaviors did not change in the comparison group. Treatment-group parents rated the overall value of the program at 6.89 on a 7-point Likert scale.

Conclusions:

Results of this pilot study suggest that an intervention comprised of parent education sessions in conjunction with small group and individual parent-child coaching sessions can successfully modify the ways in which parents provide verbal language input to their young children with ASD.

140.003 JumpStart Learning to Learn: One Week Intensive Parent Training and Diagnostic Therapy for Autism. B. Siegel*[1], T. Sendowski[1], L. Fancy[2] and D. Neufeld[3], (1)*UC San Francisco*, (2)*JumpStart Learning-to-Learn*, (3)*University of California, Berkeley*

Background:
JumpStart Learning to Learn is an intensive evidence-based one-week manualized developmental-behavioral protocol that teaches parents alongside their newly-diagnosed child with an autistic spectrum disorder (ASD). Parents receive one-to-one technical assistance for developing their 18-36 month-old child's language and play while increasing instructional readiness and decreasing behavior incompatible with instruction and learning techniques to create a more supportive, constructive family environment.

Objectives:
1. To increase instructional control through teaching pivotal responses to high interest functional materials and activities that are part of daily home life (e.g., Schriebman, 2000).
2. To increase capacity for reciprocal interaction through joint parent-child play with high value activities around the home using principles of DIR (e.g.,Greenspan & Weider, 1998) .
3. To increase spontaneous communication using a visually-based augmentative communicative protocol that shapes behavioral components of joint attention in the context of requesting high value objects and activities using a natural environment teaching paradigm (e.g., Koegel, Carter & Koegel, 2003).
4. To increase parent expertise through teaching of special parenting techniques (per 1-3, above) to improve home interactions a) to increase treatment intensity, b) decrease family stress, and c) guide parents in becoming informed consumers of autism services that fit their child's neurodevelopmental profile.

Methods:
Study Design: We will present preliminary data from a RCT of JSLTL v a 6 month waiting-list control receiving TAU in the community. Baseline and 6 month post-JSLTL data on parent knowledge of autism, family functioning, dyadic adjustment and depression will be presented to address whether there are psycho-social benefits to JSLTL that may be expected to drive improved autism-specific child-rearing practices.

Intervention: Parents and their child attend alternating one-to-one sessions with behavioral, play and language coaches who first demonstrate and then coach parents in techniques to increase the child's compliance, joint attention, imitation and spontaneous communication. The program is comprised of two daily 2-1/2 hour blocks for 4 days inter-weaved with 1 or more hours of direct didactic sessions on autism from coaches and program director. The final day is a half-day of wrap-up with the program director including scoring of a learning profile matrix and a half-day of 'docent-ing'—visiting potential placements to learn how to assess their child's fit to his/her learning profile matrix.

Results:
Data to be presented will be on parents 6 months post JSLTL (N=25) compared to a matched group of parents (N=25) matched for time since diagnosis who have never received JSLTL. Data will be from the 'Living with Autism' questionnaire devised for this study that measures acceptance of the diagnosis of autism, the Beck Depression Inventory-II, Beck, Steer, & Brown, (1996), the Family Empowerment Scale (Koren, DeChillo, & Friesen1992), and the Dyadic Adjustment Scale-4 (Sabourin, Valois, & Lussier, 2005).

Conclusions:
Data collection for the comparison group is on-going. Data on the JSLTL group

is complete. We hypothesize that parents who have received JSLTL will have more resolved grief around the diagnosis, be less depressed, and report better marital and family functioning compared to un-intervened families.

140.004 Arbaclofen for the Treatment of Children and Adults with Fragile X Syndrome: Results of a Phase 2, Randomized, Double-Blind, Placebo-Controlled, Crossover Study. E. Berry-Kravis*[1], M. Cherubini[2], P. Zarevics[2], B. Rathmell[2], P. P. Wang[2], R. Carpenter[2], M. Bear[3] and R. Hagerman[4], (1)*Rush University Medical Center*, (2)*Seaside Therapeutics*, (3)*MIT*, (4)*UC Davis*

Background: Fragile X syndrome (FXS) is the most common known genetic cause of autism, and about 25% of males with FXS meet full criteria for autism. According to the "mGluR theory" of FXS, absence of the FX gene product (FMRP) results in dysregulation of dendritic protein synthesis and consequent abnormalities of synaptic plasticity. It is hypothesized that other etiologies of autism may also be characterized by "synapsopathies" (disorders of synaptic function).

The rationale for studying arbaclofen (the active entantiomer of racemic baclofen) in FXS and autism is multifold. First, racemic baclofen anecdotally improves behavior in both FXS and autism. Second, racemic baclofen ameliorates abnormal phenotypes in several animal models of FXS, including audiogenic seizures and hyperactivity in the FXS mouse. Third, transcranial magnetic stimulation studies show that racemic baclofen modulates cortical plasticity in healthy control subjects. Lastly, in both human and animal studies, arbaclofen appears better tolerated and more efficacious than racemic baclofen.

Objectives: To assess the efficacy, safety and tolerability of arbaclofen for the treatment of irritability in FXS. The effects of arbaclofen on other behavioral and cognitive measures also were explored.

Methods: A double-blind, placebo-controlled, crossover trial in subjects with FXS, aged 6 to 40, was conducted at 12 sites in the USA (clinicaltrials.gov NCT00788073). Subjects were randomized to receive either placebo or arbaclofen. After 4 weeks treatment, subjects tapered off medication, entered a washout period, and then began treatment with the other blinded medication.

The primary efficacy endpoint was the Irritability subscale of the Aberrant Behavior Checklist. A sample size of n=60 provided 90% power to detect an effect size of 0.6. Study enrollment was restricted to subjects age 12 – 40 until a planned interim safety review by an independent monitor, to examine data from the first 10 study completers, and to consider extending enrollment to age 6.

Results: The interim safety review determined that adverse events were predominantly attributed to pre-existing conditions or viral infections, and none were unanticipated, given the known side effects of baclofen. One subject experienced a serious adverse event, increased irritability, when tapering off study medication (subsequently unblinded and determined to be arbaclofen). Other subjects showed similar deterioration when blinded study medication was titrated downward. On the independent monitor's recommendation, enrollment was then extended to age 6.

The study completed enrollment on 06Nov2009. Of 63 subjects randomized, 55 were male. There were 23 subjects aged 6-11 years, another 23 aged 12-17 years, and 17 aged 18-40 years. Full efficacy and safety results are anticipated in April 2010.

Conclusions: Advances in the neurobiological understanding of FXS and autism are now leading to the development of targeted pharmacotherapeutics for these conditions. Abundant challenges remain in the translation of neurobiology to clinical therapy, but trials of some rationally-justified agents are already underway. Interim results indicate that arbaclofen shows good safety and tolerability in subjects with FX aged 6 to 40 years. Full efficacy and safety results will be presented.

140.005 Effect of Propranolol On Eye Contact in Autism Spectrum Disorder. S. S. Saklayen*[1], K. Higgins[2], A. Narayanan[1], S. E. Christ[2] and D. Q. Beversdorf[2], (1)*The Ohio State University*, (2)*University of Missouri*

Background: Individuals with autism spectrum disorder (ASD) exhibit poor eye contact with others from an early age. Recent physiological evidence suggests that direct eye contact may be physiologically stressful to those affected by ASD. Stress is well known to activate the noradrenergic system. Therefore, an agent that could decrease the stress related to eye contact by acting to block noradrenergic activation might increase eye contact in ASD. Propranolol, a nonselective beta blocker, produces noradrenergic blockade with central and peripheral nervous system effects. Propranolol is commonly prescribed for situational anxiety (stage fright, test anxiety, etc). Thus, we wished to determine the effect of propranolol on eye contact in ASD.

Objectives: To determine the effect of propranolol on eye contact in ASD.

Methods: Fourteen individuals with ASD (mean age 18.9 years, mean FSIQ 104, 10 male) participated in the two separate eye tracking sessions. One was performed one hour after 40mg propranolol and the other was performed one hour after placebo, with the order of drug administration counterbalanced. At each session, subjects were asked to look at a series of 10-second video clips of novel faces with neutral expressions. An ASL eye tracker was used to monitor and record participants' eye movement scan patterns while viewing the video. Eyetracker data was analyzed using the EyeNal and FixPlot programs with ASL. Time spent looking at the eyes, the mouth area, and the remainder of the face was computed and compared between drug conditions. Heart rate and blood pressure were also compared between conditions.

Results: T-tests revealed a significant decrease in amount of time fixating on the mouth ($t(13) = 3.851$, $p = .001$) and an increase in amount of time fixating the eyes ($t(13) = 2.473$, $p = .014$) with propranolol as compared to the placebo condition. There was no effect of drug on time spent looking at the remainder of the face. Systolic blood pressure and heart rate were also significantly lower on propranolol as compared to placebo.

Conclusions: Preliminary evidence from the present study using video clips of faces suggests that propranolol may improve eye contact in ASD. Further studies will need to explore its effects on other aspects of impaired social interaction in ASD. Given the previously demonstrated cognitive effects of propranolol in ASD, further exploration of the clinical effects of this drug is warranted.

140.006 Factors Influencing Placebo Response in the STAART Citalopram Trial. B. King*[1], K. Dukes[2], C. Donnelly[3], J. McCracken[4], L. Scahill[5], L. Sikich[6], J. Bregman[7], E. Hollander[8], L. Ritz[9], E. Anagnostou[10], A. Wagner[9], F. Robinson[2], D. Hirtz[11] and L. Sullivan[12], (1)*University of Washington and Children's Hospital and Regional Medical Center*, (2)*DM-STAT, Inc*, (3)*Dartmouth Medical School*, (4)*University of California, Los Angeles*, (5)*Yale University School of Medicine*, (6)*University of North Carolina*, (7)*North Shore–Long Island Jewish Health System*, (8)*Albert Einstein College of Medicine*, (9)*National Institute of Mental Health*, (10)*Bloorview Research Institute, Bloorview Kids Rehab*, (11)*National Institutes of Health*, (12)*Boston University*

Background: As part of the STAART network funded by the National Institutes of Health, a multi-site clinical trial designed to assess both the efficacy and safety of the SSRI, citalopram, for a population of children and adolescents with autism and high levels of repetitive behavior was conducted. Objectives: Citalopram did not show benefit over placebo in this trial, however a third of each treatment group did experience clinical improvement. We thus sought to evaluate whether there were factors that predicted the likelihood of a placebo response at study entry. Methods: One hundred forty-nine subjects 5 to 17 years old inclusive were randomized to receive citalopram (n = 73) or placebo (n = 76). Participants had autistic spectrum disorders, Asperger disorder, or pervasive developmental disorder, not otherwise specified; illness severity ratings of moderate or greater on the Clinical Global Impressions, Severity of Illness Scale; and moderate or greater scores on the Children's Yale-Brown Obsessive Compulsive Scales modified for pervasive developmental disorders (CY-BOCS). The study lasted 12 weeks achieving a mean final dose of citalopram of 16 mg daily. Bivariate associations between responders and non-responders for potential baseline predictors were performed as well as between

responders and non-responders within treatment group. These potential predictors included demographic factors such as IQ, age, race, gender, autism clinical global severity rating (CGI-S), behavioral ratings from the Aberrant Behavior Checklist, the Child and Adolescent Symptom Inventory, Repetitive Behavior Scale, Caregiver Strain Index and Vineland Adaptive Behavior Scale. Results: A number of significant differences emerged which differentiated placebo and citalopram responders from non-responders at baseline including scores on the hyperactivity and irritability subscales of the ABC, scores on the CASI ADHD items, and Caregiver Strain. In these and other items that will be presented, subjects who went on to experience a positive treatment response tended to have lower scores at study entry than did non-responders. There was no evidence of randomization bias between citalopram and placebo groups for any of these measures. Conclusions: These findings suggest that it may be possible to reduce the likelihood of nonspecific responses to treatment in clinical trials by identifying and controlling for symptom burden and other factors at study entry.

140.007 The Gluten Free and Casein Free (GFCF) Diet: A Double Blind, Placebo Controlled Challenge Study. S. Hyman*, P. A. Stewart, T. Smith, J. Foley, U. Cain, R. Peck, D. D. Morris and H. Wang, *University of Rochester*

Background: Approximately 1/3 of children with ASD receive dietary interventions. While families report dramatic clinical effects, two prior trials do not confirm these positive outcomes. Neither examined nutritional sufficiency or controlled for other interventions. This study was undertaken to examine the behavioral and physiologic effects of the GFCF diet and assess its nutritional adequacy.
Objectives: To evaluate the nutritional adequacy, physiological effects, and efficacy of the GFCF diet on symptoms of ASD using randomized double blind placebo controlled challenges in preschool children with ASD.
Methods: ADI-R/ADOS positive children ages 30-54 months receiving at least 10 hours/week of early intensive behavioral intervention (EIBI) were recruited. They were screened for milk/wheat allergies, celiac disease, and anemia/iron status by RAST, TTG and CBC/ferritin respectively. After a strict GFCF diet for at least 4 weeks, they received weekly, grouped, randomized double blind challenges containing either 20 g wheat flour, 20 g evaporated milk, both, or neither on three separate occasions over 12 weeks . The challenges appeared identical and were similar in taste and texture. Laboratory monitoring and BMI recording occurred at baseline, 6,18,and 30 weeks. Behavioral data was collected at these times plus the day before then 2 and 24 hours after each challenge, Measures included: Bristol Stool Scale, Sleep Diaries, Actigraphy, Conners Abbreviated Rating Scale, and Target Symptoms Scale. Ritvo Freeman Real Life Rating Scales (RFRLRS) were recorded at 2 and 24 hours post challenge. Challenges occurred only if measures were at baseline levels. Data were analyzed by group and for individual children comparing baseline with 4 weeks on diet and then pre/post challenges.
Results: Twenty one children were recruited. Two were excluded for positive TTG, one for anemia. Four additional children were unable to establish the diet or left EIBI. Group data on the 14 successful participants (43.5 months, range 35-54 ; 12 males) demonstrated no statistical change in frequency or quality of stools, sleep, actigraphy for activity, or parent/teacher/observer scores of attention/activity for baseline/ diet or in pre/post challenge ratings. The group RFRLRS data 2 hours post challenge were higher after placebo than after challenges of casein ($p=.013$), gluten ($p=0.024$) or gluten + casein ($p= 0.021$). These differences were not present 24 hours post challenge. Single case analysis will be presented. All children were maintained within acceptable ranges for micro/macronutrients with intense weekly dietary monitoring.
Conclusions: This is the first study to examine the behavioral effects of a nutritionally monitored GFCF diet on attention, sleep, stool pattern, and core symptoms of ASD. While no favorable effects of the GFCF diet on attention, sleep and stool patterns were identified in group analyses, such effects may occur for individuals or for subgroups of children (e.g. with significant GI disease), providing the basis for positive

anecdotal reports. Future studies need to address the potential effects of nutrition on behavior in children with ASD and be powered to evaluate subtle changes in core symptoms.

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140.008 The Relative and Combined Effects of a Diet and a Behavioural Intervention for Behaviour and Sleep Problems in Four Boys with Asperger's Disorder. M. J. Schelleman*[1] and A. L. Richdale[2], (1)*RMIT University*, (2)*La Trobe University*

Background: Sleep and behaviour problems are common in children with an autism spectrum disorder (ASD) and are often related. Although behavioural interventions, including Behavioural Parent Training (BPT) programs, can be effective in alleviating both problems, parents often try alternative treatments such as diets. Thus accurate information regarding the effectiveness of dietary interventions for behaviour and sleep problems, both relative to, and compared with, behavioural interventions is needed. There is some evidence that various elimination diets can improve behaviour and sleep, however the relative impact of a BPT and diet on behaviour in general and the impact of diet on sleep problems is unknown. Objectives: To investigate the relative and combined effects of a BPT program and the Simplified Elimination Diet (SED) on daytime behaviour and sleep in children with a range of challenging behaviours, including sleep problems. The SED excludes food additives, salicylates, amines, and glutamates, while the BPT teaches parents standard behavioural principles to manage their child's difficult behaviours. Methods: Four boys with Asperger's Disorder aged 4:6, 6:8, 7:11, and 10:5 years participated in this study. They had an IQ > 85 and challenging behaviour, defined by a score ≥ 85th percentile on the Rowe Behaviour Rating Inventory (RBRI). Participants were randomly allocated to the BPT (Boys 1 and 2) or the SED (Boys 3 and 4) group (Phase 2). Children from the BPT group then completed the SED and those from the SED completed the BPT program (Phase 3); participants maintained the Phase 2 intervention. Measures were taken before (Phase 1) and following Phase 2, and following Phase 3. Children's general challenging behaviour and compliance and the RBRI were also measured weekly throughout the study. As well as the RBRI, which includes a sleep subscale, the Children's Sleep-Wake Scale, Conners Parent Rating Scale, Child Behavior Checklist, Home Situations Questionnaire and Social Skills Rating Scale were completed. Results: There were no changes in Boy 1's behaviour or sleep following the BPT intervention, however Boy 2 showed some positive behaviour changes and his sleep problems reduced to zero. There were significant improvements in behaviour following the SED for Boys 1 and 2 and sleep problems for Boy 1 reduced to zero. Behaviour problems improved significantly with the SED for Boys 3 and 4 and sleep problems reduced to zero. After the BPT program Boy 4 showed further improvement in some behaviours. Two of the four boys completed an open food challenge and both behaviour and sleep problems returned during the challenge phase. Conclusions: The SED was more effective than a BPT in reducing both sleep and behaviour problems in 3 of 4 boys with AD. The fourth boy's sleep problems responded to the BPT but the SED was more effective in dealing with his challenging behaviour in general. Thus, this study provides evidence that, at least some in children with AD both sleep and behaviour problems may be related to diet. This requires further investigation, including determining which dietary constituents are responsible for these effects.