Keynote Address Program

100 Time to give up on a single explanation for autism?

Speaker: F. Happé*Institute of Psychiatry, KCL*

In this talk I will suggest that we should abandon the search for a single unifying cause for the diverse symptoms defining autism. I will present recent evidence of behavioural fractionation of social impairment, communication difficulties and rigid and repetitive behaviours in a population-based sample. Twin analyses in the same sample suggest largely nonoverlapping genes acting on each of these traits. At the cognitive level, too, attempts at a single explanation for the symptoms of autism appear to have failed. Instead, different cognitive accounts are needed for the different aspects of autism, and distinct neural systems appear to be involved. Implications and future research directions will be discussed.

100.1 Introduction by Sir Leszek Borysiewicz (Chief Executive Medical Research Council).

100.2 Keynote Address.

Invited Educational Symposia Program

101 Immunity in Autism: A New Page with Fresh Insights

Organizer: G. Rall*Fox Chase Cancer Center*

Speakers: L. Boulanger[1]P. Patterson[2]C. A. Pardo[3]R. S. Fujinami[4](1)*University of California, San Diego*, (2)*Biology Division*, (3)*Jonhs Hopkins University School of Medicine*, (4)*University of Utah*

What role, if any, the host immune response plays in the etiology of autism has been a controversial and understudied aspect of autism research. Recently, the advent of novel mouse models, powerful cell culture systems, and creative human-based studies has substantiated a critical role for the immune response in autism. The goal of this session is to highlight some of these recent and diverse contributions.

101.1 Introductory Remarks.

101.2 Regulation of Glutamatergic Synaptic Transmission and Plasticity by MHC class I. L. M. Boulanger*, *University of California, San Diego*

Disruption of glutamatergic synaptic transmission is a consistent finding in autism, and alterations in ionotropic glutamate receptors have also been reported in related disorders, including Rett syndrome and tuberous sclerosis, but the cause of these changes remains unknown. Maternal viral infection is a risk factor for autism, and recent studies in animal models implicate the immune response, not the virus itself, in disruption of fetal brain development. Here we report that changes in the levels of specific immune proteins, members of the major histocompatibility class I (MHCI), are sufficient to induce abnormalities in glutamatergic synaptic transmission and synaptic plasticity in developing and adult hippocampal neurons.

In mice genetically deficient for cell surface MHCI, hippocampal synaptic plasticity driven by activation of NMDA-type glutamate receptors (NMDARs) is selectively shifted in favor of potentiation. Concomitantly, trafficking of AMPA-type glutamate receptors (AMPARs), which is thought to underlie changes in synaptic strength in the adult hippocampus, is altered in these transgenics. In particular, LTD induction protocols, which normally decrease cell surface AMPARs, instead increase cell surface AMPARs in MHCI-deficient animals, paralleling the observed shift in plasticity. In these same animals, activity-dependent remodeling of developing projections is disrupted. Together, these results suggest that changes in MHCI levels may mechanistically link maternal immune challenge, a risk factor for autism, with glutamatergic dysfunction and altered synaptic connectivity, common symptomatic correlates of this disorder. Clarifying this link could lead to novel, immune-based strategies for the diagnosis, treatment, and prevention of autism.

101.3 THE MECHANISM OF PATHOGENESIS OF AN AUTISM RISK FACTOR: ACTIVATION OF THE MATERNAL IMMUNE SYSTEM ALTERS FETAL BRAIN DEVELOPMENT VIA IL-6. P. Patterson*, *Biology Division*

Maternal infection is associated with increased autism and schizophrenia in the offspring. In a mouse model of this risk factor, infection with influenza virus at mid-gestation leads to post-pubertal onset of behavioral abnormalities in the offspring that are consistent with abnormalities seen in these mental disorders. There is also neuropathology that is consistent with that seen in schizophrenia and autism. The cause of these abnormalities is maternal immune activation (MIA), as treatment of uninfected, pregnant mice with the dsRNA, polyI:C, which evokes an anti-viral-like immune response, mimics the effects of infection on the offspring. Since infection and polyI:C induce cytokines, we asked whether these proteins mediate the effects of MIA on the fetal brain. After testing a variety of cytokines, we found that injection of IL-6 in normal pregnant mice causes behavioral deficits in the offspring similar to those caused by MIA. In the converse experiment, co-injection of anti-IL-6 antibody (but not anti-IFN) with polyI:C in pregnant mice strongly attenuates the effects of MIA on the behavior of the offspring. Moreover, maternal anti-IL-6 blocks the changes in gene expression in the brains of adult offspring that are caused by maternal polyI:C treatment. Finally, the offspring of polyI:C-treated IL-6 knockout mice do not display behavioral abnormalities. Thus, the cytokine IL-6 is a key mediator of the effects of MIA on fetal brain development. Additional new findings with the adult offspring of MIA mothers that are relevant for autism and schizophrenia include abnormalities in eyeblink conditioning, hippocampal CA1 neuron responses to dopamine, and a delay in the migration of late-born cortical neurons.

101.4 THE ROLES OF NEUROGLIA AND NEUROIMMUNE MODULATORS IN PATHOGENESIS OF ASD. C. A. Pardo*, *Jonhs Hopkins University School of Medicine*

Autism spectrum disorders (ASD) are complex neurodevelopmental disorders of early onset that are highly variable in their clinical presentation. Although the causes of autism in most patients remain unknown, several lines of research support the view that polygenic and environmental factors influence the development of dysfunctional cortical circuitry that underlies the abnormal cognitive processes and behaviors in ASD. Our research has focused on immunopathological studies of brain and cerebrospinal fluid (CSF) to investigate the role of neuroimmune factors in ASD. Characterization of microglial and astroglial responses as well as profiles of immune mediators (e.g., cytokine/chemokines and oxidative stress) in brain tissues of ASD patients were performed by immunomorphological, protein and lipidomic profiling methods. Marked increased in microglial and astroglial responses were found in selected areas of the brain such as anterior cingulate and midfrontal gyri as well as cerebellum. These cellular responses were also associated to increases in pro-inflammatory (e.g. IL-6, MCP-1), anti-inflammatory cytokines (e.g., TGFβ1) and increased oxidative stress markers (e.g. 4-HNE, isoprostanes). Similarly, CSF from patients with autism reveled also a pro-inflammatory profile with increases in cytokines such as IL-6, interferon-γ, MCP-1 and other immune mediators. Our studies demonstrate involvement of neuroglial and cytokine/chemokine responses in pathogenic mechanisms in ASD and suggest the role of innate neuroimmune pathways in processes of synaptic and dendritic organization as well neuronal dysfunction. These observations support the view that non-genetic factors influences such as neuroimmune and environmental factors are involved in pathogenesis of neurobiological abnormalities in ASD.

101.5 IMMUNE RESPONSES TO CENTRAL NERVOUS SYSTEM PROTEINS AND VIRUSES IN INDIVIDUALS WITH AUTISM. R. S. Fujinami*, J. E. Libbey, H. H. Coon, N. J. Kirkman, T. L. Sweeten, J. N. Miller, J. E. Lainhart and W. M. McMahon, *University of Utah*

There have been several reports that viral infections and autoimmune responses to central nervous system (CNS) proteins contribute to the pathogenesis of autism. These stem from the hypothesis that immune responses and/or viral infections early in life

could alter the development of the nervous system leading to autism. There has been controversy over the presence of autoantibodies to CNS proteins and viruses in autism. To further investigate this question we have measured autoantibody titers to glial fibrillary acidic protein (GFAP) and myelin basic protein (MBP) in 33 sera from children with classic onset, 26 children with regressive onset autism and 25 healthy age- and gender-matched subjects. Antibody titers were measured by enzyme-linked immunosorbent assay (ELISA). We did not find a significant difference between the control, classic autism and regression groups. This was confirmed by Western blot analyses. Similarly we did not find a significant difference in antibody titer to MBP between the different groups, which were also confirmed by Western blot analyses. We conclude that antibodies to MBP that may be present in individuals with autism do not contribute to alterations in myelin within the CNS. We also measured antibodies to measles, mumps and rubella viruses using ELISA. No significant differences in antibody titers to measles, mumps and rubella viruses were found among the groups. In addition, there were no significant differences among the groups for total immunoglobulin (Ig)G or IgM. Interestingly, about 25% of individuals with autism had very low or no antibody to rubella virus. We are further exploring how antibodies to rubella virus could contribute to the pathogenesis of autism in this subset of individuals.

Oral Presentations Program

102 Cognition 1

102.1 "I know that face" – A comparison of face learning and recognition abilities in children with Autistic Spectrum Disorders, Developmental Delay, and Typical Development. R. Wilson*, M. Blades and O. Pascalis, *University of Sheffield*

Background: Face recognition is essential for effective socialisation and communication, however children with ASD have been shown to display deficits in face recognition. Most studies have focussed on unfamiliar face processing with little research on recognition of familiar faces and the process by which a face becomes familiar. Objectives: This set of studies aimed to provide a comprehensive account of recognition of unfamiliar faces, through face learning to recognition of familiar faces in ASD, DD and TD children aged 5-11 years. Methods: Forced choice recognition (FCR) tasks were used with all studies, requiring children to select the recognised face from a choice of two photographs. Unfamiliar face recognition involved 3-second video exposure followed by FCR. Face learning involved three days video exposure to a set of six faces with FCR tasks. Familiar face recognition involved recognition of familiar school staff in a FCR task. All FCR tasks included full-face photographs, internal and external face parts. 176 children participated across the three studies (ASD=56, DD=47, TD=73). Results: No ASD-specific deficits were found on any of the studies. All children (ASD, DD, TD) showed better recognition of unfamiliar faces by full and external face parts, and better recognition of familiar faces by full and internal face parts, indicating a difference in processing strategy with familiarity. All children showed learning of faces on all face parts except the youngest TD children, and DD children. Children with ASD showed similar processing strategy to TD and DD children and similar levels of recognition accuracy to DD controls. Conclusions: Children with ASD recognise faces using the same strategy as TD and DD children. Children with ASD show the same level of proficiency in face recognition as DD controls. In low task demand conditions no evidence of ASD specific deficits were found.

102.2 Investigating the cognitive phenotype of autism: a 3-year prospective longitudinal study. E. Pellicano*, *University of Bristol*

Background: Researchers have proposed that the core features of autism are caused by multiple independent cognitive atypicalities, including capabilities in piecemeal processing combined with difficulties in theory of mind and executive control. No study has examined the validity of this 'multiple-deficits' account with respect to developmental persistence, universality, and developmental (causal) relations across cognitive domains.

Objectives: The aims of this longitudinal study were threefold: (1) to establish whether this

specific cognitive profile remains stable over time, (2) to determine the universality of this cognitive profile, and (3) to determine whether individual differences in early cognitive skills were predictive of later differences both within and across cognitive domains.

Methods: Sixty-nine children (38 children with autism and 31 typically developing children) involved in an earlier study on cognitive skills in autism were followed prospectively and reassessed 3 years later on visuospatial coherence tasks, simple and more advanced tests of theory of mind, and tests of executive function (specifically tapping planning ability and cognitive flexibility).

Results: At the group level, children with autism continued to show strengths in local processing and weaknesses in theory of mind and executive control, relative to typically developing children. At the individual level, however, this cognitive profile was not present in all children at either time point, especially at follow-up. Also, while individual differences within cognitive domains were reasonably stable over time, early theory of mind skills were found to be predictive of later executive function, but not vice versa.

Conclusions: These results of the group as a whole suggest that the cognitive profile in autism persists with development. Yet, the results on individual patterns of performance present a challenge for a multiple-deficits view of autism, and indicate that the developmental relationships between cognitive atypicalities are more complicated than presupposed.

102.3 ATTENUATED BINDING OF FEATURAL INFORMATION IN INDIVIDUALS WITH AUTISM SPECTRUM DISORDER. D. M. Bowler*, J. M. Gardiner and S. B. Gaigg, *City University, London*

Background: Extensive evidence indicates that individuals from across the autism spectrum exhibit memory difficulties that mimic those observed in typical aging. For example, both populations show disproportionate difficulties on tests of free recall as compared to tests of recognition, both populations display impairments on episodic memory measures, and both groups exhibit problems in the sequential retrieval of information. This parallel is informative because it offers a useful heuristic device for further study and because it sheds light on possible neural mechanisms underlying the memory difficulties present in ASD.

Objectives: To further explore the usefulness of the aging analogy to the study of memory in ASD by drawing on a paradigm developed by Chalfonte and Johnson (1996). These authors showed that compared to younger participants, older typical adults had intact memory for individual features (i.e. colour, identity, location) of a complex stimulus (a grid of coloured line drawings) but were impaired in their memory for combined features (i.e. colour-identity, location-identity).

Methods: A sample of participants with ASD and typical individuals, matched on age and full-scale IQ, took part in the current investigation. On each of 5 separate testing sessions, participants were presented with 21 uniquely coloured line-drawings that appeared simultaneously for 1 minute in random locations of a 6x6 grid. Following Chalfonte and Johnson (1996), their memory was tested either for individual features only or for combinations of these features.

Results: Our results show that individuals with ASD in comparison to typical individuals exhibit a marked decrement in their memory for combinations of features despite showing intact memory for the features themselves.

Conclusions: Our findings further support a parallel between the memory difficulties evident in typically aging populations and those exhibited by individuals with ASD. We discuss these findings in the context of a 'relational binding' hypothesis of ASD.

102.4 Pre-Conceptual Self-Awareness of own Agency in Autism Spectrum Disorder. D. Williams*[1] and F. Happé[2], (1)*University College London*, (2)*Institute of Psychiatry, Kings College London*

Background: The self-monitoring-deficit view of ASD (e.g., Russell & Hill, 2001), proposes a primary impairment in pre-conceptual self-awareness of own agency and actions. This leaves affected individuals with little feeling of

responsibility for their own actions 'from the inside'. By contrast, Williams and Happé (at IMFAR 2007) suggested their findings of ASD-specific deficits in reflexive self-awareness were better explained by an extension of the 'Theory of Mind' account of ASD.
Objectives: To assess whether deficits in self-monitoring characterize ASD and what implications such difficulties may have for theory and intervention.

Methods: Sixteen individuals with ASD and 16 IQ-matched comparison participants took part in each study. In Study 1, participants completed a computerized task, based on that implemented by Russell and Hill (2001) but designed to produce greater variation in performance. The aim was to identify which of several coloured squares was under the participants' control, through movements of the mouse (Self condition) and which were controlled by the computer. In an 'Other-person' condition, the participant held the mouse but the experimenter was in control of its movements. The task here was to detect the other's agency. In Study 2, participants completed a self-other source memory test for cards laid on a picture board by themselves or by the experimenter.

Results: Participants with ASD performed similarly in terms of levels and, importantly, *patterns* of performance to comparison participants. In Study 1, each group found it easier to monitor their own actions/agency than to monitor the agency of the experimenter. Both groups also showed a 'self-reference effect' in Study 2, recalling the cards laid by themselves more reliably than those laid by the experimenter.

Conclusions: Although deficits in conceptual 'theory of *own* mind' characterize ASD (Williams & Happé, 2007), difficulties in self-awareness at the pre-conceptual level of action monitoring are not apparent.

102.5 CHILDREN WITH AUTISM DISENGAGE FROM A SOCIAL STIMULUS SLOWER THAN TYPICALLY DEVELOPING CONTROLS. J. T. Elison*[1], J. S. Reznick[1], T. N. Holtzclaw[1], J. Piven[2] and J. W. Bodfish[1], (1)*University of North Carolina - Chapel Hill*, (2)*University of North Carolina*

Background: Impaired disengagement of visual attention has been demonstrated in children and adults with autism through the use of the gap-overlap paradigm. However, research has not demonstrated the effect of stimulus type on disengagement patterns.

Objectives: This study was designed to investigate whether social or nonsocial stimuli elicit differential disengagement patterns in children with autism by comparing saccadic reaction times (SRTs) between a group of school-aged children with autism (n=13, M=136.5 months; sd=24) and a group of typically developing control children (n=14, M=166.5 months; sd=28).

Methods: Data were recorded on a Tobii 1750 eye-tracker. Diagnosis of the autism group was confirmed with an ADI-R and all children had IQs > 70. The gap-overlap paradigm consists of a gap condition in which a central stimulus disappears before the onset of a peripheral target, and an overlap condition in which the central stimulus remains visible after the onset of the peripheral target. Disengagement was operationalized as the latency to initiate an eye movement from the center of the array toward the peripheral target.

Results: Both groups demonstrated the gap effect, defined as increased SRTs in the overlap condition. The autism group had significantly increased SRTs in both the overlap and the gap condition when compared to the control group. In the overlap condition, the control group disengaged significantly faster from social stimuli, whereas the autism group disengaged equally slow from social and nonsocial central stimuli. Interestingly, the groups did not differ in SRT in the nonsocial overlap condition.

Conclusions: Typical children disengaged their attention faster from a social stimulus (e.g. a face), but children with autism disengaged slower than typically developing children regardless of the nature of the central stimulus. Disengaging visual attention is a primary component of cognition that may contribute to the deficits in social behavior observed in autism.

102.6 Enhanced Rationality & Behavioral Invariance in Autism. N. A. Harrison*, B. De Martino, S. Knafo, G. Bird and R. J. Dolan, *University College London*

Background:Decisions in healthy humans are intimately interwoven with their context or 'frame' in a manner that can lead to logically inconsistent choices. A recent study suggests that 'framing effects' result from amygdala activity which serves as a simplifying affect heuristic rapidly guiding context specific behavior. Autistic individuals show a marked inability to integrate incoming perceptual information (weak central coherence) however their susceptibility to framing effects are unknown.

Objectives: To determine whether choice behavior in Autism is less susceptibility to frame effects leading to decision invariance or 'hyper-rationality' that may underlie Autism associated behavioral rigidity and social impairment.

Methods: Fourteen Autistic and 15 control subjects were compared on susceptibility to frame using a financial task involving a choice between risky and sure options in 'gain' and 'loss' frames. Subjects were age, sex and I.Q. matched. Skin conductance response (SCR) was recorded throughout. 'Need for Cognition' (NFC) and 'Cognitive Reflection Tests' (CRT) questionnaires and Autism Diagnostic Observation Schedule (ADOS) were also completed.

Results: Autistic subjects showed a striking reduced susceptibility to frame compared to controls ($p<0.1$). Further SCR responses in controls but not Autism differentiated 'gain' from 'loss' frames (Interaction $p=0.3$). Decision invariance was independent of risk behavior and did not correlate with NFC, CRT or ADOS sub-scores.

Conclusions: Inability to incorporate contextual information including subtle social cues may underlie behavioral invariance and impaired social interaction that characterizes Autistic disorders. Failure to mount an SCR suggests this may result from impaired generation or integration of amygdala based signals.

102.7 Lack of Local Bias during Selective Attention Global-Local Processing in Autism Spectrum Disorders. S. A. Johnson*[1], L. M. Blaha[2], R. R. Murphy[2], J. T. Townsend[2], V. A. Bruce[3] and J. C. Stout[4], (1)*Dalhousie University*, (2)*Indiana University*, (3)*University of Windsor*, (4)*Monash University*

Background: Previous studies of global-local (GL) processing in autism spectrum disorders (ASD; Rinehart et al., 2000; Plaisted et al., 1999) suggest a lack of both global advantage and global interference. However, their methods differed fundamentally (including unlimited stimulus presentation time, lack of spatial uncertainty, few trials) from traditional designs of GL studies. Studies of controls have indicated that such changes in GL task parameters significantly alter performance (Kimchi, 1992).

Objectives: In the current study, we characterized GL processing in ASD during selective attention tasks using traditional cognitive science methods.

Methods: Sixteen high-functioning individuals with an ASD and 16 age- and IQ-matched comparison subjects completed eight selective attention GL tasks. Four tasks used hierarchical letter stimuli and four used number stimuli. For each type of stimulus, we employed two methodologies: 1) replication of methods used in previous ASD GL studies, but with a greater number of trials and 2) methods consistent with traditional designs of GL studies, incorporating brief presentation times, spatial uncertainty, and backward masking.

Results: Repeated measures ANOVAs revealed main effects for attended dimension with faster response times for the global versus local dimension for both groups on all tasks. Contrary to findings from previous ASD studies, global interference effects were demonstrated by both groups for both replication and traditional GL tasks, and neither group demonstrated local interference. Analyses at the individual level indicated that few participants responded faster when attending to local versus global information. When present, this atypical result occurred at the same rate in both groups. Similarly, only a

few control and ASD participants showed local interference.

Conclusions: We found typical GL processing in high-functioning ASD participants. Both control and ASD groups demonstrated global advantage, global interference, and lack of local interference. Findings are discussed in light of cognitive theories of ASD and methodological considerations.

102.8 Mechanisms underlying deficits in autobiographical memory retrieval in Autism Spectrum Disorders. L. Goddard*[1], B. Dritschel[2], P. Howlin[3] and S. Robinson[1], (1)*Goldsmiths, University of London*, (2)*University of St. Andrews*, (3)*INSTITUTE OF PSYCHIATRY, KING'S COLLEGE LONDON*

Background: Autobiographical memory (AM) retrieval is an essential human ability, important for understanding oneself as an enduring entity and understanding how other people think, feel and act. AM comprises two components: semantic AM which encompasses biographical personal information (e.g., names, addresses and trait information) and episodic AM which contains personally experienced events. While there is evidence for a specific (i.e., episodic) memory deficit in adults with ASD (Goddard et al, 2007), there is some indication that memory for personal semantic information is preserved (Crane & Goddard, in press).

Objectives:

We explored the nature of AM deficits in children with ASD, focusing on different time periods and the semantic/episodic components of AM. We also investigated the potential mechanisms underlying AM difficulties, in particular, central executive function, visual memory and emotion processing.

Methods:

35 children with an ASD between the ages of 8 and 16 and 35 typically developing children matched for age, gender and IQ participated in this study. Memory was assessed on a word cueing task, and two semi structured interviews: one examining memory for recent and remote events and the other systematically examining semantic and episodic memory across different life time periods. Control measures included verbal fluency, vocabulary and general memory. Components of central executive function were examined with the Wisconsin Card Sorting, Stroop, Tower of London and Junior Hayling tasks.
Results: The ASD group showed difficulties in retrieving both episodic and semantic AMs and also required substantially more prompting. These effects were largely independent of general memory ability. The strongest predictor of poor autobiographical memory was performance on the Wisconsin Card Sorting and Tower of London tasks

Conclusions: Certain components of central executive function, i.e., set shifting and planning, underlie difficulties in autobiographical memory retrieval in children with an ASD. The developmental pathway of these deficits is discussed.

Oral Presentations Program

103 Intervention

103.1 Early Intervention Outcomes Before and After EIBI Termination and School Entry. P. Mirenda* and K. D. Bopp, *University of British Columbia*

Background: The long-term outcomes associated with early intensive behavioral intervention (EIBI) have been documented in only a few studies to date. There is a need for follow-up research to examine children's progress following EIBI termination at school entry.

Objectives: To examine the rates of change (RoC) during and following EIBI, using multi-wave measures of expressive and receptive language and adaptive behavior obtained over 4-5 years.

Methods: Data were collected for 53 children with ASD prior to the initiation of EIBI (T1) and 6, 12, 24, 32, and 53 months later, using the Peabody Picture Vocabulary Test (PPVT), Expressive One-Word Picture Vocabulary Test, Preschool Language Scale, and Vineland Adaptive Behavior Scale (VABS). SAS proc mixed analyses were used to examine the

developmental trajectories for each outcome measure during and post EIBI. Chronological age (CA) was used as a measure of time and nonverbal IQ (NVIQ) and autism severity scores at T1 were examined as predictors of the intercepts and slopes. Developmental trajectories were also estimated for typical children, using information from relevant test manuals.

Results: On all measures except the VABS communication and socialization subscales, RoCs for the autism sample approached or exceeded those of typically developing children of the same CA during 2 years of EIBI. On the two VABS subscales, this was also true for children with NVIQ scores ≥50. Following EIBI termination, RoCs for all measures except PPVT decreased to 25%-50% of the EIBI rates.

Conclusions: This sample of children receiving eclectic EIBI demonstrated greatly accelerated language and adaptive skill development over 2 years. However, these gains were not maintained at the same rate after EIBI was discontinued at school entry. This suggests that terminating EIBI at age 6 may not maximize children's developmental potential.

103.2 A New Way to Study and to Treat Autism Spectrum Conditions: Video Games for Ecologically Valid Measurement and Therapy. M. K. Belmonte*, *Cornell University*

Background: Integrative studies of autism across levels and domains of cognition demand that subjects remain on task throughout large numbers of experimental trials and paradigms. Such lengthy, demanding and tedious experiments can place experimental control at odds with ecological validity. A way between the horns of this dilemma is offered by embedding experiments within the motivating, engaging, yet strongly regular and systematic environment of a video game.
Objectives: Develop freely available, open-source, extensible software that encapsulates a battery of perceptual, attentional, executive and social cognitive tasks in a video-game format suitable for behavioural and physiological measurements and extensible for therapeutic interventions. Correlate behavioural and EEG measures across cognitive domains, in autism-spectrum probands, their clinically unaffected siblings, and unrelated normal controls.
Methods: A suite of mini-games is themed round a space colony simulator. The format is person-centred and event-driven rather than computer-centred and timed, encouraging players to apply skills at their own pace and on their own terms. Predictable and anxiety-minimising perceptual and social environments afford opportunities not only to demonstrate skills but also to develop them. Measures include motion coherence threshold, go/no-go inhibition, focused and distributed visual and multimodal attention, perceptual disembedding, and first- and second-order "theory of mind." Game events are transparently logged for offline analysis, and can be synchronised with physiological recordings.
Results: Preliminary behavioural and EEG data in autism (joint work with the UCSD Research on Aging and Development Laboratory) suggest elevated motion coherence thresholds, delayed and abbreviated beta EEG suppression and gamma activation in response to coherent motion, and absent frontal N2 during behavioural inhibition. EEG phase coherence analysis and behavioural correlations across task domains are being explored.
Conclusions: Video games offer a new, integrative tool to examine the true nature of autistic cognitive skills behaviourally and physiologically, and the potential to develop these skills therapeutically.

103.3 Friendship Training for Children With High Functioning Autism: The UCLA PEERS Program. E. Laugeson*, C. Mogil, A. R. Dillon and F. Frankel, *UCLA Semel Institute for Neuroscience & Human Behavior*

Background:

Social skills training has increasingly become a common method for assisting adolescents with Autism Spectrum Disorders (ASD) more effectively adapt to their social environment. Yet, the majority of treatment intervention studies in this area have focused on improving the social skills of younger children with ASD. Among the few social skills intervention studies conducted with older adolescents, most have not been formally tested in terms of their efficacy in developing close friendships,

nor do they assess social functioning from independent observers, such as teachers.

Objectives:

This study examines the efficacy of a manualized evidence-based parent-assisted social skills intervention, known as the UCLA PEERS Program, in improving overall social skills and friendship quality among teens 13-17 years of age with high-functioning autism or Asperger's Disorder.

Methods:

30 participants and their parents were randomly assigned to a treatment with follow-up condition or a delayed treatment control condition. Participants attended weekly 90-minute group treatment sessions over a 14-week period. Targeted skills included: conversational skills; peer entry and exiting skills; appropriate use of humor; developing and expanding friendship networks; good host behavior during get-togethers; good sportsmanship; strategies for handling rejection including teasing, bullying, arguments, and rumors/gossip; and strategies for changing bad reputations. Skills were taught through didactic instruction using concrete rules and steps of social etiquette in conjunction with role-playing exercises. Teen participants practiced newly learned skills during behavioral rehearsal exercises within the group, and parent-assisted weekly socialization homework assignments outside of the group.

Results:

Findings suggest that teens exhibited significant improvement in social functioning and friendship skills following the treatment intervention, according to self-report, parent-reports, and independent teacher reports.

Conclusions:

These findings suggest that the use of PEERS, a parent-assisted manualized social skills intervention, is efficacious in improving the social competence and friendship skills of teens with ASD.

103.4 Let's Face It! A Computer-Based Intervention for Strengthening Face Processing Skills in Individuals with Autism Spectrum Disorders. J. M. Wolf*[1], J. Tanaka[2], C. Klaiman[3], K. Koenig[1], J. Cockburn[2], L. E. Herlihy[1], C. Brown[1], S. S. Stahl[1], M. South[4], J. McPartland[1] and R. T. Schultz[5], (1)*Yale Child Study Center*, (2)*University of Victoria*, (3)*Children's Health Council*, (4)*Brigham Young University*, (5)*Children's Hospital of Philadelphia and the University of Pennsylvania*

Background: A large literature suggests that individuals with autism spectrum disorders (ASD) have deficits in face processing ability. Yet few interventions to remediate these deficits have been developed and evaluated in a randomized clinical trial. We have developed a comprehensive and engaging computer-game intervention ("Let's Face It!") that targets face processing skills.

Objectives: The present study investigated whether individuals with ASD demonstrated improvement in their face processing skills following the "Let's Face It!" intervention.

Methods: Participants with ASD were randomly assigned to either an active treatment group (N=45) or a waitlist control group (N=39). Active treatment involved 20 hours of home-based intervention over a several month period, monitored by parents, and closely supervised by research staff. The outcome measure was the Victoria/Yale Face Processing Battery (VYFPB), which includes measures of face identity (including parts/whole and eye/mouth processing) and expression recognition.

Results: Separate analyses of variance for each of the 11 subtests of the VYFPB were conducted with treatment condition (active, waitlist) and time point (pre-, post-) as independent variables, and total test score as the dependent measure. One subtest, Part-Whole Identity, demonstrated a significant interaction (with Bonferroni adjustment) between treatment condition and time point ($p=.002$), such that the active treatment group improved to a significantly greater degree than did the waitlist control group. This result held for eye, mouth, and part conditions, and was nearly significant for whole conditions.

Conclusions: "Let's Face It!" shows promise as an intervention to improve face processing skills in individuals with ASD. This was a fairly low intensity intervention (20 hours total); these results therefore serve as a proof of principle, suggesting that a more intensive intervention might yield more widespread gains. In addition, further research is needed to explore the generalizability of these improvements.

103.5 Replication Study of Face Expertise Training in Adults with High Functioning Autism Spectrum Disorders. S. Faja*, S. J. Webb, K. Merkle, D. E. Kamara, E. H. Aylward and G. Dawson, *University of Washington*

Background: Numerous investigations have demonstrated that individuals with autism employ non-expert strategies to recognize and remember faces, compared with controls. A pilot investigation of expertise training demonstrated that individuals with autism could become experts at recognizing a set of novel faces and increase their awareness of configural information contained in the face. However, training did not improve performance on standardized measures of face recognition (Faja et al., 2008).

Objectives: The current study tested the effects of expertise training with faces or houses on adults with ASDs who were impaired on standardized measures of face recognition. Methods: Participants were randomly assigned to training group (10 Face, 9 House) and received 5-8 hours of computerized training. Behavior was examined before and after training using standardized tests of recognition and recall and experimental measures of configural awareness, holistic processing and the inversion effect. ERPs to faces and houses were also collected at baseline and after training.

Results: All but one participant met criteria for expertise (Tanaka & Taylor, 1991). Post training, there were no significant differences between groups in performance on the standardized face recognition measure. No changes were found in accuracy for recognizing manipulations of configural information, increased holistic processing or inversion effect. Performance of both groups improved on the standardized measure of face memory, $t(16) = 2.14$, $p < .5$ and for accuracy in configural recognition, $t(14) = 2.22$, $p < .5$. Results of the ERP data will also be discussed.

Conclusions: These results are consistent with previous findings of improvement resulting from expertise training, compared to a no training condition. Yet, expertise training in general appears to have an effect rather than training with faces, *per se*.

103.6 THE EFFECTIVENESS OF COMMUNITY-BASED EARLY INTENSIVE BEHAVIOURAL INTERVENTION: A WAITLIST COMPARISON STUDY. H. E. Flanagan*[1], A. Perry[1], N. L. Freeman[2] and J. Bebko[1], (1)*York University*, (2)*Surrey Place Centre*

Background: Early Intensive Behavioural Intervention (EIBI) has been recognized as the treatment of choice for young children with autism. However, additional research is needed that examines treatment benefits in large community samples using comparison groups.

Objectives: 1) To examine the impact of community-based EIBI on autism severity, adaptive functioning and cognitive skills using a well-matched waitlist comparison group; 2) To determine whether younger age and higher initial skill level predict greater improvement.

Methods: Information was obtained through file review at a treatment agency providing publicly funded EIBI to a diverse urban population. Sixty-four preschool-aged children on a waitlist for treatment were individually matched to 64 children receiving EIBI (initial age within 4 months). Although random assignment was not possible, a standardized waitlist management system was used that did not include any prioritization other than time of referral. Prior to the treatment/waitlist period, autism severity and adaptive functioning were assessed and diagnosis (autism or PDD-NOS) was confirmed. Measures were re-administered following the treatment/waitlist period and cognitive skills were evaluated (available at time 2 only). The treatment period tended to be longer than the waitlist period and this difference was controlled in analyses.

Results: Prior to the treatment/waitlist period, groups did not differ with respect to age, autism severity, adaptive functioning, and parent stress. Children in the treatment group experienced greater improvement in autism severity and adaptive functioning. In addition, they had higher cognitive skills following the treatment/waitlist period. Initial age and skill level predicted outcome in some domains but not others.

Conclusions: This research supports the effectiveness of community-based EIBI for preschool-aged children with autism.

103.7 Variability in intervention outcomes for young children with ASD. D. A. Zachor*[1] and E. Ben Itzchak[2], (1)*Tel Aviv University / Assaf Harofeh Medical Center*, (2)*Ariel University Center of Samaria*

Background: Few studies have examined the variability in intervention outcomes of very young children with ASD.

Objectives: which child characteristics affect progress with intervention?

Methods: 79 children (mean age: 25.6, SD=4.2 months), meeting the cut-off points for autism on the ADI, were assessed at pre and post one year of intervention in center-based early intervention programs. Autism severity, cognitive and adaptive skills were measured by standardized tests [Mullen; Vineland; Autism Diagnosis Observation Schedule (ADOS)].

Results: Significant improvement was documented in: autism severity -ADOS scores in all domains ($p<.001$); cognitive abilities - Mullen standard scores: Visual perception ($p<.5$), Receptive and Expressive Language ($p<.001$); adaptive skills- Vineland scores in all domains, $p<.001$). Correlations between pre-intervention (PRI) autism severity and progress in expressive language and visual domains were significant ($p<.1$). No significant correlation was found between the PRI cognitive ability and the pre-post-intervention change in autism severity. Comparing PRI autism severity of children that mostly improved (upper third) in expressive language and visual domains with children that improved the least (lowest third), revealed that ADOS scores of the better group were significantly lower ($p<.1$). No significant differences were found in the PRI cognitive ability between the group that mostly or least improved in their autism severity (ADOS). Regarding cognitive profiles, [verbal/non-verbal (V/NV)], the V>NV group (n=9) had better PRI reciprocal-social scores and significantly better pre-post-intervention improvement in this domain than the V=NV (n=33) and V<NV (n=25) groups ($p<.5$). Age effect: children that improved the most in pre-post ADOS scores were significantly younger (M=24.5, SD=4.1) than those who less improved (M=27.2, SD=4.2).

Conclusions: Autism severity, cognitive and adaptive skills improve significantly with intervention in young children with ASD. PRI characteristics in social skills and overall autism severity affect post-intervention cognitive outcome. PRI age and cognitive profiles are related to post-intervention change in autism symptoms.

103.8 Designing Social Competence Interventions to Match ASD Subtype Characteristics: A Pilot Study. J. Stichter*, K. Visovsky, C. Schmidt, N. Gage and T. Crowe, *Thompson Center for Autism and Neurodevelpmental Disabilities*

Background: Youth with ASD experience social competence deficits that impact their ability to make and sustain friendships, initiate and maintain social interactions, and understand emotions in themselves and others. Without targeted intervention services, these youth often exhibit problematic social behaviors and can become socially withdrawn, which negatively impacts their quality of life and can lead to other developmental skill deficits.

Objectives: This study piloted a Social Competence Intervention (SCI), designed to impact social competence performance for a specific ASD subtype characterized by a diagnosis of an ASD, a FS IQ 75+, and the ability to pass a first order theory of mind assessment and the Faux Pas Test. The curriculum utilized primarily cognitive-behavioral intervention targeting social cognition deficits as characterized by a theory of mind deficit (TOM), deficits in executive

functioning (EF) and an inability to recognize emotions (Soloman et al, 2004).

Methods: The pilot study employed a three-tiered assessment methodology to determine programmatic effectiveness, and the impact of the intervention curriculum on functional characteristics of the subtype. Common screening and standardized tools designed to assess ToM, EF and facial recognition were administered pre and post. Curriculum based measures assess key programmatic features at specific points during the 10 weeks, and individualized measures monitoring individualized goals.

Results: Initial results on seven 11-14 year old males in the subtype indicate substantial growth on the SRS (Constantino, 2002), with a mean raw score decrease(improvement) of 33 points. Mean improvement on the TOPS was 13.5%; on the Faux Pas test was 9.6%; and on the Reading the Mind in the Eyes test was 7.1%. Additional analyses are pending on the DANVA and the BRIEF.

Conclusions: Results indicate promise for enhanced response to treatment in the area of designing interventions that target ASD subtypes. Implications for interdisciplinary research in this area should be streamlined.

Poster Presentations Program

104 Communication Posters 1

1 104.1 Joint Attention Revisited: Examining heterogeneity among children with autism. S. Hurwitz*, *University of North Carolina at Chapel Hill*

Background: The joint attention (JA) deficit in autism has been well established. JA is predictive of language abilities and may be a pivotal skill necessary for language development. Yet some children with autism display JA abilities. Objectives: This study examines the heterogeneity among children with autism in order to determine how language abilities of children who exhibit JA skills compare to children with similar chronological and mental ages but no JA skills. Methods: Thirty-four children with autism (confirmed by the ADOS and ADI-R) were grouped according to their ability to respond to JA. They were administered the ADOS—Module 1, the ADI-R, the Preschool Language Scale (PLS-4) and the Mullen Scales of Early Development. Module 1 of the ADOS has a JA probe used to place children in the Yes-JA group or the No-JA group. The two groups of children were then compared. Chronological age (CA), nonverbal mental age (MA), and total language age equivalent score were examined. Results: There were 17 children in the Yes-JA group and 17 in the No-JA group. Findings showed that the groups were not significantly different with regard to CA (mean= 42.88 and 42.71 months) or MA (17.6 and 14.6 months respectively) but had significantly different language scores (mean= 16.65 and 9.88 months). Conclusions: This study demonstrates that there is more to JA acquisition in autism than CA or MA. Even from a sample of children with autism who had low mental ages (mean 15.56, range 4-30 months), half of the group demonstrated an ability to respond to JA. This group had considerably superior language than the group without JA. This supports the theory that JA is a pivotal skill for learning language. Children with autism who have JA skills may take a different developmental path then those without, resulting in enhanced language development.

2 104.2 Weighted frequency of triadic communication growth rate predicts endpoint atypicality within a sample of infant siblings of children with ASD. P. Yoder*, W. Stone and T. Walden, *Vanderbilt University*

Background: Later-born siblings of children with ASD (Sibs-ASD) are at elevated risk for autism and related developmental disorders. However, it is currently unclear how to predict which Sibs-ASD will have compromised developmental outcomes at an age when diagnoses tend to be stable (i.e., after 30 months).

Objectives: We predicted that Sibs-ASD with faster growth rate for triadic communication between the ages of 15 and 34 months would have more optimal diagnostic outcomes than those with a slower growth rate.

Methods: Forty-four Sibs-ASD (initial CA = 15.1 mos; SD = 3 mos) were tested using the Screening Tool for Autism in Two-year-old (STAT) at 3 to 5 periods with approximately 4 – 8-month inter-test intervals. Frequency of triadic communication (i.e., communication about an object to a message recipient) was coded from the STAT. A weighted frequency score was also derived by multiplying each communication act by the behavior used to communicate (nonverbal = 1, single word = 2, multiword = 3). Child diagnoses were determined by psychologists at the last data point (i.e., M = 33.7, SD = 4.1 mos) on the basis of standard cognitive and diagnostic measures. The "atypical" subgroup (n = 15) were those with diagnoses of language impairment, developmental delay, autism, PDD/NOS, or the broader autism phenotype (i.e., clinical level of concern regarding social communication, no other diagnosis, and scores above the cutoff on the ADOS social domain).

Results: Sibs-ASD with faster growth in weighted frequency of triadic communication were less likely to have "atypical" diagnoses at the final evaluation (pseudo-R^2 = .28). Neither the initial value of weighted triadic communication nor any aspect of unweighted triadic communication growth predicted diagnostic subgroup.

Conclusions: If replicated, growth rate of weighted frequency of triadic communication between 15 and 24 months will be a strong predictor of which Sibs-ASD need treatment.

3 104.3 Gesture and Speech Integration in High-Functioning Autism. L. B. Silverman*[1], E. Campana[2], L. Bennetto[3] and M. K. Tanenhaus[3], (1)*University of Rochester Medical Center*, (2)*Arizona State University*, (3)*University of Rochester*

Background: Iconic gestures routinely accompany speech, are ubiquitous, and provide vital communicative information to the listener. Individuals with autism show a constellation of social and communicative impairments, yet it is unknown whether difficulties with iconic gesture comprehension contribute to the core features of autism.

Objectives: The purpose of this study was to examine iconic gesture comprehension in autism, and to assess whether cross-modal processing difficulties may impede gesture and speech integration in this population.

Methods: Participants were 19 adolescents with high-functioning autism (mean age:15.6 yrs) and 20 typically developing controls (mean age:15.2 yrs), matched on age, gender, VIQ, and SES. Iconic gesture comprehension was assessed through quantitative analyses of eye fixations during a video-based task. Participants watched videos of a woman describing one of four shapes shown on a computer screen. Half of the videos depicted natural speech-and-gesture combinations, while the other half depicted speech-only descriptions (using comparable verbal information). Participants clicked on the shape that the speaker described. Since gesture typically precedes speech, we hypothesized that typically developing controls would visually fixate on the target shape earlier on speech-and-gesture trials compared to speech-only trials, indicating immediate integration of visual and auditory information across sensory modalities. We further hypothesized that participants with autism would not show this effect.

Results: Analyses of eye movements revealed that controls identified the target more quickly when iconic gestures accompanied speech. Conversely, individuals with autism showed slowed comprehension when gestures were present compared to when speech occurred alone. This effect was not accounted for by unimodal speech-only or gesture-only processing difficulties.

Conclusions: These findings suggest that individuals with autism have cross-modal processing difficulties that significantly hinder gesture and speech comprehension. They also implicate brain regions responsible for social cognition and biological motion perception.

4 104.4 USING COMIC STRIP CONVERSATIONS TO PROMOTE APPROPRIATE SOCIAL BEHAVIOURS FOR CHILDREN WITH AUTISM. G. M. Guazzo*, *Integrated Centre for the Autism Study (ICAS)*

Background:
Children with Autism Spectrum Disorder (ASD) often lack the appropriate communication and reciprocal social interaction skills that lay the groundwork for school-based learning of literacy and for later academic and social achievement.

Objectives:
Our focus in this paper is to understand and diminish deficits in reciprocal social interaction and social communication in high-functioning children with ASD using Comic Strip Conversations (CSC). CSC is a conversation between two or more people that incorporates the use of simple drawings. The visual representation can include symbols, drawing and written words.

Methods:
Three boys, who were between 9 and 11 years old, were diagnosed according to the National Society for Autistic Children's criteria (Ritvo & Freeman, 1978) and the DSM IV (American Psychiatric Association, 1994). All children were verbal and could answer simple questions, generally in three- or four-word phrases. An ABAB research design was used.

Results:
With such intervention, it has attempted to upgrade the conversational abilities through the strengthening of the intrinsic motivation. Through this strategy, it has attempted to hold account of the peculiar cognitive characteristics of these persons and possibility has given to them it to experience a positive communicative loop increasing therefore also the relational life.In particular, to the end of the participation all the subjects introduced an improvement in the following abilities: use of the gestures and the look, structuring of a phrase more articulated (use than functors), starter of one conversation (to attract the attention, to use comments, to ask information), maintenance of one conversation (to recognise comments, to make questions, to answer).

Conclusions:
In conclusion, only through the repetition of interactive experiences (initially "simulated" with "scripts of routine social experiences", and then with natural social experiences), the persons with autism will have the possibility to learn these abilities.

5 104.5 Performance of identifying a conversation partner by facial gestures in individuals with high-functioning pervasive developmental disorders: An experiment using two-person dialogue scenes. J. Adachi*, *Hokkaido University of Education*

Background: Synchronous aspects of nonverbal communication and smoothness of the exchange during interaction tend to be poor in individuals with pervasive developmental disorder (PDD) (Garcia-Perez et al., 2007).

Objectives: The study aimed to investigate whether there was any difference in perception of interactional synchrony between PDD and non-PDD groups.

Methods: 26 adults(14 with PDD and 12 without PDD) with typical IQ participated in a visual task. They were shown a movie assembled from three sectional videos located in the middle left, the upper right and the lower right of the movie screen. In the experimental condition, the left video showed one of the two interactants while each of the right videos showed the other one. In the control condition, the left video showed the bottom-side of a drum being hit with a drumstick while each of the right videos showed small pieces of paper being scattered on the top-side of the drum. In both conditions, the two right videos were muted and only one of them was synchronized to the left video. The task of participants was to find out which of the right videos synchronized. Reaction time (RT) and eye movement during the task were recorded.

Results:In the experimental condition, RT in the PDD group was significantly longer than in the non-PDD group. In the control condition, RTs in both groups were not significantly different. In the experimental condition, the number of fixations in the PDD group was significantly bigger than in the non-PDD group. In the control condition, the numbers of fixations in both groups were not significantly different. In both control and experimental conditions, fixation durations in both PDD and non-PDD groups were not significantly different.

Conclusions:The findings suggested that in the experimental condition, the perception of synchrony was worse in the PDD group than in the non-PDD group.

6 104.6 Expression of distress in children with Autism Spectrum Disorder. G. Esposito*[1], P. Venuti[2] and S. De Falco[2], (1)*University of Trento, Italy*, (2)*University of Trento*

Background: Autism Spectrum Disorder (ASD) is a disorder that affects communication and social skills to varying degrees. While many studies have concentrated on examining the patterns of behavior and development in the context of speaking and interacting, very few studies have investigated the specificity of cry in infants with ASD. And this is very peculiar considering that cry can be viewed as both the first communicative system and the first social structure in human development.
Objectives: Aim of this research project is to investigate how is perceived the crying of children with ASD, as opposed to TD children or children with other Developmental Disability (DD).
Methods: Different methodologies are being used in this research project: (i) a "Listen & Response" experiment for testing whether the atypical structure of autistic cry can bias the parents' perception, (ii) an Observational Study, to analyze the caregiver behaviour in a real scenario.
Results: We found considerable agreement between the results of the 2 studies. The methodologies showed that cry episodes of ASD were considered to be the same as those of younger TD and DD children. Balanced for age, ASD cries elicited negative patterns of emotional states as compared to parents' responses to the cries of TD and DD children. These data highlight that the cry of children with ASD are not well identified. Moreover, the ASD cries elicited negative feelings.
Conclusions: ASD cries have ambiguous patterns, and therefore may not seem understandable. Parents' reactions to autistic cries are qualitatively different from their responses to cries of children with TD and DD of the same age. This difference can be an additional cause of difficulty in sharing feelings and developing inter-subjectivity processes.

7 104.7 Attachment behaviours and parent-child interaction in pre-school autism. L. Blazey[1], K. Leadbitter[2], C. Holt*[1] and J. Green[1], (1)*University of Manchester*, (2)*Lancaster University*

Background: Children with autism suffer from significant social impairments that affect social interactions and relationships with others, yet evidence suggests they are still capable of forming secure attachments to their caregivers. The origins and consequences of this paradox have been insufficiently studied. In non-autistic populations, parental sensitivity, mutuality and affect have been identified as key factors associated with attachment security. Few studies have directly examined these constructs in children with autism.

Objectives:

1) To examine the relationship between attachment security in autism and parent-child interaction in areas of: parental sensitivity, mutuality, parent affect, and child affect.

2) To compare children with autism and a group of typically-developing controls on these constructs.

Methods: Baseline data from 27 children with autism (mean age = 46 months, SD = 7.83) participating in the Pre-school Autism Communication Trial (PACT, www.manchester.ac.uk/medicine/pact) were examined and compared with data from a group of 24 typically-developing children (mean age = 23 months, SD = 6.50) group-matched on non-verbal ability. Both groups participated in a video-recorded free-play session with their parents. A ten minute sample of the play session was coded using a modified version of Coding of Attachment-Related Parenting. Attachment security was measured using the Brief Attachment Screening Questionnaire.

Results: In the autism group, attachment security was significantly associated with high mutuality and low child negative affect. Compared to typically-developing controls, the autism group showed significantly lower

parental sensitivity, mutuality, parent positive affect and child positive affect.

Conclusions:

Attachment security in autism is, in part, associated with key features of parent-child interaction in expected ways. However, parent-child interactions differ in autism compared to typical development in ways that may affect the development of attachment security. To fully understand the origins and consequences of attachment security in autism, longitudinal studies that examine these effects across time are required.

8 104.8 Nonverbal Processing Skill and Social Adjustment in Preschoolers with Autism. D. C. Carey* and S. Nowicki, *Emory University*

Background: Despite the variety and range of impairments that may exist in children with autism, the most significant deficits involve social interaction and communication, as these span across developmental stages and occur regardless of cognitive abilities. It is thought that difficulites in the social-communicative realm may stem from a deficit in nonverbal processing, however previous research in this area has produced equivocal results.

Objectives:The purpose of this study was to compare the receptive nonverbal processing ability of ASD and typical preschool children and its association to their social adjustment. It was predicted that children with autism would be less proficient than typical peers in reading nonverbal cues of emotion, and that scores on the nonverbal processing measure would relate to the participant's social adjustment ratings, as nonverbal processing abilities are necessary for effective interpersonal interactions (Nowicki, 2007).

Methods:Participants were 18 preschool children (14 boys and 4 girls, *M* age = 56.8 months). The Diagnostic Analysis of Nonverbal Accuracy (DANVA2; Nowicki & Duke, 1994) subtests of child and adult faces and paralanguage were used to assess nonverbal processing skill. Social adjustment was measured by a teacher's rating of social skills and problem behaviors.

Results:The results provided some support for the hypothesis that autistic children compared to typical children are worse at decoding emotion, especially emotions expressed through the paralanguage channel and at high intensity, although some differences diminished when controlling for cognitive ability. Poorer nonverbal processing skill was associated with poorer social adjustment for both groups of children, especially for the autistic group.

Conclusions: The finding that preschool children with ASD have difficulties identifying simple emotions and high intensity emotions provides evidence for a core emotional deficit in autism, which may impair their social adjustment. The possible existence of a nonverbal deficit in young children may be important for future diagnosis and intervention.

9 104.9 Effects of Picture Exchange Communication System on Verbal and non-Verbal Communication Skills and Problem Behaviors of Iranian Children with Autism Spectrum Disorders. H. R. Pouretemad[1], F. Ahmadi*[2], K. Khoushabi[3] and M. Mamaghanieh[2], (1)*Shaheed Beheshti University*, (2)*University of Shaheed Beheshti*, (3)*University of Social Welfare and Rehabilitation Sciences*

Background: Picture Exchange Communication System (PECS) is an picture-aided augmentative and alternative communication tool to help with developing the communication skills of children with autism. It is advantageous due to having the least number of prerequisites and the fact that it teaches requesting to the children. Despite of the increasing prevalence of Autism Spectrum Disorders (ASD) in Iran, there has been no report investigating effect of PECS in Iranian children with Autism.

Objectives: We have studied the applicability of PECS as well as the effect on communication skills and problem behaviors of Iranian children with ASD.

Methods: The participants, 4 children of 3-7 year old, were taught phases 1-4 of PECS for 42 sessions and the changes in verbal and

non-verbal communication skills, as well as problem behavior parameters were recorded before and throughout the study using Autism Treatment Evaluation Checklist and Communication Skills Development Questionnaire.

Results: At the end of the study three subjects entered phase 3 of PECS and one could gain proficiency in phase 3 and enter phase 4. Two children showed improvement in verbal communication, 3 had increased values in parameters of non-verbal communication and 3 had attenuated problem behaviors.

Conclusions: The acquisition of PECS skills and the effects of autism impairments in studied children were discussed in the context of Iranian culture and Farsi language.

10 104.10 Increasing Requesting Skills in Individuals with Autism: Animated Pictures vs. Video Modeling. L. Spencer*, *Armstrong Atlantic State University*

Background:

Teachers commonly use visually-based strategies with students with ASD. In this session, results will be presented from two studies which compared static pictures to animated visual cues (i.e., video to determine if one was more effective for teaching body part recognition and requesting skills. Implications for classroom use will be discussed.

Objectives:

· Increase understanding of the pros and cons of two types of visually-based strategies for students with ASD

· Discuss differentiated effectiveness for two groups of children with ASD

· Describe leaner characteristics which may influence strategy effectiveness

Methods:

An alternating treatment with replication within a multiple probe design across participants was used to compare the use of static pictures and video modeling to determine if one method was more efficient than the other.

Results:

Results indicated all of the participants improved their ability to request. There was a significant difference in the data between the two interventions for three of the four participants. However two of the participants performed better during the sessions using static pictures. One participant performed better during the sessions using video modeling. The data for the fourth participant did not show a significant difference between the two interventions.

Conclusions:

· All participants improved in their ability to request

· Participants with higher verbal abilities and higher adaptive behavior scores experienced some success with video modeling

· Participants that experienced success with video modeling reported watching TV. at home

· Participants that did not experience success with video modeling were not reported to have watched TV. at home

· Imitation from a live model does not equal imitation from video model

· Two teachers participated in the study

· Both teachers indicated an interest in both strategies of instruction

· One teacher preferred the intervention utilizing static pictures

· One teacher preferred the intervention utilizing video modeling

11 104.11 Measuring change in parent child communicative interaction during pre-school treatment for autism. C. R. Aldred* and J. Green, *University of Manchester*

Background: Comprehensive parent training studies generally define the specific intervention, measure moderating variables such as child ability or parent education, and relate these to child outcome variables. Despite a number of studies reporting positive gains from communication focussed parent training programmes, there is a lack of intervention trials which analyse change in parent and child dyadic interaction as a mediator of outcome. No adequate standardised dyadic interaction measure of this kind exists in the autism literature. The Parent Child Interaction (PCI) measure was developed during a pilot RCT of a parent-mediated communication intervention for pre-school autism (Aldred et al 2004). It integrates measures of synchronous and asynchronous parental communication acts (Shapiro et.al. 1987); semantic contingency of parental verbal responses from (Conti-Ramsden 1990); and duration of shared attention (Watson, 1998).

Objectives: To investigate change in parent-child interaction during preschool parental intervention.
To relate any change to overall change in child autism symptomatology and communication functioning.

Methods: Detailed PCI data on 28 children 2-5yrs diagnosed with core autism included in the pilot RCT were analysed using 2 group pre-post comparisons and regression analysis to investigate change effects.

Results: The study found significant relative improvements in parent adapted communication and child communication initiation which correlated with standardised measures showing significant improvements in autism-specific symptoms on standardised tests following a 12 month intervention.

Conclusions: The results suggest utility of this PCI video measure. The converging PCI process measure and standardised child and parent results suggest a relationship between changes in parent adapted communication targeted in therapy and gains in child reciprocal social interaction, language and communication initiation.

12 104.12 THE CRITERION-RELATED VALIDITY OF THE MODIFIED CLASSROOM OBSERVATION SCHEDULE TO MEASURE INTENTIONAL COMMUNICATION (M-COSMIC): A PRELIMINARY STUDY.

S. Clifford*[1], L. Brown[1], K. Hudry[1], G. Pasco[2] and T. Charman[1], (1)*UCL Institute of Child Health*, (2)*Autism Research Centre, University of Cambridge*

Background: The M-COSMIC was devised to extend the original COSMIC (Pasco et al, submitted) observational measure of the intentional communication of children with autism in an unstructured classroom setting. The original COSMIC was designed for use with children with low cognitive ability and no or limited speech. The M-COSMIC sought to extend this measure by including further items relating to early social communication which could be used to assess children with a wider range of cognitive and language abilities in naturalistic classroom settings.
Objectives: To investigate the psychometric properties of the M-COSMIC, including criterion-related validity and inter-rater reliability.
Methods: Participants consisted of 25 children with autism who were seen as part of the Preschool Autism Communication Trial (PACT: http://www.medicine.manchester.ac.uk/pact/) . Children received the Autism Diagnostic Observation Schedule – Generic (ADOS-G, Lord et al., 2000), standardised language assessments, and the M-COSMIC at the same time and thus constituted a concurrent criterion-related validity sample. The children, aged 3 years 6 months to 6 years were videoed during teaching and free play activities at nursery/school, and frequency counts of intentional communication behaviours as defined by the M-COSMIC were taken from the videos. To examine the validity of this measure, scores from the M-COSMIC will be correlated with relevant scores from the ADOS-G and standardised language and communication measures (PLS, VABS).
Results: Data from approximately 25 children with autism will be presented. Pearson correlations and regression analyses will be used to analyse the concurrent validity. Inter-rater reliability results will be measured using

intra-class correlations.
Conclusions: It is anticipated that the results will inform us of the potential use of this ecological measure as an outcome measure for communication-focused intervention trails. It is also expected that the measure will have research and clinical value in assessing social communication behaviours in a naturalistic setting.

13 104.13 PRODUCTION OF EMOTIONAL PROSODY AND FACIAL EXPRESSIONS IN ADOLESCENTS WITH AUTISM. R. B. Grossman*[1], L. R. Edelson[1], L. B. Rubinstein[2], J. Lomibao[3], S. Borawski[1] and H. Tager-Flusberg[1], (1)*Boston University School of Medicine*, (2)*Boston University*, (3)*Boston Autism Consortium*

Background: Studies of affective prosody production in individuals with autism spectrum disorder (ASD) have described subjective and objective differences in pitch and volume, indicating both more monotonous productions and greater expressive range in non-monotonous utterances (Shriberg et al. 2001, Hubbard & Trauner, 2007). Macdonald et al. (1989) found similar differences in productions of affect across voice and face.

Objectives: To capture and analyze productions of affective vocal prosody and facial expressions among adolescents with ASD.

Methods: Adolescents with ASD and typically developing (TD) controls (age 10-19) were asked to retell four brief, highly animated first-person stories containing happy, angry, surprised and fearful emotions presented on video tape by an adolescent actor. We digitally recorded prosody of 17 participants with ASD and 13 TD controls and facial expressions from 15 ASD and 14 TD adolescents. Voice information was analyzed using PRAAT software. Three independent coders blind to diagnosis and target emotion coded facial expressions for emotion, expressiveness (flat, mild, moderate, extreme), naturalness (natural, slightly awkward, very awkward, unnatural) and eye gaze (on, away) on a second-by-second basis.
Results: We found slower, higher, softer voices and more monotonous productions in the ASD group. In utterances showing noticeable emotion, vocal pitch and intensity ranges were significantly larger in the ASD group. The ASD participants' facial expressions were judged as expressive as their TD peers', but significantly more awkward, and with eye gaze more focussed on the camera. Both groups displayed significantly more affect in their voices than on their faces.

Conclusions: Adolescents with ASD display qualitative and quantitative differences from their typical peers in vocal expressive range and naturalness of face during affective narrative productions. Both groups have significantly higher percentages of animated vocal performances than animated facial expressions, indicating a higher threshold for affective modulation of face than voice.

14 104.14 Do joint attention problems persist in verbal children with autism?. K. Leadbitter* and C. Lewis, *Lancaster University*

Background:

The extent and nature of the joint attention impairment in autism varies across development. Joint attention encompasses a range of social-communicative functions, forms and motivations which may develop independently. Explaining the successful development of some facets of joint attention alongside enduring areas of impairment is fundamental to theoretical accounts of autism. Two accounts which offer such explanations invoke reduced self-initiation (Klin, 2003; Mundy, 2003) and reduced interpersonal engagement (Hobson, 2002).

Objectives:

1) To show that verbal children with autism demonstrate joint attentional abilities: in terms of response to the bids of others and production of the surface forms of pointing and showing when prompted.

2) To test whether these joint attention skills are characterised by:

a) reduced spontaneous initiation of joint attention or

b) diminished interpersonal engagement (shared affect and directedness of body, gestures, eye gaze and language).

Methods:

20 children with autism and 20 children with learning difficulties (6-13 years; language above 3.5 years; matched on age, gender and language; diagnoses confirmed) took part in semi-structured interactive tasks with the researcher involving proximal and distal objects of interest. The frequency of joint attentional responses and initations and the presence and quality of communicative forms were coded from video-tape.

Results:

All children in both groups responded to joint attention within two bids. Data will be presented on group comparisons in the frequencies of spontaneous and prompted joint attentional acts and in behavioural and subjective ratings of shared affect and directedness within those acts.

Conclusions:

The results show that joint attention is not globally impaired in autism as previously reported (e.g. Baron-Cohen, 1995). They also allow us to evaluate whether theoretical accounts centred on initiation (Klin, 2003; Mundy, 2003) or interpersonal engagement (Hobson, 2002) adequately explain the development of some facets of joint attention alongside enduring impairment.

15 104.15 Acquisition of Social-Communicative Behavior in Toddlers at Risk for Autism Spectrum Disorders. W. J. Guthrie*[1], C. Lord[1], M. Coffing[2], R. Petrak[1], R. Niehus[1] and S. Risi[1], (1)*University of Michigan Autism and Communication Disorders Center*, (2)*Vanderbilt University*

Background: A number of studies have examined the social-communicative behavior patterns of children with ASD under 2 (e.g. Wetherby et al., 2007) and have indicated that these young children use a variety of behaviors in order to communicate, but the patterns and frequency of use differ from children without ASD.

Objectives: To use a longitudinal dataset with monthly time points between 12 and 36 months to identify patterns in age of acquisition of social-communicative behaviors, and patterns of relationships between these behaviors; and to examine their predictive value in toddlers.

Methods: Participants were identified from an ongoing longitudinal study, which follows children monthly who have been referred for possible autism, or have a sibling with ASD. Data were used from 25 children who had at least five administrations of the Autism Diagnostic Observation Schedule – Toddler module (ADOS-T) between 12 and 30 months. At the most recent assessment, 12 children were diagnosed with an autism spectrum disorder, 9 with a non-spectrum disorder, and 4 as typically developing (19 males, 6 females). The mean age of first ADOS-T assessment was 14.20 months (2.27).

Results: Analyses indicated predictable patterns of acquisition (defined by 2 scores of 0 on individual items in successive ADOS-T administrations) of many social-communicative behaviors (e.g. Response to Name, Response to Joint Attention, Initiation of Joint Attention, Requesting, and Integration of Gaze and Other Behaviors). A progression occurred from partial to full acquisition for many skills. Individual differences in behaviors and children will be examined in detail using growth curves.

Conclusions: Timing of acquisition of different behaviors was similar for some skills (e.g. Response to Joint Attention and Integration of Gaze and Other Behaviors) and varied considerably for others (e.g. Response to Name). Implications in the very early diagnosis and treatment of children with ASD will be discussed.

16 104.16 Joint Attention in Infants and Toddlers with an Autism Spectrum Disorder: Research into the Underlying Processes. I. Schietecatte* and H. Roeyers, *Ghent University*

Background: It is generally accepted that joint attention is impaired in children with an autism spectrum disorder (ASD). A better understanding of this impairment could have positive implications for early detection and intervention. Objectives: In order to get a better understanding of problems with joint attention in children with ASD, the current research investigates underlying processes of joint attention, namely the understanding of intentionality, attentional skills and the orientation towards social stimuli. Methods: Children with a (suspicion of an) ASD and children with a typical development at the age of 24 and 36 months, were invited to do a series of tasks. The understanding of intentionality was measured by observing the behavioural responses of children towards an adult who was either unwilling or unable to give them a toy. Attentional skills (e.g. disengaging, shifting) were measured by a visual cueing paradigm and the orientation towards social stimuli was studied by a visual preference paradigm with social and non-social stimuli. Several joint attention tasks were included. Results: Data are being collected and will be available at IMFAR. It is expected that typically developing children will have a better understanding of intentionality, better attentional skills and a more pronounced social preference than children with ASD. According to our hypothesis, these skills are associated with the quality of joint attention behaviour. Conclusions: Implications for understanding joint attention impairments in children with an ASD will be discussed.

Poster Presentations Program

105 Human Genetics Posters 1

17 105.1 The DLX1and DLX2 Genes and Susceptibility to Autism Spectrum Disorders. X. Liu*[1], N. Novosedlik[1], M. Hudson[1], A. Wang[1], I. L. Cohen[2], A. Chudley[3], C. Forster-Gibson[1], S. M. Lewis[4] and J. J. Holden[1], (1)*Queen's Univerity*, (2)*NYS Institute for Basic Research in Developmental Disabilities*, (3)*University of Manitoba*, (4)*University of British Columbia*

Background: An imbalance between excitation and inhibition in the cortex has been suggested as a possible etiology of autism. The *DLX* genes encode homeobox transcription factors that have been implicated in the development of the *GABAergic* system. The *DLX1* and *DLX2* genes lie head-to- head in 2q32, a region associated with autism susceptibility.

Objectives: To investigated the *DLX1* and *DLX2* genes in ASD families for association with susceptibility to autism

Methods: We genotyped 6 Tag SNPs covering the *DLX1* and *DLX2* genes in TEST and REPLICATION cohorts of Multiplex (MPX) familie and a group of Simplex (SPX) families as well as a control sample. We performed both family-based association and population-based case-control analyses.

Results: Family-based association tests showed strong association with 5 of the 6 SNPs. The common alleles of *rs743605* and *rs4519482* were significantly associated with autism (P<0.12) in a TEST sample of 138 MPX families. Testing in a REPLICATION sample of 169 MPX families not only confirmed the association at *rs4519482* (P =0.34) but also showed strong allelic association of the common alleles at *rs788172, rs788173* and *rs813720* (all P<0.1). In the combined sample of 307 MPX families, the common alleles were all significantly associated with autism (P< 0.1). Haplotype analysis identified a common risk allele containing GGGTG haplotype that was significantly over-transmitted in the two MPX cohorts and the combined samples (P<0.1). Further testing in 306 Simplex families replicated only the association at *rs4519482* (P =0.33) in single SNP analysis and the over-transmission of the GGGTG haplotype (P=0.12) with the significance being lower than that in the MPX families.

Conclusions: The results suggest that genetic variants in the *DLX1/DLX2* genes may affect susceptibility or cause autism in families where there is a genetic loading for these conditions.

18 105.2 Yield of Standard Genetic Testing in a Large Autism Diagnostic Clinic. P. Manning-Courtney* and J. Ruschman, *University of Cincinnati*

Background:Children with possible ASD routinely undergo genetic testing as part of a diagnostic assessment. Reports vary regarding the diagnostic yield of genetic testing. Objectives: Review yield of genetic testing in a large diagnostic clinic for children with ASD. Methods: Records of 360 children (316 male) diagnosed with ASD via ADOS and clinical evaluation were reviewed (group 1). Frequency of genetic testing being obtained was assessed, and abnormal results were tallied. Records of 52 additional children, referred for expanded cytogenetic microarray testing because of a formal or suspected diagnosis of autism were also reviewed (group 2).

Results: 61.4% of group 1 underwent routine chromosome analysis, with a yield of one abnormal result. 57% of group 1 underwent DNA probe for FX syndrome, with one abnormal result. Four patients in group 2 (7.6%) had abnormal results on expanded cytogenetic microarray, including 22q13 deletion,15q11.2 duplication,10q23 duplication and 1q12q21.3 duplication. One of these patients was found to not have autism according to ADOS. Remaining 3 patients had final diagnoses of autism based on ADOS and/or clinical evaluation. Additional cases to be added at time of presentation.

Conclusions:Yield of routine chromosome analysis and DNA probe for FX in children with ASD may be lower than that of expanded cytogenetic microarray.

19 105.3 BIOCHEMICAL AND GENETIC STUDIES OF THE MITOCHONDRIAL ASPARTATE/GLUTAMATE CARRIER AGC1. L. Palmieri[1], V. Papaleo[2], V. Porcelli[1], P. Scarcia[1], R. Sacco[2], J. Hager[3], F. Rousseau[3] and A. M. Persico*[2], (1)*Univ. of Bari*, (2)*Univ. Campus Bio-Medico*, (3)*IntegraGen*

Background: the *SLC25A12* gene encodes the brain isoform of the mitochondrial asp/glu carrier (AGC), a key molecule in the malate/aspartate NADH shuttle and in energy metabolism. *SLC25A12* gene variants were found associated with autism (Ramoz et al., 2004).

Objectives: to correlate asp/glu transport rates and *SLC25A12* gene variants in postmortem brains of autistic patients and controls.

Methods: temporocortical gray matter (BA 41/42) from six patient-control pairs was used to measure reconstituted AGC1 activity from tissue homogenates or isolated mitochondria; cDNAs were sequenced and a family-based association study was performed on 246 simplex and 9 multiplex families.

Results: AGC transport rates were significantly higher in tissue homogenates from all six autistic patients, including those with no history of seizures and with normal EEGs prior to death. This increase was consistently blunted by the Ca^{2+} chelator EGTA; no difference in AGC transport rates was found in isolated mitochondria from patients and controls; mitochondria from each control showed increased AGC activity when exposed to the post-mitochondrial supernatant of his/her matched patient than to his/her own supernatant. AGC1 expression and cytochrome c oxidase activity were both increased; oxidized mitochondrial proteins were markedly increased in four of the six patients. *SLC25A12* gene variants were neither correlated with AGC activation nor associated with autism, while a protective gene variant may be present among unaffected siblings.

Conclusions:excessive Ca^{2+} entry or release from intracellular stores boosts AGC activity, mitochondrial metabolism and, to a more variable degree, oxidative stress in autistic brains. The modulation of AGC and/or Ca^{2+} homeostasis could provide new preventive and therapeutic strategies.

20 105.4 REELIN GENE EXPRESSION AND EPIGENETIC STATUS IN TEMPORAL CORTEX OF AUTISTIC BRAINS. C. Lintas*[1], K. Garbett[2], K. Mirnics[2] and A. M. Persico[1], (1)*Univ. Campus Bio-Medico*, (2)*Vanderbilt Univ.*

Background: Reelin plays a pivotal role in neurodevelopment and has been implicated in autism pathogenesis. The methylation status of the reelin gene (*RELN*) promoter regulates gene expression and *RELN* promoter

hypermethylation has been found in *post-mortem* brains of schizophrenic and bipolar patients.

Objectives: to correlate *RELN* gene expression with promoter methylation status in the same post-mortem termporocortical tissue samples (BA41/42 or 22) of 9 patient-control pairs (M:F=7:2, pre:post-puberal=3:6).

Methods: gene expression was assessed by oligonucleotide DNA microarray analysis followed by real-time qPCR. *RELN* promoter methylation status was verified by bisulphite treatment, amplification by nested PCR and DNA sequencing of 17-22 clones/subject.

Results: *RELN* gene expression was reduced on average by 47% using oligonucleotide DNA microarray analysis. Compared to controls, *RELN* mRNA was significantly reduced in postpuberal (N=6 pairs, P<0.5), but not in prepuberal patients (N=3 pairs, P=0.51). Postpuberal patients and controls did not differ in mean total number of methylated clones, but patients displayed much heavier methylation at the 5' promoter end compared to controls (P<0.000001). Conversely, postpuberal controls displayed heavier methylation at the 3' promoter end (P<0.000001). No significant correlation was found between *RELN* mRNA levels and *RELN* promoter methylation, regardless of status, promoter region and age.

Conclusions: sex hormones seemingly trigger *RELN* promoter methylation both in normal individuals and in autistic patients; there is a highly significant difference in methyl CpG distributions between autistic and control brains. The lack of correlation between *RELN* mRNA levels and *RELN* promoter methylation could be due to higher level epigenetic mechanisms, such as histone acetylation. This hypothesis is currently being explored.

21 105.5 A genome-wide association study of autism. X. Q. Liu*[1], A. P. Thompson[2], D. Pinto[1], J. Skaug[1], L. Zwaigenbaum[3], W. Roberts[1], S. W. Scherer[1], P. Szatmari[2] and A. D. Paterson[1], (1)*The Hospital for Sick Children*, (2)*Offord Centre for Child Studies, McMaster University*, (3)*Glenrose Rehab Hospital/ University of Alberta*

Background: Genetic heterogeneity and weak effects of individual genes have been the major factors that hinder the search for susceptibility genes in autism spectrum disorders (ASD).

Objectives: To identify the ASD susceptibility genes in homogeneous subgroups using genome-wide association methods.

Methods: We will perform a genome-wide association study using 500 unrelated ASD cases and two sets of controls (500 controls from Germany and 1,000 controls from North America). We have finished the genotyping using the Affymetrix GeneChip Human Mapping 500K Array. The genome-wide association data from the Autism Genetic Resource Exchange Consortium (525 families) will be used to replicate the results from this study. Homogeneous subgroups based on IQ, language and family history will be used in the above analyses.

Results: The results will be reported at the meeting.

Conclusions: The conclusions will be reported at the meeting.

22 105.6 COGNITIVE AND BEHAVIORAL CHARACTERIZATION OF THE POTOCKI-LUPSKI SYNDROME. D. E. Treadwell-Deering*[1], M. P. Powell[1], J. R. Lupski[2] and L. Potocki[1], (1)*Texas Children's Hospital, Baylor College of Medicine*, (2)*Baylor College of Medicine*

Background: Potocki-Lupski Syndrome (PTLS; duplication 17p11.2) the homologous recombination reciprocal of the Smith-Magenis (SMS) microdeletion, is a recently recognized multiple congenital anomalies and mental retardation syndrome. Many patients have escaped ascertainment when assessed by routine cytogenetic methods. It was hypothesized that the phenotype of PTLS would be milder than SMS as genomic duplication is generally better tolerated than deletion; mild to borderline intellectual

disability and hyperactive and inattentive behavioral difficulties were anticipated. The availability of targeted array-based comparative genomic hybridization in clinical diagnostic laboratories has led to a greater sensitivity in diagnosis.

Objectives: To further characterize PTLS and to aid in clinical diagnosis, parent counseling and patient management.

Methods: Fifteen patients participated in a clinical protocol that included developmental and cognitive profiles, psychiatric assessment, and extensive medical evaluations. Assessment tools included the Mullen Scales of Early Learning or Stanford-Binet Intelligence Scales and Leiter International Performance Scales; Vineland Adaptive Behavior Scales; Behavioral Rating Inventory of Executive Functions; Behavior Assessment System for Children; Aberrant Behavior Checklist, and Short Sensory Profile; the ADI-R and ADOS-G were added after the first seven evaluations. Cytogenetic and molecular analyses were performed on all patients to establish genotype.

Results: The majority of patients (12/15) presented with intellectual disability in the moderate range of impairment and autistic symptoms; unexpectedly, two-thirds (10/15) met strict diagnostic criteria for autism or pervasive developmental disorder, NOS. The most common medical clinical features in these patients included hypotonia, failure to thrive in infancy, obstructive and central sleep apnea, EEG abnormalities, and cardiovascular anomalies.

Conclusions: Although unanticipated, PTLS appears to be very highly associated with autistic spectrum disorders. Continued assessment of patients will allow for clarification of this association and may contribute to our knowledge regarding the etiology of the pervasive developmental disorders.

23 105.7 Descriptive Analysis of 252 Twin Sets Recruited Through a National Online ASD Registry and Research Database. K. Law*, A. Marvin, C. Anderson, C. Cohen and P. Law, *Kennedy Krieger Institute*

Background: Twin studies provide an opportunity for researchers to disentangle genetic and environmental factors related to Autism Spectrum Disorders (ASD). Multiple twin studies report much higher concordance rates for monozygotic (MZ) twins compared to dizygotic (DZ) twins, supporting a strong genetic component to the disorder. The small sample size in twin studies, however, limits further exploration of many research questions. Recruitment of twin sets continues to be a challenge for autism researchers.

Objectives: To present baseline characteristics, demographics and other preliminary analysis on 252 twin sets enrolled in the Interactive Autism Network (IAN) research registry and database.

Methods: IAN is an initiative intended to accelerate autism research through an online registry and research database. Questionnaires are used to collect data from families, including the child with ASD, unaffected siblings and biological/adoptive parents. More than 20,000 individuals are enrolled. The database is an open resource, providing de-identified data and recruitment assistance to autism researchers.

Results: In less than 9 months, 252 twin sets (55 MZ and 197 DZ) enrolled in the IAN research protocol. This is the largest collection of twins in published autism research. Basic demographics such as age, gender, race, and ethnicity will be presented. Similar to other published findings, concordance rates are 81% for MZ and 18% for DZ twins. Preliminary analysis shows that gender does not predict concordance in either MZ or DZ twins. Concordance rates were not affected by age of twins. Among all twin sets, only 6.8% reported prior genetics research participation.

Conclusions:This study demonstrates successful recruitment of an unprecedented number of twin sets in a short time using internet-mediated research. A large number of twin sets are required to explore the complex genetic and non-genetic factors contributing to ASD. Future use of this database by autism researchers will demonstrate the long-term value of the resource.

24 105.8 Human Cerebellar Malformations and Autism Share Susceptibility Loci. K. A. Aldinger*[1], I. D. Krantz[2], W. B. Dobyns[1] and K. J. Millen[1], (1)*The University of Chicago*, (2)*The Children's Hospital of Phialdelphia*

Background: Post-mortem and MRI studies have identified several neural structures that are anatomically abnormal in autism patients, including the cerebellum. Posterior cerebellar hypoplasia and a decrease in the number of Purkinje cells have consistently been reported in the autistic brain. These are neural developmental phenotypes, suggesting that genes regulating cerebellar development may confer autism susceptibility. Few human cerebellar developmental genes have been described. We recently characterized a new human cerebellar malformation (CbM) locus on chromosome 6p25 at the molecular level by deletion mapping. Furthermore, we are systematically searching for CbM genes, generating the only DNA and clinical databank for CbMs.
Objectives: To determine the overlap between CbM loci and autism loci throughout the genome.
Methods: We performed exhaustive literature and database searches to identify cytogenetic abnormalities, copy number variants, or linkage at all 20 CbM cytogenetic loci in patients with autism.
Results: Among patients with autism we identified 5 with cytogenetic abnormalities and 9 with copy number variants of 6p25. Suggestive linkage to 6p25 in autism has also been reported. CT or MRI scans were not readily available for most autism patients to evaluate for CbM. Notably, however, the CbM patient with the smallest 6p25 deletion has a sibling with the identical 6p25 deletion and a diagnosis of autism, firmly establishing a link between CbM and autism at this locus. We further identified all 20 CbM loci in patients with autism. 18/20 (90%) CbM loci have at least 2 independent lines of evidence that they are also autism loci.
Conclusions: Cerebellar developmental phenotypes have been consistently reported in patients with autism suggesting that genes involved in cerebellar development may also contribute to autism pathophysiology. We recommend screening 6p25 deletion patients for CbMs and evaluating for autism. Our data further suggest that CbM patients may characterize a subset of autism patients.

25 105.9 Replication and Association Analysis of a 1p13-q12 Locus for Nonverbal Communication Deficits in Autism Spectrum Disorder. J. L. Yoon, M. Alarcon, D. Geschwind and R. M. Cantor*, *UCLA*

Background: The heritability of Autism Spectrum Disorder(ASD) is well established; however, inconsistent linkage and association results reveal its genetic complexity. Analysis of individual heritable quantitative features of ASD offers an opportunity to reduce complexity and increase consistency. Applying this strategy, the deficit in nonverbal communication (NVC) was quantified in children from 236 families in the Autism Genetics Resource Exchange(AGRE) using an Autism Diagnostic Instrument Revised sub-score. A nonparametric multipoint whole genome linkage analysis of the 299 sibpairs revealed an NVC quantitative trait locus(QTL) at 1p13-q12($p < .0001$), among others(Chen et. al., Mol Psych, 2006).
Objectives: To replicate the NVC QTL in a whole genome scan analysis of an independent sample of AGRE families and to identify genes predisposing to deficits in NVC by conducting association analyses in the replicated QTL.
Methods: A nonparametric QTL analysis was conducted using the Genehunter software in an independent sample of 219 AGRE families with 274 sibpairs. To identify genes associated with NVC, empiric family based analysis was conducted with the FBAT software on the 12,019 Affymetrix 550K SNPs located in the 1p13-q12 QTL on 680 children from 286 AGRE families.
Results: The 1p13-q12 NVC QTL was replicated($p < .0001$), providing strong evidence that genes in this region predispose to deficits in NVC. Setting .0001 as the level of significance, SNPs in or near 3 genes within the QTL were associated with NVC, with one SNP exceeding a Bonferroni correction($p<.000004$). Associated haplotypes were detected ($p < .0001$), and a haplotype within one of the genes was also associated with ASD($p<.00007$).
Conclusions: Gene(s) in 1p13-q12 contribute

to deficits in NVC. Conducting QTL analyses of heritable quantitative features of ASD, filtering by replication, and following with targeted association studies is an effective strategy to identify genes predisposing to features of ASD as well as the disorder itself.

26 105.10 Detecting Cognitive Endophenotypes for Autism Using a General Population Twin Family Sample. R. A. Hoekstra*[1], M. Bartels[2], G. F. Estourgie-van Burk[2], S. Baron-Cohen[1] and D. I. Boomsma[2], (1)*University of Cambridge*, (2)*VU University*

Background: The uneven cognitive profile of autism spectrum conditions (ASC) is illustrated by relative peak performance on tasks such as Block Design and Embedded Figures and poor performance on Verbal Fluency and social cognition tests. Studies of the Broader Autism Phenotype show that a similar uneven cognitive profile may also characterize first-degree relatives of people with ASC, suggesting familial influences. Whether these cognitive strengths and weaknesses correlate with autistic traits in the general population is unknown. Moreover, the nature of the association between this cognitive profile and autistic traits remains elusive.

Objectives: To explore the association between autistic traits and performance on cognitive tests in a general population sample; and to examine whether this association is due to shared genetic or environmental influences. A genetic link between certain cognitive abilities and autistic traits would point to these being promising endophenotypes for autism.

Methods: Autism-Spectrum Quotient scores (AQ, a quantitative measure of autistic traits) and performance on an extensive cognitive test battery (11 Wechsler subtests and tests of verbal/ spatial memory, processing speed, Stroop-interference and verbal fluency) were assessed in 18-year-old twins (n = 374) and their siblings (n = 96). Genetic vs. environmental covariance was estimated using structural equation modelling.

Results: Performance on the Block Design and Information subtests of the Wechsler intelligence scale was positively related to the Attention to Detail subscale of the AQ (both r=.16). Poor performance on the Wechsler Vocabulary subtest (r=-.25) and Verbal Fluency (r=-.21) predicted social interaction difficulties. The associations between these tests and autistic traits were explained by both genetic and environmental influences.

Conclusions: General population autistic traits covary with the same cognitive strengths and weaknesses as observed in clinical ASC. The relationship between autistic traits and the uneven cognitive profile is partly genetic, suggesting these may be promising endophenotypes for autism.

27 105.11 The relationship between molecular subtype and autism symptom severity in Angelman Syndrome. S. U. Peters*[1], L. M. Bird[2], R. Barbieri-Welge[2], W. H. Tan[3], R. Hundley[3], S. Skinner[4], A. Bauer-Carlin[4], T. Sahoo[1] and C. A. Bacino[1], (1)*Baylor College of Medicine*, (2)*Rady Children's Hospital San Diego*, (3)*Childrens Hospital Boston/Harvard Medical School*, (4)*Greenwood Genetics Center*

Background: Angelman Syndrome (AS) is a neurodevelopmental disorder characterized by mental retardation, absent speech, ataxia, seizures, and a distinct behavioral phenotype. Previous studies, focused primarily on deletion positive patients, indicated that a significant proportion of patients with AS also meet criteria for autism.

Objectives: To compare symptoms of autism and associated developmental and behavioral domains among the molecular subtypes and deletion subclasses of AS.

Methods: Patients were assessed with the ADI-R and ADOS-G, the Bayley Scales of Infant Development-III, Vineland Adaptive Behavior Scales, and the Aberrant Behavior Checklist (ABC). Deletion-positive patients underwent a microarray-based comparative genomic hybridization assay.

Results: 72 patients with AS (53 deletion, 11 *UBE3A* mutation, 4 uniparental disomy, and 4 imprinting center defect) were evaluated. Only deletion positive patients exceeded ADOS cutoff scores for autism or autism spectrum disorder (ASD). Those with larger, Class I

deletions were more likely to exceed criteria for autism/ASD (p=.5) compared to smaller, Class II deletions. Differences in ADOS socialization scores accounted for differences in autism diagnosis by deletion class, with Class I patients achieving more severe scores (p=.5). Significant differences were noted for cognition (p<.1), expressive language (p<.1), and fine motor skills (p<.5) between AS patients with co-morbid autism/ASD and those without. Significant, positive partial correlations were noted between ADOS communication and socialization scores and the Lethargy/Withdrawal domain of the ABC (r=.30; r=.35) and the Stereotypy domain (r=.25; r=.34) of the ABC.

Conclusions: Severity of autism symptoms in AS is associated with deletion size and with a more aloof/withdrawn behavioral phenotype. There are four genes (*NIPA 1*, *NIPA 2*, *CYFIP1*, & *GCP5*) missing in Class I and present in Class II deletions, one or more of which may have a role in the development of socialization skills.

28 105.12 Differences in Clinical Presentation of Trisomy 21 with and without Autism. C. A. Molloy*[1], D. S. Murray[1], H. Castillo[1], F. J. Hickey[1], B. Patterson[1] and A. Kinsman[2], (1)*Cincinnati Children's Hospital Medical Center*, (2)*Greenville Hospital System Children's Hospital*

Background: A strategy that has been advocated to elucidate mechanisms underlying specific types of autism is to focus on the presentation of autism in well characterized genetic syndromes such as Down syndrome.

Objectives: To identify characteristics differentiating children with Down syndrome with and without autism.

Methods: Children with trisomy 21 (n = 20) and autism were compared to children with trisomy 21 without autism matched on chronologic age, race and gender. Communication, cognitive and adaptive behavior skills were assessed with standardized instruments. Medical history was reviewed and medical records were examined for head growth in the first 3 yrs of life. Paired t-tests were conducted to evaluate case-control differences on all standardized test scores. Proportions in each group having specific medical conditions were compared with a chi square statistic. Differences in head circumference growth velocity were evaluated with a repeated measures model using generalized estimating equations.

Results: Cases ranged in age from 4.3yr to 16.8yr (median = 9.1yr). Controls matched within 12 mo. Mean case-control difference in age equivalent scores for receptive language was -26.7mo (SEM = 15.6; p<0.0001); for expressive language it was -25.4mo (SEM = 16.8; p < 0.0001). Mean difference in full scale change sensitive score from the SB5 was -40 (SEM = 6.1; p<0.0001). Mean difference for the Adaptive Behavior Composite was -21.4 (SEM = 2.3; p<0.0001). Seven cases had a history of seizures compared to 1 control (p=0.4). All participants had decreased head size consistent with Down syndrome, with no case-control differences.

Conclusions: Children with Down syndrome and autism have more severe, widespread deficits than children with Down syndrome alone. Their presentation does not include increased head size but does include an increased risk for seizures that may indicate a more widespread loss of functional connectivity in the brain.

29 105.13 CADHERIN-11 as a possible candidate gene for autism. A. C. Crepel*[1], H. Peeters[1], J. R. Vermeesch[1], J. Steyaert[2], D. Walleghem[3] and K. Devriendt[1], (1)*University of Leuven*, (2)*University of Leuven, and Dept. Clinical Genetics, University of Maastricht, Netherlands*, (3)*University Center for Child and Youth Psychiatry*

Background:
Positional cloning of chromosomal translocation breakpoints in autism patients is a valuable strategy towards the identification of candidate genes, especially in isolated autism, and when the aberration is de novo and family history is negative for autism. (1)
Objectives:
We describe a nondysmorphic patient with autism and full scale IQ of 76, who carries a

complex translocation involving chromosomes 3,5,16 and a pericentromeric inversion on chromosome 4.
Methods:
1Mb BAC array-CHG was performed to uncover possible submicroscopic imbalances. The breakpoints were finemapped with FISH.
Results:
On array-CGH, a ~1Mb microdeletion encompassing the clone NONSC8G10 was detected. Only 1 gene, cadherin-11 (CDH11) was located in this region. Of the remaining 6 breakpoints, one disrupted the AK13094 gene, another was near GFOD and RANBP10.
Conclusions:
In this patient with a complex chromosomal aberration, the CDH11 gene was found to be deleted on one allele. Cdh11 is expressed in the lymbic system and hippocampus in mice and may play a role in the organisation of central synapses.(2) Interestingly, there is evidence that altered synaptogenesis is implicated in the pathogenesis of autism. For instance, the post-synaptic cell adhesion molecules NLGN-3 and -4 are implicated in autism through their role in the establishment of fully functional presynaptic terminals in contacting axons.(3) Thus, CHD11 represents both a positional and functional candidate gene for autism. Mutation screening in a larger cohort of autism patients is ongoing.
(1)Castermans D et al (2003) The neurobeachin gene is disrupted by a translocation in a patient with idiopathic autism. J Med Genet 40(5) 352-6
(2)Manabe T et al (2000) Loss of cadherin-11 adhesion receptor enhances plastic changes in hippocampal synapses and modifies behavioral responses. J Mol Neurosci 15(6) 534-46
(3) Persico AM, Bourgeron T (2006) Searching for ways out of the autism maze: genetic, epigenetic and environmental clues. Trends Neurosci 29(7) 349-58

30 105.14 Association of MET with Autism Spectrum Disorder and Co-Occurring Gastrointestinal Symptoms. D. B. Campbell*[1], T. M. Buie[2], H. S. Winter[2], M. Bauman[2], J. S. Sutcliffe[1], J. M. Perrin[2] and P. Levitt[1], (1)*Vanderbilt University*, (2)*Massachusetts General Hospital for Children*

Background:
In addition to the core behavioral symptoms of autism spectrum disorder (ASD), a subgroup of patients present with chronic gastrointestinal (GI) dysfunction. We recently reported association of a functional *MET* gene variant with ASD and significantly decreased expression of MET receptor tyrosine kinase protein in temporal cortex of individuals with ASD. MET is a pleiotropic receptor that functions in both brain development and GI repair.
Objectives:
To determine if association of the ASD-associated *MET* promoter variant may be enriched in a subset of individuals with co-occurring ASD and GI symptoms.
Methods:
Presence of GI symptoms was determined from medical records available from the Autism Genetics Resource Exchange (AGRE). Genetic association analysis was performed on genotypes at the *MET* promoter variant rs1858830 using the family based association test (FBAT).
Results:
In a sample of 194 families for which GI symptom diagnosis was available, parent-to-child genetic transmission indicated association of the *MET* rs1858830 'C' allele with both ASD (P=0.44) and GI symptoms (P=0.001). In 99 families containing at least one child with co-occurring ASD and GI symptoms, the *MET* 'C' allele was associated with both ASD (P=0.002) and GI symptoms (P=0.002). In contrast, there was no association of the *MET* promoter variant in the 95 families lacking a child with co-occurring ASD and GI symptoms (P=0.918). In addition, GI symptoms were more common in individuals of *MET* rs1858830 genotype C/C in both strata. Thus, GI symptoms were present in 39% of individuals with genotype C/C and 25% of individuals of genotype G/G (χ^2=5.447; P=0.20).
Conclusions:
Replication will be necessary, but these data suggest that disrupted MET signaling may contribute to both behavioral and medical dysfunctions, providing increased sensitivity in stratification of children with ASD into unique subgroups for improved treatment.
Supported by: NIMH MH65299 and the Marino Autism Research Institute (PL).

31 105.15 GENOMIC COPY NUMBER AND PHENOTYPIC VARIABILITY OF THE AUTISM SPECTRUM DISORDERS. Y. Qiao*[1], X. Liu[2], M. Koochek[1], N. Riendeau[1], P. Malenfant[2], C. Harvard[1], J. Hildebrand[1], J. J. Holden[2], E. Rajcan-Separovic[1] and S. M. Lewis[1], (1)*University of British Columbia*, (2)*Queen's Univerity*

Background:

Autism Spectrum Disorders (ASDs) are heritable and complex neurodevelopmental conditions with unknown aetiology because of their significant clinical and genetic heterogeneity. Clinically relevant genomic copy number variants (CNVs) have been detected in 10~27% of ASD subjects studied in 3 different whole genome screening studies.

Objectives: To investigate the correlation between clinically relevant CNVs and the phenotypes of ASD subjects.

Methods:

We used commercial whole genome 1Mb BAC array comparative genomic hybridization (array-CGH) (Spectral Genomics) to screen for CNVs in 99 subjects with idiopathic autism (78 males and 21 females). FISH and real-time quantitative PCRs were used to validate the array-CGH results.

Results: Nine pathogenic CNVs (7 de novo, 1 inherited and 1 unknown origin) were detected in 9 individuals studied (9%). They include 2 unrelated cases with overlapping regions of de novo del(2)(p15-16.1) (4.5 and 5.7 Mb); an aunt and niece with de novo del(14)(q14.2) (0.7 Mb) and de novo dup(15)(q11) (10 Mb); a boy with de novo del(5)(p15.2-15.31) (2.4 Mb) and de novo del(3)(p24.3) (0.1 Mb); a boy with a de novo dup(18)(p11.3); a girl with unknown familial origin of dup(7)(q11); and two brothers with a maternally inherited del(X)(p11.22) (470 Kb). The 9 pathogenic CNVs were found in 9% of simplex, 6.9% of multiplex-immediate (1st degree co-relationship) and 13% of multiplex-extended (≥ 2nd degree co-relationship) families. No significant difference was noticed between parental age at conception and CNV frequency. The severity of clinical phenotype appears to be directly related to the gene content instead of the size of the pathogenic CNV.

Conclusions:

CNVs found in individuals with ASDs signal the locations of ASD-related culprit genes, and whole genome screening coupled with extensive phenotyping including medical and morphological assessments, is an effective and cost-efficient approach to improve prediction of candidate genes and detect those of mild to moderate effect.

32 105.16 Rate of Chromosomal Anomalies in an Iranian Autism Sample. A. Tolouei[1], R. Sasanfar[2], S. Haddad[3], M. Houshmand[4], M. Rostami[5] and S. L. Santangelo*[2], (1)*Special Education Organization of Iran*, (2)*Harvard Medical School*, (3)*Center for Human Genetic Research*, (4)*National Institute for Genetic Engineering and Biotechnology*, (5)*Medical Molecular Genetic Laboratory*

Background:

Approximately 2% - 5% of individuals with autism spectrum disorder (ASD) have some form of chromosomal abnormality; the most common location is the chromosome 15q11-q13 region.

Objectives:

The rates of chromosomal abnormalities in children with autism have never been examined in an Iranian population. This study examined how rates of chromosomal anomalies in an Iran, where the rate of consanguinity is ~ 20%, compare with those reported for other population samples.

Methods:

Cytogenetic analyses were performed on an unreferred sample of 118 children with ASD enrolled in schools for children with special needs in Iran. These were children with autistic disorder, Asperger syndrome, and PDD-NOS who had no known coexisting genetic condition. ASD diagnoses were made using standard diagnostic tools based on DSM-IV criteria. Cytogenetic analyses were

performed using peripheral blood lymphocyte cultures by standard protocols. Fragile X evaluation was done by both polymerase chain reaction and Southern blot.

Results:

Seven of the 118 children with ASD (6%) had some form of chromosomal abnormality; 2 had Fragile X syndrome, 2 had a chromosomal marker of unknown origin, 1 had a fragile site on 1p19, 1 had a fragile site on 1q11, and 1 had a fragile site on 9q11. No evidence of Idic15 or 15q11-q13 anomalies was found. The seven cases with chromosomal anomalies were not significantly different than cases without anomalies on IQ, autism symptoms, parental age, or any other measured variant.

Conclusions:

Our findings are concordant with other reports for overall prevalence of chromosomal abnormalities and fragile sites on the X chromosome in ASD subjects, except that no Idic15 or 15q11-q13 alterations were found. Differences in sample ascertainment across studies may account for this, since some prior studies have examined ASD samples that were specifically referred for cytogenetic examination, while this sample was unreferred.

33 105.17 Expression and methylation of the serotonin transporter gene in lymphoblastoïde cell lines from autistic patients carrying different genotypes for 5–HTTLPR. P. Vourc'h*[1], R. Tabagh[1], S. Védrine[1], C. Barthelemy[2], C. Moraine[1] and C. R. Andres[1], (1)*INSERM U930, University François-Rabelais de Tours*, (2)*CHRU de Tours, INSERM U930, University François-Rabelais of Tours*

Background: A role for the serotoninergic system in autism has long been suggested based on its implication in behavioural processes such as social interactions and the frequent observation of elevated levels of blood platelet serotonin in autistic patients. *Objectives:* We tested for an association between the SLC6A4 gene encoding the serotonin transporter (5-HTT) and autism or non syndromic mental deficiency (MD). We next analyzed the expression levels and methylation status of SLC6A4 in lymphoblastoïde cell lines from autistic patients.
Methods: We genotyped four functional polymorphisms (rs25531 and 5-HTTLPR in the promoter, VNTR in intron 2, rs3813034 in 3'UTR) in the SLC6A4 gene (17q12) in a population with autism (n = 103), a population with non syndromic MD (n = 100) and a control population (n = 164).
Results: We did not observe significant differences in the distributions of alleles and genotypes between patients with MD and controls. However, we found significant differences in allele frequencies for the 5-HTTLPR marker (X2=13.38, p=0.00025; Odds ratio 1.93, CI 95%:1.35-2.75) and haplotype frequencies (X2=13.93, p=0.003) between autistic patients and controls. The autistic patients showed higher frequencies of the Short (S) allele of 5-HTTLPR and the A / S haplotypes (rs25531 / 5-HTTLPR). We are currently analysing the expression level and the methylation status of the SLC6A4 gene in lymphoblastoïde cell lines from autistic patients carrying different genotypes for 5-HTTLPR (Long/Long, Long/Short, Short/Short). These experiments are performed on lymphoblastoïde cells cultured with or without brain neurotrophic factor (BDNF), molecule acting on the serotoninergic system.

Conclusions: Our results reinforce the implication of the gene encoding 5-HTT in autism vulnerability and suggest a direct role for the region carrying the Short allele of 5-HTTLPR.

34 105.18 The Association of a MET Promoter Variant with Autism is Dependent on Disease Classification. P. B. Jackson*[1], L. Boccuto[2], C. Skinner[1], J. S. Collins[1], R. E. Stevenson[1], G. Neri[2], F. Gurrieri[2] and C. E. Schwartz[1], (1)*Greenwood Genetic Center*, (2)*Catholic University*

Background: A 2006 report by Campbell et al. (PNAS) showed that a variant in the promoter region of the *MET* gene (rs1858830) on chromosome 7q31 was associated with autism.

Objectives: To replicate previous findings using South Carolina and Italian autism cohorts.

Methods: Analyses were performed using samples from 270 autism patients and 460 controls. Fifty-six patients with autism spectrum disorder (ASD) were from Italy and 162 patients with classical autism were from the South Carolina Autism Project (Schroer et al. 1998 Am J Med Genet). Control samples consisted of 91 individuals from Italy and 369 from South Carolina. The rs1858830 variant was genotyped by PCR amplification and *Eag I* digestion. Fragments were separated and scored using agarose gel electrophoresis.

Results: Italian and South Carolina patient and control populations were found to be in Hardy-Weinberg equilibrium. In the Italian cohort, no significant association with ASD was found when comparing the CC to the GG genotype (odds ratio = 1.12; 95% CI = 0.47-2.67). Chi-square tests similar to those performed by Campbell et al. were not found to be significant.

In the South Carolina cohort, a significant association with classical autism was found when comparing the CC to the GG genotype (odds ratio = 1.89; 95% CI = 1.8-3.31). This association was also significant for cases from simplex families (odds ratio = 2.3; 95% CI = 1.14-3.61). Chi-square tests similar to those performed by Campbell et al. were found to be significant.

Conclusions: The rs1858830 variant was not found to be associated with ASD in an Italian cohort. However, this variant was found to be associated with classical autism in a South Carolina cohort. Since Campbell et al. found a stronger association in families with narrowly defined autism, these results imply that the *MET* promoter variant is more strongly associated with classical autism than ASD.

35 105.19 Social behavior and autism traits in a sex chromosomal disorder: Klinefelter (47XXY) syndrome. S. Van Rijn*[1], H. Swaab[1], A. Aleman[2] and R. S. Kahn[3], (1)*Department of Clinical Child and Adolescent Studies, Leiden University*, (2)*BCN NeuroImaging Center, University of Groningen*, (3)*Department of Psychiatry, Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht*

Background: Klinefelter syndrome (47,XXY) is a sex chromosomal disorder that affects approximately 1 in 700 boys. Although there is a general impression that boys or men with Klinefelter syndrome often struggle with social situations, knowledge of the social behavioral phenotype of Klinefelter syndrome is limited. Difficulties in coping with the social environment may be indicative of an increased vulnerability for autistic traits. However, to our knowledge, there has been no study of autism-like features in a large sample of individuals with Klinefelter syndrome.
Objectives: The aim of this study was to improve our understanding of the social behavioral phenotype in Klinefelter syndrome by assessing social abilities and autism traits.
Methods: 31 XXY men and 24 non-clinical controls were included in the study. We used the Scale for Interpersonal Behavior, a quantitative measure of the degree to which individuals participate in specific social interactions and at the same time the degree to which they are distressed during these social situations. Importantly, this measure allows a quantification of social capacities that are normally distributed in the general population. We also included the Autism Spectrum Questionnaire, a dimensional measure of autistic personality traits which are distributed along a continuum in the general population.
Results: XXY men reported increased levels of distress during social interactions and less engagement in those aspects of social behavior that deal with display of negative emotions. Interestingly, we observed considerably increased levels of autistic traits across all dimensions of the autism phenotype in XXY men: social skills, communication, imagination, attention to detail and attention switching.
Conclusions: These findings call for a clinical investigation of vulnerability to autism in Klinefelter syndrome. Although our findings require replication, Klinefelter syndrome might serve as a model for studying a role of the X

chromosome in social behavioral dysfunction and autism-like behavior.

36 105.20 NLGN4X GENE OVEREXPRESSION IS ASSOCIATED WITH AUTISM AND PROFOUND MENTAL RETARDATION. H. Daoud[1], F. Bonnet-Brilhault[1], S. Védrine[1], P. Vourc'h[1], R. Tabagh[1], C. R. Andres[1], C. Barthelemy[1], P. Guérin[2], F. Laumonnier*[1] and S. Briault[3], (1)*INSERM U930, University François-Rabelais of Tours*, (2)*UDITTED, Centre Hospitalier de Chartres*, (3)*INSERM U930, CHR Orléans*

Background: Truncating mutations in the X-linked *Neuroligin 4* gene (*NLGN4X*) have been previously identified in few families with autism, Asperger syndrome and/or mental retardation (MR), suggesting that defects in its coding sequence are quite rare in these disorders. However, it could be conceivable that altered expression levels of the *NLGN4X* gene are present in autistic patients and associated with variations in regulatory sequences.

Objectives: To further investigate the role of *NLGN4X* gene in autism spectrum disorders (ASDs), we have explored its transcript level in individuals diagnosed with ASDs with a normal *NLGN4X* gene coding sequence.

Methods: We studied 96 unrelated French patients who met DSM-IV criteria for autism. Genetic disorders have been excluded by clinics and cytogenetics. Patients with FRAXA mutation were also excluded. The *NLGN4X* transcript level has been analyzed by quantitative RT-PCR using cDNA generated from lymphoblastoid cell lines (LCLs) from affected individuals.

Results: Using real time RT-PCR conditions, we identified a 3-fold increase in the *NLGN4X* transcript level compared to controls in one boy with autism and profound MR. This increased *NLGN4X* expression is associated with a *de novo* 1 bp (-335G>A) substitution which is located in the promoter region and not found in 450 normal X chromosomes. Moreover, this substitution is associated with the formation of one perfect ZID (Zinc-finger protein with Interaction Domain) binding site.

Conclusions: We report here the first description of an increased level of the *NLGN4X* transcript in LCLs from one patient with autism and profound MR. This result brings a new insight regarding the phenotypic spectrum of *NLGN4X* mutations, and suggests that the analysis of transcription level as well as regulatory sequences in this gene may reveal more individuals with mutations.

37 105.21 ASSOCIATION STUDY OF BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) AND NEURAL CELL ADHESION MOLECULE (NRCAM) POLYMORPHISMS WITH FRENCH AUTISTIC PATIENTS. F. Zaidi[1], P. Gorwood[1], B. Golse[2], L. Robel[2] and N. Ramoz*[1], (1)*INSERM*, (2)*AP-HP*

Background: Differences in the serum levels of brain-derived neurotrophic factor (BDNF) were observed between patients with autism compared to controls. Furthermore, haplotypes of *BDNF* gene were associated with autism by transmission disequilibrium test. And, variants of neural cell adhesion molecule *NRCAM* gene were found associated with autism in different reports.

Objectives: Study the genetic association between *BDNF* and *NRCAM* polymorphisms with autism in a French population.

Methods: The *BDNF* gene is located on chromosome 11p13 and corresponds to one haplotype block only. While the *NRCAM* gene is mapped on chromosome 7q31.1-q31.2 region and is encompassed by several haplotype block We performed a case-control study by genotyping two SNPs (the missense rs6265 and rs11030121) within *BDNF* gene, and the missense rs6958498 within *NRCAM* gene, using TaqMan® SNP Genotyping Assays, on 84 French autistic patients and 143 healthy controls matching for the geographic origin. Hardy-Weinberg equilibrium of SNPs was checked by using Haploview software. Distributions of alleles, genotypes and carriers were compared between patients and controls by crosstabs analysis.

Results: Each SNP followed the Hardy-Weinberg equilibrium. No significant difference of frequency for rs6265 or rs11030121 was found in patients compared to controls (81% versus 83% and 68% versus 72%, respectively for each major allele). Furthermore, no difference of distribution was found with the genotypes and carriers of each SNPs, nor with the haplotype rs6265-rs11030121. In contrast, we found a trend for association between NRCAM polymorphism and autism with an overrepresentation of the C allele (84.7% versus 77.3%, Fisher's exact test 2-sided p=0.1), corresponding to the proline amino acid.

Conclusions: This genetic analysis, on a population originating from France, does not support the association between *BDNF* gene and autism but suggests the involvement of *NRCAM* gene in autism.

38 105.22 Analysis of functional serotonin transporter polymorphisms in a German sample of patients with autism. S. M. Klauck*[1], B. Felder[1], M. Urrutia Villavicencio[1], A. Benner[1], F. Poustka[2] and A. Poustka[1], (1)*German Cancer Research Center (DKFZ)*, (2)*J.W.Goethe-University*

Background:

Biochemical studies in patients with autism spectrum disorder are indicative of the involvement of the serotonergic system in the etiology of the disorder. Specifically, selective serotonin reuptake inhibitors which target the serotonin transporter (*SLC6A4, 5-HTT*) were successfully used for treatment of autistic or concomitant symptoms such as repetitive behavior, language use or aggression. Several polymorphic loci in the *5-HTT* gene, especially the HTTLPR, affect its expression or function.

Objectives:

Several studies report significant association of HTTLPR alleles with autism. However, the preferentially transmitted allele is almost equally divided between the short (S) or the long (L) allele in these studies. Furthermore, other studies report no association finding at all. Recently, it was shown for SNP rs25531 (A/G) located within HTTLPR that only the A variant of the L allele confers to high 5-HTT mRNA levels. The G variant within the L allele behaves like the low-expressing S allele. This may have lead to contradictory association results in the past.

Methods:

To elucidate the impact of alleles at HTTLPR including the potentially functional SNP (rs25531), genotyping has been performed in a set of 180 complete trios from the German sample of patients with autism. In addition, the intron 2 VNTR and the rare gain-of-function coding mutation Ile425Val have been investigated.

Results:

We could not find association with either the HTTLPR alone or the haplotype HTTLPR-rs25531 performing TDT analysis. Furthermore, no association was evident for the intron 2 variant in our patient sample. Within the set of families no Ile425Val mutation could be found.

Conclusions:

The negative results from our study of 180 German trios rule out any association between the serotonin transporter and the autism phenotype. But there may be other functional active polymorphic sites within *5-HTT* that could confer liability to autism, which have not been tested here.

Poster Presentations Program

106 Clinical Phenotype Posters 1

40 106.2 Autism Subgroup BioMarkers: RNA Expression Studies. L. Lit[1], S. Ozonoff[2], I. Hertz-Picciotto[3], J. A. VanDeWater[3], R. Hansen[1], P. Ashwood[3], J. P. Gregg[3], R. R. Davis[3], A. Enstrom[3], I. N. Pessah[3] and F. R. Sharp*[1], (1), (2)*UC Davis M.I.N.D. Institute*, (3)*University of California at Davis*

Background: Many phenotypes are being described for children with autism, including onset type. Comparison of children with autism (AU) and pervasive developmental

disorders not otherwise specified (PDDNOS) to GP yielded 12 genes expressed in Natural Killer (NK) cells or CD8+ cytotoxic lymphocytes. Approximately 70% of AU subjects had high expression of these NK/CD8+ genes.

Objectives: Identify RNA expression biomarkers associated with AU subgroups.

Methods: 35 children ages 2-5 with autism (AU) and 14 PDDNOS children were compared to 12 typically developing children (GP). Total RNA from blood was processed on human Affymetrix microarrays.

Results: Using the 12 genes expressed in NK cells, AU children were separated into high NK and normal NK expression. Comparison of AU children with high NK to normal NK yielded hundreds of genes. Unsupervised cluster analyses revealed 3-4 subgroups. Of 10 children with early onset AU, 9 had high NK gene expression profiles. Specific comparisons of AU subjects with early onset, regression, mixed onset, and plateau clinical onset phenotypes demonstrated specific gene expression profiles for each clinically defined onset pattern of autism.

Conclusions: These studies support immune profiles associated with clinical onset definition in some children with autism. They show that a substantial proportion of children with autism – though not all – have abnormal expression of genes associated with NK/CD8+ cells. There are distinct patterns of RNA expression that are associated with at least two and perhaps as many as four types of onset of autism. The data support differences in peripheral blood RNA expression in 50-70% of children with autism compared with GP. Those children without these changes may have abnormalities confined to brain, and therefore have no observable changes in peripheral blood. Alternatively, they might have mothers with peripheral immune abnormalities that might secondarily affect the developing fetal brain with an appropriate environmental trigger.

41 106.3 Developmental trajectories in siblings of children with autism: Cognition and language from 4 months to 7 years. I. Gamliel*[1], N. Yirmiya[2], D. H. Jaffe[3] and M. Sigman[4], (1)*School of Education, The Hebrew University of Jerusalem*, (2)*Department of Psychology and School of Education, The Hebrew University of Jerusalem*, (3)*School of Public Health, The Hebrew University of Jerusalem*, (4)*Departments of Psychiatry and Psychology, UCLA*

Background: Some siblings of children with autism (SIBS-A) are characterized by the broad autism phenotype (BAP), which involves milder but qualitatively similar difficulties.

Objectives: To compare the cognitive and language skills of SIBS-A and siblings of typically developing children (SIBS-TD) from 4 months to 7 years, using growth curve analyses.

Methods: A longitudinal cohort study sample of siblings tested at ages 4, 14, 24, 36, and 54 months and 7 years (n = 41). At 7 years, 15 of the 37 SIBS-A were identified with BAP-related difficulties using parents' report and/or scores of at least 1.5 standard deviations below average on the cognitive and/or language measures (i.e., WISC-III, CELF-III). Between and within group differences were assessed with growth curve models using MLwiN repeated measures analysis for the 4-54 months data.

Results: The cognitive scores (4-54 months) of SIBS-A-BP (identified by parents' report and/or tests scores) were significantly lower (on average by 8 points) compared to SIBS-TD. However, the growth curves over time were not significantly different between SIBS-A and SIBS-TD groups. The language scores (4-54 months) of SIBS-A-BP (identified by parents' report and/or tests scores, and only by parents' report) were significantly lower (on average by 10 to 21 points) compared to SIBS-A-nonBP and SIBS-TD. The growth curve of SIBS-A-BP (identified by parents' report) indicated that these siblings developed differently than SIBS-A-nonBP and SIBS-TD. Similarly, language scores (4-54 months) of SIBS-A-nonBP (identified by test scores) were significantly lower (on average by 9 points) and their language development differed compared to SIBS-TD.

Conclusions: Language is a major area of difficulty for SIBS-A during the pre-school years. As a group, SIBS-A identified at age 7 years with BAP-related difficulties manifested lower cognitive and language abilities as well as different developmental trajectories during the pre-school years (4-54 months).

42 106.4 High Birth Weight in Children with ASD and Their Unaffected Siblings. C. Anderson*, A. Marvin, P. Law and K. Law, *Kennedy Krieger Institute*

Background: Increased head circumference and body size, as well as the presence of high levels of growth-related hormones, have been reported in autism spectrum disorders (ASD). Anthropomorphic differences may provide a clue to the underlying biology of autism.

Objectives: To compare birth weight of children with ASD, their unaffected siblings, and the general U.S. population.

Methods: Self-report data on birth weight of 4,600 children with ASD and 3,978 of their unaffected siblings was collected from families using a web-based interface. U.S. population vital statistics for 2005 were used for purposes of comparison. Birth weight was divided into five categories: Very Low (<1500 grams), Moderately Low (1500-2499 grams), Normal (2500-3999 grams), Moderately High (4000-4500 grams), and Very High (>4500 grams). Chi square analyses were performed.

Results: Compared with children of the same gender in the general U.S. population, boys and girls with ASD, as well as their male and female siblings, were more likely to have a Moderately High or Very High birth weight. 16.1% of boys with ASD and 17.6% of male siblings had a high birth weight, while only 10.5% of all male children (and 12.5% of white, non-Hispanic boys) did so. 10.9% of girls with ASD and 10.5% of female siblings likewise had a high birth weight, while only 6.3% of all female children (and 7.3% of white, non-Hispanic girls) did so. (For all comparisons, $p<.001$.)

Conclusions: Preliminary data suggest that both children with ASD and their siblings are more likely to have a Moderately High or Very High birth weight when compared with children of the same gender in the general U.S. population. These findings should be further explored using other data sources and controlling for additional potential confounders.

43 106.5 Autism Symptom Clustering Scale. M. Brimacombe* and X. Ming, *New Jersey Medical School - UMDNJ*

Background: Autism is a neurodevelopmental disorder that often has multiple medical and behavioral symptoms. Autism is now estimated to occur at a rate of more than 1/500 [1], and is currently the focus of much basic research

Objectives: A major impediment to research in autism is the lack of clinical sub-typing and the need for instruments that can be employed to more carefully sub-type the disorder under examination, creating more homogeneity in subject cohorts and less spurious variation in subsequent analysis.

Methods: Given the multi-dimensional nature of autism, its symptoms and related co-morbidities, an Autism Symptom Cluster Index (ASCI) was developed to broadly measure clinical severity on a validated set of autism cases, guided by clinical interpretation. A cohort of approximately 200 complete cases was used, with detailed information available on each subject. To develop the ASCI each symptom dimension was scored and incorporated into a weighted average to provide an overall score for each subject.

Results: The ASCI score was then shown to clearly differentiate the autism group from the PDD-NOS and Asperger's groups. Sub-scale analysis was also conducted and demographic aspects investigated.

Conclusions: The broad nature of the ASD diagnosis is often a challenge for researchers as it introduces much heterogeneity into patient cohorts. The ASCI is an instrument based on individual symptomology that will help in the clinical sub-typing of ASD.

44 106.6 Decreased serum levels of growth factors in male adults with high-functioning

autism. H. Matsuzaki*[1], Y. Iwata[1], K. J. Tsuchiya[1], G. Sugihara[1], S. Suda[1], K. Suzuki[1], T. Miyachi[1], K. Matsumoto[1], K. Nakamura[1], M. Kawai[1], M. Tsujii[1], T. Sugiyama[2], N. Takei[1] and N. Mori[1], (1)*Hamamatsu University School of Medicine*, (2)*Aichi Chilren's Health and Medical Center*

Background: The neurobiological basis for autism remains poorly understood. Given the role of growth factors in brain development, we hypothesized that some growth factors may play a role in the pathophysiology of autism.

Objectives: In this study, we examined whether serum levels of Epidermal growth factor (EGF), Hepatocyte growth factor (HGF), Insulin like growth factor 1 (IGF-1), Transforming growth factor β1 (TGF-β1) are altered in adult subjects with high-functioning autism, and analyzed correlations between serum levels of each growth factor and clinical variables, i.e. Autism Diagnostic Interview-Revised (ADI-R), Yale-Brown Obsessive Compulsive Scale (Y-BOCS), Aggression Quessionaire (AQ), Wechsler Adult Intelligence Scale-Revised (WAIS-R), Faux Pas test, etc.

Methods: We measured serum levels of EGF, HGF, IGF-1 and TGF-β1 in the 17 male subjects with high-functioning autism and 18 age-matched healthy male subjects by using ELISA kits. The data were analyzed using the Mann-Whitney U test. Among subjects with autism, relationships between serum levels of each growth factor and clinical variables were determined by Pearson or Spearman correlations. The diagnosis of autism was made on the basis of the ADI-R and the DSM-IV.

Results: The serum levels of EGF (mean ± SD = 72.4 ± 102.8 pg/mL), HGF (503.5 ± 160.5 pg/mL), TGF-β1 (7.34 ± 5.21 ng/mL) in the subjects with high-functioning autism were significantly lower ($p < 0.001$) than those (mean ± SD = 322.3 ± 122.0 pg/mL [EGF], 817.6 ± 232.4 pg/mL [HGF], 14.48 ± 1.64 ng/mL [TGF-β1]) of normal control subjects, respectively. However, serum levels of IGF-1 did not differ between groups. There were no correlations between serum levels of any growth factor and clinical variables in the subjects with autism.

Conclusions: This study suggests that decreased levels of EGF, HGF and TGF-β1 might be implicated in the pathophysiology of high-functioning autism.

45 106.7 M-CHAT and ESAT screening questionnaires at 18 months in the general population: issues of overlap and external validity. J. Buitelaar[1], K. Beuker*[1], S. Schjolberg[2], K. Kveim Lie[2], M. Hornig[3] and M. Bresnahan[3], (1)*Radboud University Nijmegen Medical Centre*, (2)*Norwegian Institute of Public Health*, (3)*Columbia University*

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 (in the absence of more final data of children with ASD identified).

Methods: The data have been collected in the context of the Autism Birth Cohort Study, an ongoing, prospective birth cohort study in Norway, funded by the Norwegian Institute of Public Health, and the National Institute of Health of the USA. 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 behaviour.

Results: The percentages screen-positive children on the ESAT (0.5%) and M-CHAT (5.4%) differed significantly from each other ($p<.1$). 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 behavioural and temperamental problems. For the M-CHAT only screen positive group there were more concerns about motor development.

Conclusions: Results of this study demonstrated overlap in identified cases by the ESAT and M-CHAT. The questionnaires differed significantly in the percentages of screen-positives. Based on the relationship with proxy-measures, the ESAT tends to pick up children with behavioral problems and emotional distress and the M-CHAT children with more general and motor developmental delays.

46 106.8 A CASE STUDY OF CHILDHOOD DISINTEGRATIVE DISORDER USING SYSTEMATIC ANALYSIS OF FAMILY HOME MOVIES. R. Palomo*[1], M. Thompson[2], C. Colombi[2], I. Cook[2], S. Goldring[2] and S. Ozonoff[2], (1)*Equipo IRIDIA*, (2)*M.I.N.D. Institute*

Background: Childhood Disintegrative Disorder (CDD) is a rare Pervasive Developmental Disorder. Like autism, it is characterised by impairments in social interaction and communication and by repetitive behaviours. In CDD, symptom emergence must be preceded by a period of at least two years of typical development and a loss of skills in several developmental domains (American Psychiatric Association, 2000). Objectives: The purpose of the case study is to examine the validity of CDD and investigate the timing of regression. Methods: We describe the development of a boy with CDD who after a period of 4 years of typical development experienced a loss of skills parallel to the emergence of autism symptoms. Moreover, unique to this study, family home movies recording his development from birth through the regression were systematically analyzed by coders unaware of the child's diagnosis or the purposes of the study, trained to reliability on an objective coding system (Werner & Dawson, 2005). Using Noldus 5.0, The Observer, the rates of gaze to people, non-word vocalizations, one-word and multi-word verbalizations, orienting to name, pointing, repetitive motor movements, repetitive actions on objects, and unusual visual behaviours were objectively quantified. Results: The systematic analysis of family home movies, as well as clinical observation, show a dramatic reduction of social orienting behaviours, pointing, and language, as well as a great increase of repetitive and unusual visual behaviours after a period of 4 years of normal development. No medical causes or correlates were found. The regression was quite abrupt in its onset and losses continued for up to a year afterward. Improvement has been limited. Conclusions: CDD validity is supported. The characteristics of the regression timing and the need of clearer diagnosis criteria due to the overlap of CDD with autism with regression are also discussed.

47 106.9 NOVEL CLUSTERING OF ITEMS FROM THE AUTISM DIAGNOSTIC INTERVIEW-REVISED TO DEFINE PHENOTYPES WITHIN AUTISM SPECTRUM DISORDERS. M. Steinberg and V. Hu*, *The George Washington University Medical Center*

Background: Heterogeneity in phenotypic presentation of ASD has been cited as one explanation for the difficulty in pinpointing specific genes involved in autism. Recent studies have attempted to reduce the "noise" in genetic and other biological data by reducing the phenotypic heterogeneity of the sample population.

Objectives: The current study uses multiple clustering methods across 123 ADI-R items which cover a broad spectrum of behaviors and functions from a large population to identify subgroups of autistic probands with clinically relevant behavioral phenotypes in order to isolate more homogeneous groups of subjects for gene expression analyses.

Methods: ADIR score sheets were downloaded for 1954 individuals with autism from the Autism Genetic Research Exchange phenotype database. The scores were modified to fit a 0-3 numerical scale and subjected to multiple clustering analyses, including principal components analysis (PCA), hierarchical

clustering (HCL), and k-means clustering (KMC) which were employed to subgroup individuals on the basis of ADIR item scores. A fitness of merit (FOM) analysis was also conducted to estimate the optimal number of clusters.

Results: This analysis demonstrated that there were easily recognizable distinctions among the groups based upon severity of scores in different domains. Based on the FOM analysis, KMC analysis was performed, dividing the samples into 4 clusters. One cluster is characterized by severe language deficits, while another exhibits milder symptoms across the domains. A third group possesses noticeable savant skills while the fourth group exhibited intermediate severity across all domains. When the clusters of the samples were superimposed upon the graph obtained by PCA, it showed a clear, though not perfect, separation among the groups.

Conclusions: Grouping autistic individuals by multivariate cluster analysis of ADI-R scores reveals meaningful phenotypes of subgroups within the autistic spectrum which we show, in a related study, to be associated with distinct gene expression profiles.

48 106.10 GENE EXPRESSION PROFILING OF LYMPHOBLASTOID CELL LINES DISTINGUISHES AUTISM CASE-CONTROLS AS WELL AS AUTISTIC PHENOTYPES. V. Hu*, T. Sarachana, K. S. Kim and N. Lee, *The George Washington University Medical Center*

Background: Autism spectrum disorders (ASD) refer to a group of related neurodevelopmental disorders characterized by delayed/abnormal language development, deficits in social interaction, repetitive behaviors and restricted interests. The heterogeneity in clinical presentation of ASD, possibly due to different etiologies, complicates genetic/biological analyses of these disorders.

Objectives: We have applied novel clustering methods to ADIR scores to identify distinct phenotypic subgroups of ASD. The purpose of this study was to identify gene expression profiles in lymphoblastoid cell lines that distinguish these subgroups from control individuals as well as to identify differentially affected pathways among the autistic groups.

Methods: DNA microarray analyses were conducted on over 115 lymphoblastoid cell lines from 3 distinct phenotypic groups of autistic individuals and age-matched, nonautistic controls from the NIMH Genetics repository. Datasets from these analyses were analyzed using Ingenuity Pathway Analysis and Pathway Studio 5 software.

Results: Comparison of gene expression profiles from control samples against all autistic samples reveals a set of genes for which gene expression level is associated with phenotypic severity. A 4-class analysis further reveals genes that separate the 3 phenotypes from each other as well as from controls. Statistical analyses of each subgroup vs. the control group identify differentially expressed genes unique to each subgroup as well as genes in common across subgroups. Bioinformatics analyses of the microarray data for each phenotypic subgroup similarly identify unique and common pathways and functions that are "enriched" in the respective gene datasets.

Conclusions: Gene expression profiles of lymphoblastoid cell lines from autistic case-controls not only discriminate between autistic and unaffected individuals but also correlate with phenotypic variants of ASD. These distinguishing genes can potentially be used to develop a diagnostic gene panel that can be used to screen for autism as well as reveal the variant of autism that is present.

49 106.11 Body Mass Index (BMI) and Related Factors in a Large-Scale Study of Children with ASD and their Unaffected Siblings. A. Marvin*, C. Anderson, C. Foster, S. S. Marvin, C. Cohen, K. Law and P. Law, *Kennedy Krieger Institute*

Background: Only a few studies have explored height, weight, and BMI in autism spectrum disorder (ASD), with contradictory findings. Since it has been suggested that anthropomorphic differences may provide clues to the underlying biology of ASD, it is

important to identify differences in BMI between affected and unaffected individuals.

Objectives: To analyze cross-sectional data on BMI, energy/activity level, and food intake for children with ASD, and their unaffected siblings, ages 3 to 17.

Methods: Parents provided data on height, weight, and related factors for 1,435 children with an ASD (85% male) and 1,011 of their unaffected siblings (47% male) using a web-based interface. Approximately half the measurements were obtained at a health provider's office. Key variables were compared by ASD status, age group, and gender. A five point Likert scale was used to measure energy/activity level and food intake.

Results: Affected children ages 6-11 and 12-17, both girls and boys, had a significantly higher BMI compared with unaffected siblings ($p<0.5$). However, this was not the case for those ages 3-5. As expected, more girls and boys who were overweight had medical problems or were taking medications that are known to affect weight and/or height ($p<0.5$). Younger children with ASD had higher levels of hyperactivity, as compared to teenage children with ASD, who had low levels of energy/activity ($p<0.001$). Similarly, younger children with ASD were reported to eat a less-than-normal amount of food, while their teenage counterparts were reported to eat a more-than-normal amount of food ($p<0.1$). In contrast, a stable, more normal energy/activity level and amount of food consumed were reported for unaffected siblings.

Conclusions: There is a need to further explore the causes of elevated BMI in autism spectrum disorders, as well as to address the health risk this may pose.

50 106.12 Latent Class Analysis of behavioural, biological and genetic information in an Autistic Cohort. F. J. Millman*[1], D. Hay[1], J. A. Bell[1], D. Groth[1], S. Heidarabady[2], N. Martin[1], C. Oliff[2], A. Kulkarni[3], D. De Lagarde[4], D. Ravine[5] and J. Wray[2], (1)*Curtin University of Technology*, (2)*State Child Development Centre*, (3)*Princess Margaret Hospital*, (4)*Western Australian Institute for Medical Research*, (5)*University of Western Australia*

Background: Autism is a complex neuro-behavioural disorder often occurring with a variety of physical and behavioural abnormalities. This has lead to a variety of mixed and complex phenotypes which has often confounded previous genetic research.

Objectives: This research aimed to harness this behavioural, biological and genetic heterogeneity as a method of creating a more powerful study, using latent class analysis to investigate the subtypes of autism.

Methods: Information was collected on a cohort of 92 Autistic children (ages 4-18yrs) regarding their family histories and development using a parental report questionnaire covering pregnancy, birth, early physical and behavioural development and abnormalities, other medical conditions, diagnosis, sibling and family conditions. Current behaviour and functioning were assessed using the Vineland Adaptive Behaviour Scales, Social Responsiveness Scales, Developmental Behaviour Checklist, Childhood Communication Checklist-2. Current physical development and the presence and status of Minor Physical Abnormalities (MPA's) were assessed by a paediatrician using a pre-determined checklist. Information pertaining to their early development was collected from postnatal and early childhood records. All children were karyotyped and urine amino acid analysis used to screen for a variety of genetic disorders.

Results: Heterogeneity of individuals was determined across behavioural domains including functioning level, biological domains including head size, presence of minor physical abnormalities and abnormal skin pigmentation, and genetic polymorphism in both coding and non-coding regions including those of CFHR, FCGR and ApoBEC. This enabled us to determine the presence of 'Autism Subtypes' which may be informative in future autism investigations. Experimental genetic assays were carried out on DNA to determine haplotypes and polymorphisms in Autism related genes.

Conclusions: Focusing on conditions comorbid with autism as a clue to distinct latent classes may lead to sub-classifications of autism and thus more powerful phenotypic and genotype studies in the future.

51 106.13 Two Biological Markers Are Not Stable Over Time in Children with Autism. S. A. Munasinghe*[1], T. Ng[1], A. Maley-Berg[1], G. O'Connor[1], C. Oliff[1], Y. McNeil[2], D. Brewster[2] and J. A. Wray[1], (1)*Princess Margaret Hospital for Children*, (2)*Royal Darwin Hospital*

Background: Various biological observations in children with autism have been reported, but there is limited longitudinal data on the specificity, stability and relationship of the abnormalities with communication and social development.
Objectives: To examine the stability over time and the clinical significance of certain biological markers in children with autism.
Methods: This paper reports the results of two studies in children with autism. In Study 1 GI permeability (Lactulose:Rhamnose ratio (LR ratio)) and antibodies to myelin basic protein were measured and social and communication data was collected, at two time points 1-2 years apart. In Study 2 a single measure of GI permeability was taken in another cohort.
Results: GI Permeability: At baseline, 6/6 (100%) of the children (average age of 46.7 months), had abnormal LR ratios. At follow-up (average age of 70 months), this figure was 1/6 (17%). Combining the results from Study 1 and 2, there was a negative correlation (Spearman's rho) between LR ratios and age ($r=-0.40$, $p<0.5$, $n=39$) with a tendency for LR ratios to decrease to the normal range with age. Anti-MBP: Ten children had antibodies to MBP measured at two time points. There was no significant difference between these time points for anti-MBP IgG or IgM. However, a significant number of children had abnormal anti-MBP IgA at baseline (50%) compared with at follow-up (10%). ($t=3.17(9)$, $p<0.5$). There was no significant correlation with either of these biomarkers and the IQ, social and communicative measures.
Conclusions: Abnormal gastro-intestinal permeability and serum antibodies to myelin basic protein (MBP) were highly prevalent in young children with autism, but were not stable over time. There was a negative correlation between LR ratios and age, with a tendency for LR ratios to normalise with age. These findings were not correlated with any of the psychometric or other biological markers measured.

52 106.14 The broader phenotype in parents of individuals with autism spectrum disorders. Y. Kawakubo*, H. Kuwabara and K. Kasai, *University of Tokyo*

Background: Relatives of individuals with autism spectrum disorders (ASD) often have mild forms of autistic–like characteristic, or what is called, the broader phenotype. Autism-Spectrum Quotient (AQ) is a self-administered instrument for measuring the degree to which an adult has the traits associated with the ASD.
Objectives: In this study, AQ-J (AQ Japanese version) was administered in parents of individuals with ASD to see whether they show features of the broader phenotype.
Methods: Participants were 72 parents of individuals with ASD (father=34, mean age=45.0, mother=38, mean age=42.3) and age-matched 89 controls (male=46, mean age=43.1, female=43, mean age=42.9). All participants gave written informed consent. The mean AQ score and five subscale scores (social skills, communication, imagination, attention to detail and attention switching) were calculated.
Results: The mean AQ score was not significantly different between the parents and the controls. On the communication subscale score, the fathers showed significantly higher scores than the control males, but the mothers did not show a significant group difference. Other subscales were not significantly different between the parents and the controls. In 34 couples of parent group, the spouse correlation for the mean AQ score was not significant.
Conclusions: These results suggest that the broader phenotype appears more in father of individuals with ASD than mothers of individuals with ASD.

53 106.15 Autism spectrum disorders in an adult psychiatric population. A naturalistic cross-

sectional controlled study. E. Rydén and S. Bejerot*, *Karolinska Institute*

Background: Autism spectrum disorders (ASD), have yet to become a focus of attention in clinical adult psychiatry. Objectives: The aims of the present study were firstly to characterize psychiatric patients with ASD in regard to demographical factors, psychiatric co-morbidity and personality traits and compare the ASD group with a psychiatric control group in these respects. Secondly, we wanted to compare differences of personality traits between females and males in the ASD group. Methods: Adult psychiatric patients where ASD or ADHD was suspected were referred to a tertiary unit in Stockholm 2001-2006. All patients diagnosed at the unit with ASD (39 females and 45 males) were consecutively included and compared to all 46 identically interviewed and assessed patients who did not receive an ASD or ADHD diagnosis. Among scales used were the GAF, SCID II Screen, and Swedish universities Scales of Personality (SSP). Results: ASD patients had an equal educational level but a lower social and occupational functioning. Their GAF scores were significantly lower compared to the control group. Prior to referral major depressive disorder and obsessive-compulsive disorders were the most common psychiatric diagnoses. In the assessment approximately 1/3 fulfilled diagnostic criteria for co-morbid ADHD. The patients with ASD also had significantly more schizotypal and avoidant personality traits according to SCID II screen. In SSP, patients with ASD rated themselves significantly higher on Stress-susceptibility, Embitterment, Detachment, Trait irritability and Lack of assertiveness than controls. Females with ASD scored significantly higher than males on borderline and passive-aggressive traits according to the SCID II Screen and on Embitterment and Trait irritability in the SSP. Conclusions:We could show that psychiatric patients with ASD have a low level of functioning and a personality profile which is gender specific. This may contribute to the identification and understanding of patients with ASD in adult psychiatry.

54 106.16 A SCALE TO ASSIST THE DIAGNOSIS OF AUTISM SPECTRUM DISORDERS IN ADULTS: PRELIMINARY RESULTS OF A MULTI-CENTER STANDARDIZATION STUDY. E. R. Ritvo*[1], R. A. Ritvo[2], M. J. Ritvo[3], D. Guthrie[1], S. Bejerot[4], K. Matsumoto[5], K. Tsuchiya[5] and M. Tsujii[6], (1)*UCLA*, (2)*UCLA SCHOOL OF MEDICINE*, (3)*HARVARD WESTLAKE SCHOOL*, (4)*Karolinska Institute*, (5)*Hamamatsu University School of Medicine*, (6)*Osaka-Hamamatsu Joint Center for Child Mental Development*

Background: The Ritvo Autism Asperger's Diagnostic Scale (RAADS) is an 80 item scale to assist clinicians diagnosing autism spectrum disorders in adults (18 years and older). It has been shown to be valid, reliable, and highly sensitive and highly specific in a limited number of subjects. Two recent peer reviewed publications present the rational, a detailed description, and a clinical research application of the scale. It is now being standardized on a larger number of subjects in an international multi center study. Objectives: ,To present the initial findings of the international multi center standardization study. Methods: Clinical data and scale scores are being obtained on the following types of subjects: A. Subjects with an autism spectrum disorder, 1) those diagnosed by research criteria, 2) those with a prior diagnosis by clinician of various professional disciplines, B. Subjects without an autism spectrum disorder, 1) those who do not and never have had a DSM-IV diagnosis, 2) those with a current Axis One DSM-IV diagnosis other that a developmental disability, 3) first degree relatives of subjects who received a research diagnosis of an Autistic Spectrum disorder. Statistical analyses of demographic factors, sensitivity and specificity, and concurrent validity (by comparison with the Constantino SRS Scale and Module 4 of the ADOS Scale) will be presented. To date over 100 autistic spectrum and 300 non-autistic spectrum subjects have been assessed, and more will be added by the time of the presentation. Results: to be determined Conclusions: These will be based on the results of the data available for

analyses on May 1, 2008, and presented at the conference.

55 106.17 Multidisciplinary search for intermediate phenotypes in autism spectrum disorders. W. De la Marche*, K. Devriendt, H. Peeters, I. Noens, J. Wagemans, C. Van Geet, K. Freson, J. W. Creemers, S. Sunaert and J. Steyaert, *Katholieke Universiteit Leuven*

Background: Phenotypic and genetic heterogeneity present major difficulties in research on the genetics of ASD and probably reflect heterogeneity in neurobiological mechanisms. Moreover, ASD traits are present in the general population in a dimensional way, with family members of individuals with ASD being more affected. Different neurocognitive and neurobiological mechanisms may be associated with different modes of (complex) inheritance. As a classical linkage approach has not led to a breakthrough, a comprehensive search for neurobiological mechanisms (intermediate phenotypes) in ASD may yield new cues towards the genetics of ASD. Two independent research groups from the Katholieke Universiteit Leuven have generated convergent results, providing strong arguments for a role of the 'regulated secretion pathway' in neurons in the pathogenesis of ASD.
Objectives: 1) Defining patterns of inheritance of (clusters of) symptoms, cognitive traits and biological markers in ASD; 2) Searching for clusters in neurocognitive and neurobiological variables in order to delineate intermediate phenotypes and use these to group families with presumably more homogenous genetic causes; 3) Screening for specific defects in one intermediate phenotype, the 'regulated secretion pathway' in a large sample of families; 4) Confirming the intermediate phenotype-hypothesis in subjects with a specific genetic condition and ASD.
Methods: In 100 multiplex families, 300 simplex families and 100 patients with known genetic syndrome associated with ASD, we administer dimensional questionnaires and interviews for the phenotyping, use novel paradigms and existing tasks to measure central coherence, face processing and executive functioning, conduct a clinical genetic examination, carry out molecular genetic testing and test platelet function as a means to functionally test the regulated secretion pathway. In a subgroup we carry out fMRI and DTI.
Results: In this poster we present our research plan and possible candidate genes for ASD.
Conclusions: Multidisciplinary research will lead to new insights in intermediate phenotypes for ASD.

56 106.18 Stability of early daignosis in autism spectrum disorders. Y. M. Hou*[1], J. H. Liu[1], C. H. Chiang[2] and C. C. Wu[2], (1)*Chiayi Christian Hospital*, (2)*National Chung Cheng University*

Background: Early diagnosis of autism in toddlers now is possible after recently vigorous investigation. However the stability of diagnosis in younger children with autism spectrum disorders (ASD) still need further researches.

Objectives: We tried to assess the stability of clinical diagnosis of ASD in Taiwanese toddlers when followed up 18- 21 months later.
Methods: We recruited 31 children aged between 24-36 months (male: female= 23: 8, with mean age=29.4 months, and mean mental age=17.5 months) from the Developmental Assessment Clinic of the Chiayi Christian Hospital, with the consent of their parents. Initially (time 1) two child psychiatrists made the clinical diagnosis by the DSM-IV diagnostic criteria of pervasive developmental disorders through interaction with children and semi-structure interview with their caregivers. 18- 21 months later (time 2) we made final diagnoses for all those children after the same diagnostic procedures and consensus meetings. Children with evident neurological disorder or sensory deficit were excluded.

Results: At time 1, according to the initial diagnosis, those children were divided into autism group (N=12), PDDNOS group (N=6), and developmental delayed group (N=13). At time 2, for the autism group, nine children still had the diagnosis of autism, and one PDDNOS and two delayed; for PDDNOS group, one child had had changed diagnosis of autism, four still PDDNOS and one delayed; and for delayed

group, none had autism, two children PDDNOS and 11 still delayed.

Conclusions: Our findings confirmed the possibility of early diagnosis of autism in children younger than 3 years old. And at our follow up study, the clinical diagnosis of either ASD or delayed group was quite stable. Further studies with larger sample size are needed.

57 106.19 Physical Examinations of children in the CHARGE Study. K. Angkustsiri*, R. S. Akins, L. Plumer, P. Krakowiak, I. Hertz-Picciotto and R. L. Hansen, *University of California at Davis*

Background: Although children with autism spectrum disorders (ASD) share core behavioral symptoms, they vary in associated clinical features that may be important in understanding underlying biological processes reflecting genetic and environmental influences on development.
Objectives: To identify differences in physical development found among children with ASD, developmental delay and typical development that may reflect disruptions in early embryological development.
Methods: Children between the ages of 2-5 years were recruited through a larger population study, the CHARGE study. The diagnosis of an ASD was confirmed with ADI-R and ADOS scores. Control groups from the same catchment area included developmentally delayed (DD) children without ASD and typically developing (TD) children from the general population. Pediatricians completed standardized physical examinations for each child. Chi square analysis was used to compare frequencies of atypical features between groups.
Results: Physical examinations for 636 children (338 ASD, 192 TD, 106 DD) were performed. Compared to typically developing children, children with ASD had significantly higher frequencies of atypical midface (8% vs. 1%, p=0.001), cheekbone (6% vs. 1%, p =0.001), maxilla (5% vs. 1%, p=0.005), ear cupping (16% vs. 7%, p=0.006), nasal root (24% vs. 10%, p <0.001), nasal bridge (20% vs. 4%, p<0.001), nasal tip (10% vs. 1%, p<0.001), single palmar crease (7% vs. 3%, p=0.5), hyperextensible joints (26% vs. 14%, p=0.001), and atypical muscle tone (21% vs. 2%, p<0.001). Rates of atypical findings were similar between children with developmental delay and ASD.
Conclusions: Children with ASD and DD show more variability than typically developing children in facial (including midface, nose and ears) and musculoskeletal (palmar crease, hyperextensibility and muscle tone) structures but are similar to each other. Further analysis will be done to determine whether specific clusters of physical features are associated with environmental exposures, medical conditions and developmental trajectories measured in the CHARGE study.

58 106.20 THE PREVALENCE OF INTELLECTUAL DISABILITY AMONG CHILDREN UNDERGOING STANDARDIZED EVALUATION FOR ASD. R. P. Goin-Kochel*[1], D. E. Treadwell-Deering[2], S. U. Peters[1], A. E. Porter[1], M. P. Powell[2], M. C. Gibbs[2] and T. M. Lyle-Lahroud[2], (1)*Baylor College of Medicine*, (2)*Texas Children's Hosptial, Baylor College of Medicine*

Background: There has been recent debate over the number of individuals with autism spectrum disorders (ASD) who also meet criteria for mental retardation (MR)—now referred to as intellectual disability (ID). Recent, limited data suggest that the prevalence of ID in ASD ranges between 25.8% and 58.5%, with co-occurrence in 66% to 70% of children who meet strict criteria for autism. Yet these estimates can be quite discrepant depending on the stringency of diagnostic criteria, child age, and informant.

Objectives: To determine the prevalence of ID among a large sample of children who underwent standardized evaluation for suspected ASD.

Methods: Data were pooled from the medical records of children who had received a research-reliable ADI-R and ADOS and a developmentally appropriate IQ test as part of their evaluation for possible ASD at Texas Children's Hospital through December 31, 2007. The prevalence of ID, as defined by IQ

scores of ≤ 70, was calculated by diagnosis (autism, ASD, neither).

Results: To date, complete data have been pooled for 192 children (84.3% male). Of these, 146 (76.0%) met strict criteria for autism, 4 (2.1%) met criteria for an ASD, and 42 (21.9%) did not meet criteria for either. The overall prevalence of ID was 59.9%; however, this differed significantly by diagnosis (Fisher's exact = 22.3, *df* = 2, $p < .0001$), with rates of 68.5%, 75%, and 28.6% for the autism, ASD, and neither autism/ASD groups, respectively.

Conclusions: The ID prevalence was comparable to that in the literature for strict autism but higher for the ASD group, which could be attributed to the small number with this diagnosis. Data collection and analyses, including ID by child age at evaluation (≤ 5 years, 5 years +), are ongoing, with an anticipated final sample of approximately 400 children.

59 106.21 Analysis of the Autism Phenotype: Identification of Distinct Sub-populations. R. Anney*, K. Tansey, M. Gill and L. Gallagher, *Trinity College Dublin, Ireland*

Background: Autism is a neurodevelopmental disorder affecting the three core areas of communication, social interaction and restrictive repetitive behaviors. It affects 1 in 1000 individuals in the general population and is known to have a highly genetic component. Advancements in genetic studies have been hindered by lack of consistency due to high heterogeneity of the phenotype. It has been hypothesized that separate dimensions of the autism phenotype may influence separate genetic and biological mechanisms. **Objectives:** Perform a principle component analysis of all the Autism Diagnostic Interview-Revised (ADI-R) data from a sample of children with autism to draw comparison between derived factors and the existing described domains. To perform a cluster analysis of the ADI-R data to identify groups of individuals with specific phenotypic patterns that would allow sub-setting into homogenous groups for the purposes of phenotype genotype analyses. **Methods:** ADI-R data from 200 individuals with autism were subjected to principal component and partition cluster analysis using STATA. **Results:** Principal component analysis identified five main factors: verbal communication, social ever, social current, insistence on sameness, and repetitive sensory motor actions. Cluster analysis identified two clusters from our sample representing a high functioning group and a low functioning group. **Conclusions:** ADI-R contains quantitative factors and there is a definable split between low and high functioning individuals.

60 106.22 Follow up of Brain Endothelial Antibodies in Children with Language Regression. K. A. McVicar*, S. Shinnar, M. D. Valicenti-McDermott, R. Steinman and S. L. Moshe, *Albert Einstein College of Medicine*

Background: A high frequency of brain endothelial antibodies (BEA) has been observed in children with language regression (LR). The persistence of these antibodies on repeated measurements is unknown.

Objectives: Describe serial measurements of serum BAE in children with LR. Methods: We measured repeat serum BEA IgM (primary) and IgG (secondary) titers in 7 children with LR whose initial BEA titers were positive. Samples were analyzed at Dr Connolly s laboratory at Washington University. Subjects were children with LR with (n=6) and without (n=1) autism recruited from the Albert Einstein College of Medicine hospital affiliates. All had a documented language regression (loss of 5 previously acquired words). Mean age at regression in those with autism was 24.6 months. The child with isolated LR was 67 months and presented with seizures. All 7 were boys.Results: Initial blood samples showed positive IgM BAE titers in all 7 children and IgG titers in 3 (2 with autism and LR and one with LR only). Mean age at first BAE titer was 74 months (range 38-154). Follow-up titers were obtained a mean of 24 months after the initial titer (range 11-43 months). Follow-up BEA titers were positive for IgM in all 7 children but only one child had positive IgG titers. That child had LR and autism. Conclusions: BAE serum antibodies are persistent. Interestingly, IgM antibodies that are usually the primary response are present

years after the regression and persist on repeat testing. In contrast, IgG antibodies that are usually a secondary response are inconsistently present and when present on one sample, may not persist. Continued immune reactivity as evidenced by persistent BAE IgM titers suggests the possibility of treatment with immune modulating agents even after the regression has already taken place.

61 106.23 Screening for Autism Spectrum Disoroders (ASD) in Flemish Day-care Centres with the Checklist for Early Signs of Developmental Disorders (CESDD). H. Roeyers*, M. Dereu, R. Raymaekers, M. Meirsschaut, G. Pattyn, I. Schietecatte and P. Warreyn, *Ghent University*

Background: Screening instruments for ASD usually rely on parents or health practitioners as informants. However, parents often lack sufficient knowledge of normal development to judge their child's behaviour and health practitioners must base their evaluation on a brief observation. Child care workers though have a good knowledge of children's development and have sufficient opportunities to observe their behaviour.

Objectives: To develop a screening instrument that can be used by child care workers in day-care centres.

Methods: Child care workers in day-care centres across Flanders received a 3-hour training. They filled out the 29-item CESDD for all children in their centre (N = 5411; mean age 17.41 months, range 3 to 36 months; M:F 1:1). Children who showed some signs of ASD or language delay were invited for a second-stage screening.

Results: Based on a preliminary cut-off score of at least 2 signs of ASD ticked on the questionnaire, the CESDD has a sensitivity of .83 and a specificity of .93. The CESDD has a good internal consistency: Cronbach's alpha is 0.70 for children younger than 12 months, 0.86 for children between 12 and 24 months and 0.89 for children older than 24 months.

Conclusions: Screening for ASD in day-care centres with the CESDD seems very promising to promote early detection of ASD in a general population sample, which is important for clinical and scientific reasons.

62 106.24 DIVERGENT EFFECTS OF PBDE-47 ON T CELL IMMUNE RESPONSES IN AUTISTIC AND TYPICALLY DEVELOPING CHILDREN. J. Van de Water*[1], P. Ashwood[1], J. Schauer[1] and I. N. Pessah[2], (1)*University of California at Davis*, (2)*University of California at Davis, M.I.N.D. Institute*

Background: Current models suggest a role for both genes and the environment in the etiology of autism. There is evidence that immune dysregulation may be a clinical feature of ASD.

Objectives: To compare the potential differential effect of a common environmental polybrominated diphenylether, PBDE-47, on the immune response in children with ASD (n=19) and age-matched typically developing controls (TD, n=18).

Methods: Peripheral blood mononuclear cells (PBMC) were exposed ex vivo to either 100 nM or 500 nM PBDE47 for 4 hrs. PBMC were then challenged with the T cell mitogen, PHA. We measured both the proliferative response and cytokine production following stimulation. The data, analyzed by Wilcoxon rank tests, took into account both the magnitude of the response, and how many responses went up or down within a subject population.

Results: There was a significant increase in the proliferative response following PHA stimulation in the presence of 100 nM PBDE-47 for the ASD group compared to a reduction in the TD controls. When the cells were pre-incubated with PBDE-47 at 500 nM, the proliferative response was not affected in the TD controls but was significantly elevated in the ASD subjects ($p < 0.5$). Regarding cytokine production, exposure to 100 nM PBDE-47 resulted in significantly lower values for IL-6, MIP-1alpha and MIP-1beta in both the TD and ASD groups. The relative responses of the ASD and TD subjects diverged in the presence of 100 nM PBDE, with TD showing greater reductions in levels of the cytokine IL-12, and the chemokines MIP-1alpha and MIP-1beta.

Conclusions: This data suggests that in vitro exposure of PBMC to PBDE-47 affects cell proliferation and cytokine production in a pediatric population. Moreover, PBMC from the ASD subjects was differentially affected when compared to the TD controls suggesting evidence of a differential sensitivity to the environmental contaminant PBDE-47.

63 106.25 Confirmation of the ADOS Module 1 Revised Algorithm in Young Children with Autism Spectrum Disorder. A. P. Thompson*[1], E. Duku[1], S. Georgiades[1], T. Bennett[1], P. Szatmari[1], S. Bryson[2], E. Fombonne[3], P. Mirenda[4], W. Roberts[5], I. M. Smith[6], T. Vaillancourt[1], J. Volden[7], C. Waddell[8], L. Zwaigenbaum[7] and P. In ASD Study Team[9], (1)*Offord Centre for Child Studies, McMaster University*, (2)*Dalhousie University/IWK Health Centre*, (3)*McGill University*, (4)*University of British Columbia*, (5)*University of Toronto*, (6)*Autism Research Centre*, (7)*University of Alberta*, (8)*Simon Fraser University*, (9)*N/A*

Background: The Autism Diagnostic Observation Schedule (Lord et al., 2000) assesses communication, social and play skills, and restrictive/repetitive behaviours in the diagnosis of ASD. Recently, Gotham et al. (2007) revised the algorithms for Modules 1, 2 and 3 based on factor analytic evidence of two domains (Social Affect, SA; Restricted, Repetitive Behaviours, RRB). Two 14-item Module 1 algorithm versions were developed depending on language ability (no words; some words) in a sample with an average age of 56 months (range=14-144).
Objectives: To test the proposed revision of the ADOS Module 1 algorithm in a population of preschoolers with ASD.
Methods: Module 1 data were available on 193 children with ASD participating in a Canadian longitudinal study (mean age=36.6 months, mean mental age=18.9 months). Due to our small sample size, it was not possible to analyze the "no words" and "some words" algorithms separately. Instead, we used only the 12 items common to both algorithms (4 language-based items were excluded). Confirmatory factor analysis was used to examine whether the 2-factor model met the acceptable model fit criteria in our sample.
Results: The model fit was good (RMSEA=0.6; CFI=0.98). The correlation between the SA and RRB factors (r=-0.15) was lower than for the "no words" (r=0.49) and "some words" (r=0.59) algorithms proposed by Gotham et al. (2007).
Conclusions: The revised 2-factor model of the ADOS Module 1 algorithm developed in older children was confirmed in our sample of preschoolers with ASD, even though only the 12 items common to both Module 1 algorithms were included in the analyses. The lack of correlation between SA and RRB factors suggests some level of independence. Further research of this longitudinal cohort is necessary to determine if the correlation between the factors changes over time.

64 106.26 EXAMINATION OF INTELLIGENCE MEASURES IN CHILDREN AND ADULTS WITH HIGH-FUNCTIONING AUTISM. K. E. Bodner*[1], D. L. Williams[2] and N. J. Minshew[3], (1)*University of Pittsburgh*, (2)*Duquesne University*, (3)*University of Pittsburgh School of Medicine*

Background: Studies of intelligence in individuals with autism have yielded inconsistent results. Some studies have indicated that individuals with autism can be characterized by VIQ

Objectives: To investigate IQ measures of the WISC-III/WAIS-III and the Raven's in relatively more able children and adults with high-functioning autism (HFA).

Methods: The age appropriate Wechsler IQ measures and the Raven's were collected on 75 children (37 HFA and 38 TD; 8–15 years; mean 11 years) and 91 adults (49 HFA and 42 TD; 16–46 years; mean 26 years). Autism diagnosis was attained through the ADOS, ADI, and clinical impression. All participants attained Full Scale IQ's>70.

Results: There was no significant difference noted in mean WISC-III and Raven's percentile scores of HFA children. However, HFA adults and TD children and adults performed significantly better on the Wechsler assessments than the Raven's. TD children and adults displayed similar results between

Wechsler Full Scale IQ and Raven's percentiles, reflecting a stable pattern of development. HFA participants did not display such similarities between the performances on the two tests.

Conclusions: The WISC-III and Raven's are both appropriate measures of intelligence in more able HFA children, yielding similar results. However, as a group, the HFA received lower scores on the Raven's than on the WAIS-III. The Raven's did not match results of the Wechsler IQ tests for this more able population. Level of verbal ability may be a factor in these results, with the possibility of inverse results in a less verbal population.

65 106.27 Script to Screen: Programming Gestation Date Calculators in Autism Studies. P. A. Thompson*, G. B. Jensen, A. E. A. Siddiqi, J. D. Bonner, J. E. Siebert, M. F. Kuhn, T. L. Holland, K. L. Marable, S. J. Sharp, P. L. Reed and M. H. Rahbar, *Michigan State University*

Background: Autism is postulated to have etiology in gestational and postnatal exposures. Determining dates of exposures during gestation demands accurate date estimates. The Center for Autism and Developmental Disabilities Research Epidemiology (CADDRE) has developed and incorporated a gestation date calculator program into the CADDRE Information System (CIS) for the Study to Explore Early Development (SEED). The development process of gestation date forms and population of dates within telephone scripts is discussed.
Objectives:- Describe development process and technical issues of programming gestation date calculation algorithms in CIS
- Describe process of data storage and populating CADDRE study interviews with algorithmically calculated gestation dates.
- Discuss potential benefits of automatically populating scripts with algorithmically estimated gestation dates versus manually entering dates from spreadsheet into CIS.
Methods: CADDRE Data Coordinating Center received a paper form with description of pregnancy questionnaire process, in addition to a spreadsheet including due date calculation macros. From these documents and spreadsheet, DCC was tasked with developing an application that would estimate due date and gestation dates. The development from spreadsheet and paper forms to application will be described. Additionally, the advantages of populating of study telephone interview scripts will be discussed.
Results: A module in the CIS application was developed to define metadata for study scripts. This module utilizes an expression evaluator for question skips, caption editing, and population of gestation date fields. Algorithmically estimated dates are calculated and stored in the CIS database, and were used to populate study scripts.
Conclusions: Initial data suggests that populating study scripts using computer-based gestation date calculations improve the reliability of dates over data entry from spreadsheet into CIS. Additionally, labor is decreased when dates are automatically imported. References to automatically imported dates should yield greater accuracy in gestational exposure assessment.

66 106.28 Structure of the Autism Diagnostic Interview - Revised. A. Snow*, L. Lecavalier and C. Houts, *Ohio State University*

Background: The Autism Diagnostic Interview–Revised (ADI-R) is one of the most widely used assessment instruments in the field. Relatively few studies have used factor analysis to assess its items. Such analyses could shed some light on the structure of autistic symptoms and on the validity of the diagnostic algorithm.
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Objectives: The purpose of the current study was to investigate further the factor structure of the ADI-R. Exploratory (EFA) and confirmatory factor analysis (CFA) were conducted on the ADI-R items (algorithm items only and all items).
Methods: Data were obtained from the Autism Genetic Resource Exchange program. The sample included 1,861 youngsters with PDDs between the ages of four and 18 years (mean=8.3, SD=3.2). The sample consisted of 1,455 males (78%) and 406 females (22%). Analyses were conducted separately for algorithm items only and for all items and according to verbal status (n=1329 verbal and n=532 non-verbal). For all analyses, EFA (Ordinary Least Squares and oblique rotations)

was conducted first on a random subsample and then followed by CFA on the entire sample. Several models were compared with the CFAs.
Results: Overall, results indicated a two-factor solution best fit all four data sets (algorithm items only/all items, verbal/nonverbal children). The first factor consisted of social items and the majority of communication items. The atypical communication items (e.g., stereotyped utterances, pronominal reversal, neologisms) and repetitive behaviors loaded onto the second factor. CFAs suggested excellent fit indices for most solutions (i.e., RMSEA<.5; SRMR<.9).
Conclusions: Data suggested that autism symptomatology can be explained statistically with a two-domain model. Analyses permitted the identification of which symptoms are most/least correlated with different domains. Factor analytical studies of this nature can assist in refining the autism phenotype and improving the diagnostic algorithm.

67 106.29 Autism Head Growth Characterized by Growth Surges Throughout Childhood. J. H. Miles*[1], M. B. Keegan[2], J. E. Farmer[1] and T. N. Takahashi[1], (1)*University of Missouri*, (2)*University of Missouri School of Medicine*

Background: Delineation of ASD heterogeneity requires characterization of biological phenotypes which occur in a significant proportion of ASD. Macrocephaly, HC ≥97%, is an endophenotype occurring in ~30% of ASD individuals and 37-47% of their parents (Miles, 2002). Longitudinal data, however, are conflicting; some report normal or low birth HC with accelerated growth in the first months or between 2 and 3 years; others gradual growth or decline.

Objectives: Better characterize the "macrocephaly" phenotype.

Methods: Examined HC curves in a homogeneous group of 63 children (58M, 5F) with classic AD, essential phenotype & birth HC plus 3+ later measurements. Followup 8.8yr ±6.

Results: Birth HC was normal in 94% (59/63) (Z=-1 to 0.5); 48% of these became macrocephalic & 52% remained normocephalic. In both groups head growth occurred in surges of >1SD throughout childhood. In those who became macrocephalic, 47% had 1 surge of > 1SD, 44% had 2 surges and 9% had 3 surges. Growth surges of >1SD also occurred in 61% of children whose HC remained in the normal range; 52% had one growth surge and 9% had two. For both groups timing of the first surge was similar: <3yr (43%, 53%), 3-8yr (38%, 42%) & >8yr (19%, 5%). Both groups also had similar parental HC profiles; 68% of macrocephalic probands had macrocephalic fathers, compared to 60% of normocephalic; 16% of macrocephalic probands had macrocephalic mothers compared to 11% of normocephalic probands. At birth few ASD probands were macrocephalic (1.6%) or microcephalic (4.7%); all 4 individuals had surges into the macrocephalic range. Ultimate head size correlated with the number of growth surges.

Conclusions: Surges in brain growth is a more informative autism endophenotype than macrocephaly and continue throughout childhood. Ultimate head size appears to be a continuous variable, which may explain why macrocephaly has not been predictive of behavioral phenotypes or outcomes.

68 106.30 AUTISM AND DELINQUENCY. A. Van der Reijken*[1] and I. A. Van Berckelaer-Onnes[2], (1)*Centrum Autisme*, (2)*Leiden University*

Background:

In the last 15 years an increasing number of papers have been published about autism in relation to delinquent behaviour. Several of these concern case histories, others concern incidence searches. The question arises whether people with autism are prone to delinquent behaviour.

Objectives:

To find out whether people with autism run the risk of delinquency and whether certain autism-specific characteristics are more likely to lead to delinquent behaviour than others.

Methods:

N=14 study. All the cases were referred to one of the authors, who acted as an expert witness in their court cases. The cases were analysed in eight areas, i.e. type of delinquent behaviour, age at the moment this behaviour started, age when the patient was diagnosed, comorbid disorders, intelligence, demographic data, concomitant circumstances and deviant behaviours shown before the committed offence. In addition, cases described in literature are compared with our group.

Results:

Violence, sexually deviant behaviour and stalking are the most frequently committed crimes in this group. Only a few cases were diagnosed with autism before the crime, although they all displayed all sorts of behavioural problems long before they were arrested. Sexual crimes and stalking seem to be the result of a combination of obsessive behaviour and social shortcomings. These individuals do not know how to satisfy their sexual needs. Violence is often the result of panic and/or obsessions.

Conclusions:

Although the number of cases is very small, the results of this study are promising. Research of more cases is needed to value the results found and to give guidelines for prevention.

69 106.31 Predictive Value Of BITSEA In Detecting ASD In French-Speaking Children Attending Daycare Settings. K. Morasse*[1], E. Gilbert[2], S. Pouliot[3], J. Lambert[1] and L. BenAmor[1], (1)*Hôtel-Dieu de Lévis*, (2)*Centre de recherche Université Laval Robert-Giffard*, (3)*Université Laval*

Background: In Quebec, a large proportion of preschool children is attending public daycare facilities. Screening for Autism Spectrum Disorders (ASD) in those institutions could considerably enhance early diagnosis. BITSEA is the brief form of ITSEA (Infant-Toddler Social and Emotional Assessment), a questionnaire assessing social-communicative functioning in preschool children. ITSEA is recognised for its sensitivity to ASD. Unpublished French versions of ITSEA-BITSEA are used in this study. Objectives: To assess the efficiency of the BITSEA in detecting ASD children in daycare settings, and to examine the relations between BITSEA and other questionnaires. Methods: 24 children were recruited in two public childcare services, in groups where children were suspected of ASD or related disorders. BITSEA were completed by the caregivers for each child. More information on everyday functioning and global development was obtained with ITSEA and ASQ (Age & Stages Questionnaire) completed by parents. Children were individually observed during a play session with a psychologist. Children showing atypical results on any of these measures were invited to a psychiatric assessment. Nine of them were met by professionals of our child psychiatry department, three receiving formal ASD diagnoses. Results: Only the ASD children were scoring above the clinical cut-off for problems on the BITSEA, and they also scored under the cut-off for competencies. Analyses on the entire sample show that Problems on BITSEA negatively correlates with Competencies on BITSEA, and with ASQ Communication, Fine motor skills and Problem resolution subscales. BITSEA Problems and Competencies correlate with Competencies and Dysregulation ITSEA subscales. Results of WPPSI-III and Vineland administered to a subgroup of children will also be discussed. Conclusions: Those results strongly suggest that the use of BITSEA in Quebec daycares can efficiently enhance early diagnosis of ASD. However, replication of this study is needed with larger samples of children and facilities.

Poster Presentations Program

107 Brain Imaging Posters 1

70 107.1 Absence of fear contagion for body expression of emotion in autism spectrum disorder. N. Hadjikhani*[1], B. Joseph[2], D. Manoach[3], R. Hoge[4], H. Tager-Flusberg[2] and B. De Gelder[5], (1)*Harvard Medical School & EPFL*, (2)*Boston University School of Medicine*, (3)*Harvard Medical School*, (4)*University of Montreal*, (5)*Tilburg University*

Background: Social-communication deficits are one of the core symptoms of autism, and a deficit in perceiving emotional signals from others may be one of the underlying causes.

Objectives: To test the hypothesis that emotion perception difficulties in autism are not confined to faces, but also include viewing emotional states of others expressed by the whole body.

Methods: We used fMRI and compared the cortical responses of individuals with autism to the bodily expression of emotion with cortical responses of neurotypicals. To test whether behavioral and functional performance in recognition of bodies expressing emotion is associated with amygdala microstructure, we used DTI and examined differences in FA between ASD and neurotypicals.

Results: We found a lack of condition-specific activity associated with seeing fearful bodily expressions as compared to images of meaningful neutral body actions in subjects with ASD. In neurotypicals, we observed an emotional modulation of the mirror neurons system (MNS) and other brain areas, but this emotional modulation was almost absent in ASD. In addition, we found structural differences in the amygdala between subjects with ASD and neurotypicals, and observed that performance in an emotional behavioral task is correlated with amygdala microstructure.

Conclusions: Emotion expressed by the whole body (but excluding facial expressions) fails to modulate activation in visual areas and the MNS, contrary to what is found in neurotypicals. The synergies between the mechanisms underlying recognition of facial expressions and body expressions may have their source in the amygdala. An abnormality of the amygdala, by compromising basic stimulus-reward learning could lead to a lack of development of areas involved in emotional evaluation, including the MNS. An inappropriate emotional response and a deficient MNS could lead to a lack of mirror activity that could then fail to evoke somatic markers important to the generation of the feeling of emotion.

71 107.2 Dysfunctional mirror neurons and Autism – A doubtful connection. I. Dinstein*[1], C. Thomas[2], K. Humphreys[3], N. Minshew[4], M. Behrmann[5] and D. J. Heeger[1], (1)*New York University*, (2)*Harvard Medical School*, (3)*Institute of Psychiatry*, (4)*University of Pittsburgh*, (5)*Carnegie Mellon University*

Background: It has been hypothesized that core symptoms in autism result from a specific dysfunction in mirror neuron activity. However, the experimental protocols commonly used to assess mirror neuron activity in humans are not capable of isolating their responses from the many other visual and motor neurons that coexist in the same cortical areas.
Objectives: To better isolate mirror neuron responses in high functioning individuals with autism we used an fMRI adaptation protocol designed to assess the selectivity of neurons for observed and executed movements; a defining feature of mirror neuron physiology.
Methods: In the first experiment, subjects were asked to observe, execute, or imitate the rock, paper, and scissors hand movements (from the children's game). Activity during each condition was compared with rest to assess "mirror system" activity. In the other experiments, subjects were asked to observe or execute a single repeating hand posture or a sequence of different hand postures. Activity during blocks of different postures was compared with that of repeated posture to measure visual and motor adaptation.
Results: Responses across the whole cortex including candidate mirror system areas (defined using the common imitation protocol: anterior intraparietal sulcus and ventral premotor) were comparable across autism and comparison groups in all three experiments. Individuals with autism, however, exhibited more variable fMRI responses both within and across subjects, across the whole cortex.
Conclusions: High functioning individuals with autism exhibited normal cortical responses, on average, in candidate mirror system areas. Furthermore, these individuals exhibited fMRI adaptation during both observation and execution of movements, indicative of normal underlying movement-selective neural responses. Such selective responses are

crucial for proper movement perception as hypothesized by "mirror system" theories. Our results therefore suggest that dysfunctional mirror neurons are not the underlying physiological basis of core autism symptoms.

72 107.3 The Effect of Handedness on fMRI Language Activation in Adolescents with Autism Spectrum Disorder. T. A. Knaus*, A. M. Silver, K. A. Lindgren, M. Kennedy, J. Siegel and H. Tager-Flusberg, *Boston University School of Medicine*

Background: Handedness and language functions are highly associated, although the exact nature of this relationship remains unclear. Language deficits are one of the core features of autism spectrum disorder (ASD) and previous studies have demonstrated an increased rate of left-handedness in this disorder. Although studies have examined language laterality in typically developing right- and left-handers, few studies have examined language laterality and handedness in ASD.

Objectives: The purpose of this study was to examine brain activation during a language task in left- and right-handers with ASD and typically developing left- and right-handers.

Methods: We used fMRI to examine activation during a visual response naming task in a small sample of left-handed boys with ASD (n = 6), left-handed typically developing boys (n = 6), right-handed boys with ASD (n = 6), and right-handed typically developing boys (n = 6). Percent signal change was calculated in 2 regions of interest, frontal language regions (pars triangularis and pars opercularis) and temporal language areas (posterior superior temporal gyrus, including the planum temporale), in each hemisphere and asymmetry quotients (AQs) were calculated.

Results: In left-handers, there were significant group differences for the temporal region (p = .005). Left-handed controls had leftward asymmetry of activation while ASD left-handers showed rightward asymmetry. In contrast, in right-handers, there were no significant AQ differences between ASD and controls. When right- and left-handers were compared, in the ASD group, temporal AQs were significantly different (p = .003), with left-handers demonstrating rightward asymmetry and right-handers having leftward asymmetry. In the control group, there were not significant differences between right- and left-handers.

Conclusions: These findings suggest that language functions may be different in left-handers with ASD. Differences were found relative to typically developing individuals as well as compared to right-handers with ASD, emphasizing the importance of examining left- and right-handers separately.

73 107.4 Mindblindness in relation to oneself: Individual differences in alexithymia modulate neural response to self-reflective mentalizing in autism and neurotypical adults. M. V. Lombardo*[1], B. Chakrabarti[1], S. A. Sadek[1], G. Pasco[1], S. J. Wheelwright[1], J. Suckling[2], E. Bullmore[2], S. Baron-Cohen[1] and ,. MRC AIMS Consortium[3], (1)*Autism Research Centre, University of Cambridge*, (2)*Brain Mapping Unit, University of Cambridge*, (3)*University of Cambridge; Institute of Psychiatry, King's College London; University of Oxford*

Background: A little over a decade ago, the term "mindblindness" was coined to characterize the impairments in understanding mental states by individuals with autism spectrum conditions (ASC) (Baron-Cohen, 1995). Most research however, has tested mindblindness in relation to other's minds. More recently, studies have begun to focus on the difficulty individuals with ASC have in introspecting on their own thoughts and emotions (a trait know as 'alexithymia') (Lombardo et al., 2007, PLoS One).

Objectives: To assess how the neural response to self-mentalizing is modulated by individual differences in alexithymia.

Methods: 23 adult males (18-45 years old) with a diagnosis of Asperger Syndrome and 23 age-, sex-, and IQ-matched neurotypical adults were scanned at 3T during fMRI while making mentalizing judgments about themselves or a non-close other. Alexithymia

was measured using the Toronto Alexithymia Scale (TAS-20).

Results: Among neurotypical adults, alexithymia positively correlated with self-mentalizing BOLD response in the caudal anterior cingulate cortex (cACC; r = 0.78) and anterior insula (AI; r = 0.59). In ASC, alexithymia positively correlated with self-mentalizing BOLD response in ventral medial prefrontal cortex (VMPFC; r = 0.62). Alexithymia differently modulated activity in cACC depending on diagnostic status. Neurotypical participants activated cACC more with increasing alexithymia, while in ASC, cACC was less active with increasing alexithymia.

Conclusions: Our results highlight the importance of cACC in self-referential cognitive difficulties. The cACC is highly involved during interoceptive awareness (Critchley et al., 2004, Nat Neurosci) and affective processing of pain (Singer et al., 2004, Science). While neurotypical individuals tend to use cACC more with increasing levels of alexithymia, individuals with ASC use cACC less as alexithymia increases. We conclude that mindblindness in relation to the self in ASC is related to decreased recruitment of a brain region essential for reading one's own bodily states and emotions.

74 107.5 Autistic Subjects Classification Based on PET Images. E. Duchesnay[1], A. Cachia[2], N. Chabane[3], N. Boddaert[4], J. F. Mangin[1], J. L. Martinot[2] and M. Zilbovicius*[2], (1)*Research Unit U797 "Neuroimaging and Psychiatry", CEA - INSERM and NeuroSpin, CEA*, (2)*Research Unit U797 "Neuroimaging and Psychiatry", CEA - INSERM*, (3)*Hospital Robert Debre*, (4)*Hospital Necker*

Background:Most of recent brain imaging studies of autism are based on methods that look for abnormalities at a voxel level ignoring distributed pattern abnormalities. A second limitation of those methods is that they only enable group analysis (eg.: control vs. patient) of populations.

Objectives:Conversely to voxel-based method we propose a method that simultaneously considers several brain regions taking into account their informative interrelations in order to improve the sensitivity of abnormalities detection. Moreover, such method enables individual analysis, which offers new perspectives like the evaluation the efficiency of a treatment on a single subject.

Methods:Rest cerebral blood flow (CBF) images of 45 (5 to 12 years) children with primary autistic disorder and 13 nonautistic (5 to 15 years) children with idiopathic mental retardation were measured with a positron emission tomography (PET) camera. We propose a multi-stages pattern recognition method. Early stages aim to identify autism discriminant regions. Later stage selects the most discriminant combination of those regions to build a autism vs. control classifier. Finally, the classifier is applied to new individual images and the prediction (autistic, control) is compared with the true clinical outcome to evaluate the accuracy of the individual classifier.

Results:The classification system identified two regions: (i) right superior temporal sulcus (hypoperfusion in autism) (ii) The left postcentral gyrus (hyperperfusion in autism). The validation of the method yielded to 91% (41/45, P=0.4) of correct classification of autistic subjects and 77% (10/13, $P=5.10^{-9}$) for mental retardation subjects.

Conclusions:Efficient individual detection of rest CBF abnormalities in children with autism may be obtained from PET images without any a priori manually defined ROIs.

75 107.6 Association Between Amygdala Activation in Response to Emotional Faces and Social Anxiety in ASD. E. H. Aylward*, N. Kleinhans, T. R. Richards, C. Johnson, J. Greenson and G. Dawson, *University of Washington*

Background: Difficulty evaluating and interpreting facial expressions has been reported in autism spectrum disorders (ASD) and is thought to be associated with amygdala abnormality. However, previous fMRI studies of emotional face matching in ASD have reported reduced fusiform activation and

increased activation of the precuneus, but no difference in amygdala activation.

Objectives: fMRI was used to explore the neural basis of abnormal emotional face processing in ASD and to determine the effect of social anxiety on amygdala activation.

Methods: During fMRI scanning, 29 individuals with ASD and 25 normal controls viewed Ekman faces depicting fear or anger. Subjects were instructed to select which of two faces at the bottom of the screen portrayed the same emotion as the face at the top of the screen. The control condition consisted of a simple shape-matching task. In addition, participants were administered the Social Avoidance and Distress Scale (SADS).

Results: The ASD group reported significantly more social avoidance and distress on the SADS than the control group ($p < 0001$). For the comparison of emotional faces vs. shapes, controls evidenced significantly more left prefrontal activation than the ASD group and significantly less activation in the left precuneus, left cuneus, and bilateral lingual gyri. fMRI analyses were also conducted with the SADS total score entered as an independent variable. For the ASD group, greater social avoidance and distress was associated with increased activation in right amygdala and decreased activation in fusiform face area.

Conclusions: Overall, these findings support previous work indicating that individuals with ASD exhibit reduced prefrontal activation and increased activation in sensory cortices while performing cognitive tasks, in comparison with typically developing controls. The correlation between social anxiety and activation in the fusiform and amygdala suggests that level of social anxiety is critically related to functional abnormalities in these brain regions.

76 107.7 fMRI investigation of decision making, temporal foresight & reward evaluation in Asperger's syndrome. C. Murphy*, A. Christakou, D. Murphy and K. Rubia, *Institute of Psychiatry*

Background:

There is evidence that people with autistic spectrum disorder (ASD) have deficits in cognitive flexibility, planning & response to reward. Competent planning is crucial to decision making, and involves inter-temporal bridging - making future choices based on experience and outcome evaluations and understanding future consequences of one's actions.

Objectives:

Investigate brain function in individuals with Asperger's and healthy Controls during a gambling task that measures outcome evaluation and reward-related inter-temporal decision making.

Methods:

Nine individuals with Asperger's and twenty matched Controls completed an event-related adaptation of the The Iowa Gambling Task on a 3T magnetic resonance imaging (MRI) scanner. The task involves choosing between card decks that result in high immediate monetary gain, but larger future loss ("risky": long-term loss), or low immediate gain, with larger final reward ("safe": long-term gain). Data were analysed using non-parametric image analysis (XBAM).

Results: In Controls, preference for "safe" choices, reflecting forward thinking and inter-temporal competence, when contrasted with disadvantageous risky choices, elicited activation in ventromedial prefrontal, anterior cingulate, and parietal cortices and mid-cerebellum. Monetary wins, compared to losses, showed increased activation in the caudate, anterior cingulate and cerebellar hemispheres, whilst losses compared to wins showed increased activation in the bilateral inferior prefrontal, insular and cingulate cortices.

In individuals with Asperger's, preliminary analyses show abnormal brain activation in the neural networks activated in controls during "safe"decisions, and in relation to reward. Detailed results will be provided at the conference.

Conclusions:

We hypothesise that individuals with Asperger's will have; i) reduced number of reflective, advantageous choices, ii) reduced dorsolateral and orbital prefrontal brain activation during these choices & iii) blunted brain activation response to both positive and negative reward feedback. Final analyses on a larger sample of 20 patients will be presented at the conference and implications of the findings will be discussed.

77 **107.8** Low form coherence thresholds associated with increased fMRI responses and gray matter density in Asperger's syndrome. S. Tsermentseli*, J. Spencer and J. O'Brien, *Brunel University*

Background: Increasing evidence show atypical visual processing in autism; this pattern of atypical performances has lead to the development of neurobehavioral theories of autism describing these anomalies as consequences of an abnormal multimodal structure of information in the visual modality.
Objectives: To explore motion-coherence and form-coherence processing in Asperger's disorder (AS) using psychophysics and fMRI and to examine whether morphological differences are related to regions of altered activation.
Methods: We measured form and motion thresholds for detecting a Glass stimulus of varying coherence in a field of random dots in a group of adults diagnosed with Asperger's syndrome and a normal control group matched for chronological and mental age. A coherent visual patch was depicted by dots separated by a rotational transformation in space (form coherence) or space-time (motion coherence). Stimuli were presented for 0.25s to prevent serial search strategies. Coherence was progressively reduced from 1.0 until an error was made, in the manner of a 2-up, 1-down staircase. In a parallel event-related fMRI study, participants performed the same task in the scanner at fixed coherence levels (0, 0.125, 0.25, 0.5, 1.0). Voxel-based Morphometry (VBM) was implemented to compare structural differences between the two groups.
Results: Results from the psychophysical and fMRI data showed that adults with AS perform at the same level as controls in motion processing, replicating previous studies with children. However, it was found for the first time that individuals with Asperger's show lower form coherence thresholds. In addition, increased fMRI BOLD responses to form coherence in the middle occipital gyrus, the intraparietal sulcus and the ventral surface were reported in the AS group. VBM indicated significantly higher levels of global grey matter density in Asperger.
Conclusions: The results represent a contribution towards better understanding of the mechanisms mediating visual information processing in autistic spectrum disorders.

78 **107.9** The Effect of Tryptophan Depletion on Inhibitory Brain Function in Asperger's Syndrome. D. A. Sauter*[1], E. Daly[2], K. Rubia[3] and D. Murphy[3], (1)*Institute of Psychiatry, London*, (2)*Institute of Psychiatry, King's College London*, (3)*Institute of Psychiatry*

Background: The serotonergic system, involved in aggression and impulse control, has been implicated in Autism Spectrum Disorder (ASD), and has been linked to some typical symptoms, such as repetitive behaviours. Although a number of studies have found differences between ASD and controls on biological measures of serotonin, little is known about the effect of these differences in the serotonergic system on brain function of people with ASD during cognitive tasks.
Objectives: This study investigated the differential effects of acute tryptophan depletion (ATD) on the brain function of adult males, 12 with and 12 without Asperger's syndrome, during the performance of an inhibitory task.
Methods: Participants performed an event-related go/no-go task in two functional magnetic resonance imaging (fMRI) scanning sessions in a 1.5T scanner. In a double-blind, counterbalanced design, participants consumed either a tryptophan-free or a balanced amino acid drink at each session. The task required subjects to selectively execute or inhibit a motor response.
Results: Levels of neural activation in dorsolateral pre-frontal cortex and right temporal regions were differentially affected by tryptophan depletion in the two groups;

after ATD, activation increased in these regions in controls, but decreased in the Asperger's group.
Conclusions: These findings provide neuro-functional evidence of differential modulatory effects of serotonin on inhibitory neuronetworks in Asperger's syndrome.

79 107.10 Inhomogeneous Somatic Maps in Autism. B. Sheth*[1], M. A. Coskun[1], L. Varghese[1], S. Reddoch[2], E. M. Castillo[2], D. A. Pearson[2], K. A. Loveland[2] and A. C. Papanicolaou[2], (1)*University of Houston*, (2)*Univ. of Texas Med. Sch. at Houston*

Background: Current research points to a deficit in connectivity in the brains of individuals with autism. There has been more progress on functional long-range connectivity between different brain areas in autism than on local connectivity within a brain area. Studies have focused on the neural basis of "core characteristics," particularly social-emotional differences in autism. The comorbidity of diverse impairments such as sensorimotor differences and social-emotional deficits suggests that abnormalities in brain development of a more general nature such as differences in local and long-range circuitry affect multiple different functions.

Objectives: We explored somatic maps in AD as reflective of abnormalities in circuitry.

Methods: Using magnetoencephalography (MEG), we examined the cortical response to tactile stimulation of the thumb (D1) and index finger (D2) of the dominant hand and lip of young adult observers (18 individuals with autism disorder or ADs and 17 typically developing persons or TDs). Automatically fitting a single current source model to the evoked potential data, we obtained the cortical representation corresponding to each body part stimulated.

Results: The somatic maps revealed two differences. i) The distance between the representations in cortex of D1 and the lip was significantly larger in ADs compared with TDs ($p < 0.001$). The difference was significant, even after normalizing by head volume. ii) Typically, D2 is farther from the lip than is D1. This was reversed in ADs. The ratio of the distance of each finger from the lip was significantly different between the two populations.

Conclusions:The twin findings of atypical somatic map extent in autism reflect atypical local connectivity. Synchronous development of a larger head with the stabilization of a somatic cortical map during early childhood in ADs could have left behind an inhomogeneous somatic map. The present findings are a functional imprint of past reports of abnormal anatomy and morphology in autism.

80 107.11 GOAL-DIRECTED ACTIONS IN AUTISM: IMPLICATION OF MIRROR AND CANONICAL NEURONS SYSTEMS. J. Martineau*, N. Hernandez, J. P. Cottier and C. Destrieux, *INSERM U 930*

Background: Abnormal motor control appears to be one of the elementary dysfunctions in autism and may lead to language and social cognition impairments. Imitation disorders, abnormal posture, facial mimicry and motricity observed in autism plead for an abnormality of sensorimotor integration.

Objectives: The present investigation examined functional activations of autistic patients and healthy subjects performing goal-directed actions.

Methods: Twenty right-handed male participants aged 20 to 34 years were included: ten autistic patients with normal IQ and ten healthy subjects. Subjects were scanned for anatomical and fMRI with a GE Signa 1.5 T system using a head gradient coil. Two experiments were performed using a blocked design. *Experiment 1*. Five conditions were proposed during 5 runs: visual perception of a real object in a box, visually-guided grasping of this object in the box, blind grasping of this object in the box, reaching this object in the box, mime of the grasping gesture without the object in the box. *Experiment 2*. Three video sequences were proposed: observation of a moving hand, of a moving object and of a hand manipulating the object. Data were analyzed using the freesurfer-fsfast package using a GLM and visualized on a flat representation of the cerebral cortex. Group analysis was performed

using a surfacic coordinate system for coregistration and a random model effect.

Results: Both groups showed normal activations in left motor cortices in grasping experiments. Parietal (IPS) and occipital (EBA and LOC) activations were lower in the autism group than in the comparison group. During action observation tasks, inferior frontal, superior parietal and intraparietal were also less activated than in the control group. Conclusions: This suggests an impairment of the neuronal system linking action perception and execution (canonical neurons and mirror neurons systems) usually activated during the goal-directed actions in the autistic pathology.

81 107.12 Motor Activity During the Observation of Dynamic Emotional Facial Expressions Is Intact in Autism Spectrum Disorder. J. A. C. J. Bastiaansen*[1], M. A. Thioux[2] and C. Keysers[2], (1)*Lentis*, (2)*University Medical Center Groningen*

Background: According to the mirror neuron theory of autism spectrum disorder (ASD), ASD is characterized by reduced activity in neural systems that mirror observed actions, sensations and emotions in typically developing individuals (TDs). Observation of facial emotional expressions involves two types of mirroring: 1) activation of motor areas involved in producing facial expressions and 2) activation of areas involved in experiencing the same emotion.

Objectives: With this fMRI study we tested whether adults with ASD activate their motor system as much as TDs while viewing movies of facial expressions.

Methods: We scanned 17 high functioning adults with ASD and 17 age and IQ matched TDs while they passively viewed movies of pleased, disgusted and neutral facial expressions and while they performed a simple motor task (pulling up the nose).

Results: The motor task showed no significant differences between groups (p>.001), so we created a single motor mask (facial movement – baseline) combining all participants. Several areas within this mask were active for ASD adults during facial expression observation relative to baseline, including right insula, BA44, MI, premotor/supplementary motor cortex and right STS. Importantly, there were no significant differences in these areas between groups (p>.005). Lowering the threshold revealed stronger activations for ASD in a between-group comparison. Disregarding the mask, ASD adults demonstrated stronger activations in amongst others emotional and mentalizing areas, particularly while viewing disgusted expressions (p<.005).

Conclusions: We found that adults with ASD activate their motor system at least as strongly as TDs when observing dynamic facial expressions. This result challenges the mirror neuron theory of autism. Hyperactivation of emotional and mentalizing areas suggests people with ASD may react excessively to emotional facial expressions, and therefore turn away from other people's faces. Alternatively, they may compensate less efficient processing by recruiting more neural resources or might be more motivated.

82 107.13 A DTI tractography study of young children with autism. M. Weinstein*[1], L. Ben-Sira[2], V. Kronfeld-Duenias[3], T. Hendler[4], D. A. Zachor[5], P. M. Eksteine[6], Y. Levy[7] and D. Ben Bashat[2], (1)*The Hebrew University*, (2)*Functional Brain Mapping Unit- the Wohl Institute for Advanced Imaging, Tel Aviv Sourasky Medical Center*, (3)*Functional Brain Mapping Unit-the Wohl Institute for Advanced Imaging, Tel Aviv Sourasky Medical Center*, (4)*Functional Brain Mapping Unit- the Wohl Institute for Advanced Imaging,Tel Aviv Sourasky Medical Center.*, (5)*Sackler Faculty of Medicine, Tel Aviv University,Department of Pediatric, Autism center, Assaf Harofe Medical Center*, (6)*Department of Anesthesia and critical care, Tel Aviv Sourasky Medical Center*, (7)*The Hebrew University, Jerusalem*

Background: Accelerated brain growth in autism has been amply documented in the first 2-4 years of life (1-4). Several studies used DTI to examine white matter structure in subjects with autism (5-7), yet most studies were performed with older children or adults.

In our earlier work, we presented the first evidence of over restriction of white matter in young children with autism, providing quantitative information regarding white matter integrity (8). Objectives: To examine white matter integrity in young children with autism using DTI tractography. Methods: DTI data was acquired for subjects who met ADI-R and ADOS criteria for autism (AUT, n=8, age: 2.78±0.66) and typically developing control subjects (TD, n=9, age: 2.47±0.67). Three major fiber bundles were extracted: the corpus callosum, the cortico-spinal tract (cst) and the superior longitudinal fasciculus (slf). Further segmentation of the corpus callosum (cc) was conducted according to the method in Witelson (9). Streamline fiber tracking method based on fiber assignment by continuous tracking (FACT) was applied using DTI Studio software (Johns Hopkins University, Baltimore, MD, USA). For the tracking of white matter fibers, the multiple regions of interest method was applied. Mean diffusivity, FA, eigen values (0,1,2), axial and radial diffusivities were calculated for each fiber segment and were compared between the groups. Results: Although results did not reach statistical significance, consistently higher eigen values for the AUT group were found in the body of cc (Witelson2, 3 and 4), whereas, lower eigen values were found in the slf right and left. No between groups difference were detected in eigen values in the cst fibers. No differences in FA were found in any region. Conclusions: A distinct trend was detected in the eigen values, but not in the FA. Further exploration needs to be done in order to substantiate these results.

83 107.14 Mentalization Network Gray Matter Volumes Abnormalities in Autism Spectrum Disorders. M. Assaf*[1], K. Jagannathan[2], L. Miller[2], R. Sahl[2], R. T. Schultz[3] and G. Pearlson[1], (1)*Institute of Living, Hartford Hospital / Yale University*, (2)*Institute of Living, Hartford Hospital*, (3)*Children's Hospital of Philadelphia and the University of Pennsylvania*

Background: Autism Spectrum Disorders (ASD) share common deficits in social and communication skills. One influential cognitive theory proposed to explain these impairments is 'mind-blindness', i.e. deficiency in the ability to attribute states of mind (including emotions, desires and goals) to other people. This process, also known as Theory-of-Mind (ToM), or Mentalization, is a crucial component of social behavior allowing prediction and interpretation of others' behavior. The brain network involved in this process includes the temporoparietal junction (TPJ), temporal pole (TP) and medial prefrontal cortex (MPFC). We previously demonstrated that ASD patients underactivate this network while engaged in a social, competitive game that entails on-line mentalization. In addition, previous studies showed that ASD patients exhibit abnormal gray matter (GM) volumes in widespread brain areas. In the current study, we examined GM abnormalities of ASD patients specifically in the mentalization network.

Objectives: To compare GM volumes of ASD patients to matched healthy controls (HC) in the mentalization network (i.e. TPJ, TP and MPFC), and to investigate the relationship between ASD GM volumes of this network and the severity of patients' symptoms as measured by the ADOS.

Methods: Twenty-one high functioning ASD patients, ages 11-32, and 23 matched HC, ages 10-29, underwent an MRI scan. Structural MPRAGE T1-weighted images were acquired with a 3T scanner. Voxel-Based Morphometry (VBM) analysis was done using SPM2.

Results: Compared to HC, ASD patients showed increased GM volumes in the MPFC and bilateral TPJ, and decreased GM volumes in bilateral TP. Positive correlations were found between MPFC GM volume and patients' ADOS scores.

Conclusions: High-functioning ASD patients showed abnormal GM volumes in the mentalization network, within MPFC volumes correlated with their symptom severity. These results support the theory that neuropathologic changes in specific brain regions underlie the mentalization impairments of ASD.

84 107.15 An fMRI Study of Socially Rewarded Learning in High Functioning Autism. A. Scott*, J. R. Cohen, D. Ghahremani, R.

Poldrack, M. Dapretto and S. Y. Bookheimer, *University of California, Los Angeles*

Background: Social rewards, such as a smiling face, are often used to guide learning of appropriate behaviors during development. Computational modeling research suggests that an early deficit in reward-related learning may lead to aberrant development of joint attention and gaze following (Triesch et al., 2006), two principal characteristics of autism.

Objectives: To investigate how a social reward, a smiling face, guides implicit learning in high-functioning children with autism (HFA) and typically developing children (TD) using fMRI.

Methods: 16 HFA boys (12.4 + 2.14 years) and 16 age- and IQ-matched TD boys were scanned during a rewarded implicit learning task. Subjects were shown abstract visual stimuli and asked to respond with either a "1" or a "2" button press. Four of the 6 trial types were deterministic with respect to the outcome (1 or 2); the remainder were random. Feedback on half of the trials consisted of a social reward or punishment. The remaining trials were a neutral face with the same text. Subjects were given a post-scan test to determine if they were able to explicitly memorize the associations.

Results: Both groups performed at chance on the post-test, suggesting implicit rather than explicit learning. Task accuracy improved only in the TD group. Overall, TD children demonstrated greater activity than HFA in frontostriatal networks. During positive social rewards for deterministic trials, TDs had greater activity than HFA in dorsal and ventral striatum, anterior cingulate, and inferior frontal gyrus. Equivalent activation in bilateral fusiform gyrus during feedback ($t(30)=0.706$, $p = 0.380$) indicate that both groups processed the faces.

Conclusions: These results suggest that positive social rewards engage neural systems involved in reward processing in TD, but not HFA, children. It appears that TD children are able to incorporate this feedback to guide implicit learning whereas HFA children cannot.

85 107.16 A possible influence of the GAD2 gene on cortical brain volume in Autistic Spectrum Disorders. P. Johnston*[1], C. Ecker[1], E. Daly[1], J. P. Sinnwell[2], P. Bolton[1], J. Powell[1] and D. Murphy[1], (1)*Institute of Psychiatry*, (2)*Mayo Clinic*

Background: The GABAergic system has emerged as a candidate neurotransmitter system underpinning the pathophysiology of Autistic Spectrum Disorders (ASD). Glutamic Acid Decarboxylase (GAD) is a crucial enzyme responsible for the decarboxylation of glutamate to gamma-amino butyric acid. Two isoformes of this enzyme are present GAD1 and GAD2; two different genes found on chromosome 2 and 10 respectively encode these. Linkage analysis have identified chromosome 10 as having high association with ASD and a recent SNP association analysis within our group found a significant association with GAD2 and ASD. Post-mortem analyses have shown a reduced GAD protein levels in autistic parietal and cerebellar cortices. However nobody has related genetic variation in GAD to brain.

Objectives: To investigate the association between the GAD2 gene and cortical anatomy in ASD.

Methods: A sample of 64 individuals (42 clinically diagnosed ASD cases and 22 healthy controls) underwent a conventional SPGR scan; FreeSurfer software was used to automatically label 34 subdivisions of each hemisphere and calculate cortical volumes. Each subject was genotyped for 10 SNPs tagging the GAD2 gene using Taqman procedures. Haplo.Stats was used in conjunction with R Statistically Computing for haplotypic and statistical analysis.

Results: We found a significant decrease in cortical volume of ASD inferior parietal cortex ($p = 0.0089$). Haplo.Stats identified a significantly associated 3 marker haplotype with ASD cases. All possible haplotype combinations were identified and their frequencies calculated. Hap1 and Hap3 showed the highest frequencies and were examined further. Subjects expressing Hap3 showed a significant increase in inferior parietal cortical

volume (0.00025), however a significant reduction was noted in ASD cases expressing Hap3 (0.0005) using generalized linear regression analysis.

Conclusions: Our work adds to post mortem evidence that Cortical volume reduction in the left inferior parietal cortex of the ASD brain may be related to haplotypes of the GAD2 gene.

86 107.17 Influences of Manipulating Scanpaths on Brain Activity Evoked by Faces. E. Carter*[1], C. M. Hudac[1], S. B. Perlman[1], B. C. Vander Wyk[1], S. G. Dewhurst[1], N. Minshew[2] and K. A. Pelphrey[1], (1)*Carnegie Mellon University*, (2)*University of Pittsburgh*

Background: Individuals with autism demonstrate abnormal visual scanpaths when looking at faces (Pelphrey et al., 2002, JADD; Klin et al., 2002, AGP). Additionally, these individuals show an absence of the usual face-selective activity in the fusiform gyrus (FFG) relative to typically developing individuals (Schultz et al., 2001, AGP).

Objectives: Employing fMRI, our study explores the effects of manipulating time spent fixating upon the eyes on brain activity evoked by faces in people with and without autism.

Methods: We created a paradigm in which a crosshair moves over an image of an actor displaying a fearful facial expression. Participants push a button when the crosshair changes color (this happens infrequently) to ensure that they maintain fixation on the crosshair. Four conditions were designed by modifying the typical scanpaths over the core features of the face: Low (32 % of the time spent on the eyes relative to other features), Medium (48%), High (56%), and Free Viewing (no crosshair). At this time, three people with high-functioning autism and 10 matched neurotypical individuals have participated in this ongoing study.

Results: As predicted, typically developing individuals showed greater activation in the bilateral FFG ($p < .005$) to the High versus Low condition. Consistent with prior research, individuals with autism exhibited hypoactivation in the bilateral FFG. However, they showed greater activation in these areas in the High condition than in either the Low ($p<.5$) or Free Viewing ($p<.5$) conditions.

Conclusions: These preliminary findings suggest that by encouraging individuals with autism to look at the eyes of faces and follow more typical scanpaths, we can normalize their FFG activation. This work could have implications for the ways in which we understand the potential mechanisms underlying interventions that encourage eye contact during social interactions.

87 107.18 Callosal morphology in high functioning adolescents with autism spectrum disorders and its relation to symptomatology. M. S. Reddish[1], G. Wallace*[2], A. Martin[1] and J. N. Giedd[1], (1)*NIMH*, (2)*National Institutes for Mental health*

Background: Previous studies of subjects with autism spectrum disorders (ASDs) have demonstrated abnormalities of structural brain connectivity, particularly in the corpus callosum.

Objectives: The present study sought to examine corpus callosum morphology among adolescents with high functioning ASDs and its correlation with autism symptomatology.
Methods: T1-weighted MP-RAGE MRI volumes were acquired at 3T from 16 males with a high functioning ASD (diagnosed using DSM-IV criteria as well as scores from the Autism Diagnostic Interview and the Autism Diagnostic Observation Schedule) and from 17 typically developing males matched group-wise on age and IQ. The midsagittal area of the corpus callosum was quantified and parcellated into 7 subdivisions based on a previously developed methodology.

Results: No group differences in corpus callosum area were found; however, when accounting for group differences in total white matter volume, the corpus callosum was relatively larger among the adolescents with ASD. Within the ASD group, corpus callosum area was negatively correlated with autism symptomatology. Specifically, posterior regions of the corpus callosum were negatively correlated to measures of stereotyped behavior.

Conclusions: Intact corpus callosum area, but reduced white matter volumes may indicate aberrant connectivity in ASD. Moreover, variation in corpus callosum area may be related to autism symptoms.

88 107.19 Localization of Transverse Relaxation Time Abnormalities in Autism. Y. Gagnon*, T. Devito, J. Hendry, N. Gelman, N. Rajakumar, P. Williamson, D. Drost and R. Nicolson, *University of Western Ontario*

Background: Autism is a developmental disorder characterized by social deficits, impaired communication, and restricted and repetitive patterns of behavior. Although there is strong evidence linking autism with abnormal brain development, the anatomical extent and timing of these neurobiological differences are unknown. Transverse relaxation time (T2) is a quantitative parameter of magnetic resonance imaging (MRI) influenced by tissue water compartmentalization and concentration. We reported a global increase of white matter T2 in the first whole brain study of T2 in autism.

Objectives: The purpose of this study was to localize the areas contributing to the previously reported global T2 increase in patients with autism.

Methods: Twenty-one males with autism, aged 6 to 16, and 20 male controls in the same age range underwent a MRI scan at 3 Tesla. T2 data were acquired using a Gradient Echo Sampling of the Free Induction Decay and Echo sequence. The images were spatially normalized and region of interest masks were created to calculate the mean T2 values in the masked regions.

Results: Patients had a global increase in white matter T2 (2.9%; p=0.2) as well as an increase in white matter T2 in the left hemisphere (3.3%; p=0.004). Post-hoc analysis revealed that patients had a significant increase in frontal (3.0%; p=0.3) and parietal white matter (3.1%; p=0.003).

Conclusions: Study limitations include a small sample size and the use of an adult brain template for the spatial normalization of images. Increased T2 could be caused by increased water within the myelin layers, consistent with study data showing larger brains and defective long range brain signaling. The asymmetry of white matter T2 is consistent with findings of abnormal brain lateralization in autism. Future work will focus on specifying the tissue origin of these local T2 differences.

89 107.20 Success rate of fRMI scans in children with ASD, epilepsy, and typical development. K. F. Jankowski[1], D. Shook[2], L. Rosenberger[1], A. Della Rosa[3], B. E. Yerys*[1], M. M. Berl[1], C. J. Vaidya[2], J. W. Van Meter[4] and W. D. Gaillard[1], (1)*Children's National Medical Center*, (2)*Georgetown University*, (3)*Catholic University*, (4)*Georgetown University Medical Center*

Background: The field of pediatric functional neuroimaging is a growing method for analyzing brain development; but the feasibility of this technique in children lacks thorough investigation. The literature fails to differentiate scanning efficacy in pediatric clinical and control populations.

Objectives: The present study examined functional neuroimaging success rates in three pediatric populations: children with autism spectrum disorder (ASD), children with epilepsy (EP), and typically-developing (TD) children.

Methods: 246 children (32 ASD; 124 EP; 90 TD) ages four to eighteen years old participated in fMRI studies of language and executive control using a 3T Siemens Trio scanner. Scans included block and event-related designs for ASD and TD, and block designs for EP. Exclusionary criteria included cognitive impairment (IQ < 70). Scan success was determined by dividing the number of completed scan runs by the total attempted. When possible, reason for scanning failure (excessive motion, cognitive difficulties, or refusal) was recorded.

Results: The TD group had a higher scanning success rate (90%) than both ASD (78%) and EP (88%) groups. Children with ASD had the lowest number of successful scan trials in proportion to total number attempted.

Excessive motion was the leading cause of scanning failure, followed by refusal to participate, and cognitive difficulties.

Conclusions: Our findings suggest that imaging children from clinical groups, especially children with ASD, requires higher participant recruitment, additional scan time, and supplementary monetary funds. An analysis of the feasibility of pediatric neuroimaging serves as a valuable resource when modeling budgetary plans and research proposals.

90 107.21 Structural Brain Differences between Autistic Children and their Typically-Developing Siblings: a Voxel-Based Morphometry Analysis. K. Steinman*[1], L. Lotspeich[2], S. Patnaik[2], F. Hoeft[2] and A. Reiss[2], (1)*University of California, San Francisco*, (2)*Stanford University*

Background: Morphologic brain differences have been identified between children with autism and typically-developing children, though findings have been inconsistent across studies. One potential cause is the variability in brain morphology resulting from the influence of multiple genetic and environmental factors on brain development. A strategy to control for such factors is to compare brain structure between siblings discordant for autism.

Objectives: To assess the relationship between brain morphology and autism using voxel-based morphometry to examine siblings discordant for autism.

Methods: Participants included 27 same-gender sibships consisting of one child with autistic disorder (AU; confirmed with ADI-R and ADOS-G) and one typically-developing sibling (TD). Subjects were between 6-13 years old (AU 9.7±1.7; TD 9.1±1.9), and all pairs were less than 4 years apart. High-resolution structural magnetic resonance images were pre-processed (including modulation) and analyzed (paired t-test covarying for age, gender, and total gray/white matter volume) using SPM5 and VBM5.1 (p=0.1 corrected).

Results: AU had greater grey matter volume than TD in the right insula and posterior perisylvian region and the left insula and inferior temporal lobe. AU had greater white matter volume in the right temporal stem and inferior temporal lobe. AU had less grey matter volume than TD in bilateral anterior cingulate cortex, and less white matter volume in posterior corpus callosum and cingulate gyri and left anterior parietal lobe.

Conclusions: Volume differences found in temporal lobes, insulae, and cingulate cortices are consistent with differences found in some prior structural and functional studies of autism, and correspond to areas involved in language and social behaviors known to be abnormal in autism. Using autism-discordant siblings, we controlled for many environmental and (non-autism-causing) genetic factors which likely confounded many prior studies. These results are therefore likely more robust than those found previously. We recommend this strategy for use in future structural neuroimaging studies of autism.

91 107.22 The effect of global intellectual ability on the relationship between autistic features and prefrontal cortical folding. A. C. Stanfield*, T. W. J. Moorhead, M. D. Spencer, R. C. M. Philip, J. M. Harris, D. G. C. Owens, S. M. Lawrie and E. C. Johnstone, *University of Edinburgh*

Background: Magnetic resonance imaging (MRI) studies have suggested that aberrant patterns of cortical folding may be associated with the development of autism spectrum disorders (ASD). However, these studies have considered only individuals without global intellectual impairment, i.e. with an IQ>70. Around 70% of people with ASD are considered to be intellectually impaired, therefore the existing literature is not representative of the general autistic population.

Objectives: We set out to determine whether the relationship between autistic features and the degree of prefrontal cortical folding differs between individuals with and without global intellectual impairment.

Methods: 87 male individuals receiving special educational assistance were recruited from across Scotland. The participants were divided into two groups: those with global intellectual impairment (IQ<70, n=34) and those without global intellectual impairment (IQ>70, n=53). Autistic features were assessed using the Social Communication Questionnaire (SCQ) and each participant received a structural MRI scan. Prefrontal cortical folding was determined using automated methodology to measure the gyrification index (GI), a standard measure of cortical folding. The relationship between SCQ score and prefrontal GI was examined separately in each group and tests of interaction employed to determine if the relationship differed between the groups.

Results: SCQ scores for the group as a whole ranged between 3 and 33. A significant negative relationship was seen between SCQ score and GI among the intellectually impaired participants, whereas no significant relationship was seen in the non-intellectually impaired group ($r = -0.36$, $p=0.3$ and $r=0.3$, $p=0.81$ respectively). This difference between the groups was significant ($F=3.82$, $p=0.5$).

Conclusions: These results suggest that different, or additional, brain structural features may be associated with the expression of autistic characteristics in people with intellectual impairment compared to those without. Results from non-intellectually impaired groups may not necessarily apply to the broader population of people with ASD.

92 107.23 Diffusion Tensor Imaging of the social brain in autism. L. Poustka*[1], G. Schmötzer[2], J. Haffner[3] and B. Stieltjes[4], (1)*Central Institute of Mental Health*, (2)*J.W.Goethe University of Frankfurt*, (3)*University of Heidelberg*, (4)*German Cancer Research Center, Germany*

Background:

Autism spectrum disorders are now widely viewed as neurodevelopmental disorders, although the underlying brain basis is not entirely clear. It is hypothesized that functional underconnectivity between regions comprising the mentalizing network contribute to the social impairments in autism, especially in the earlier cerebral development.

Objectives:

To examine aspects of the orbital and medial prefrontal cortices, the amygdala and lateral aspects of the temporal cortex are target region for the so called social brain.

Methods:

Diffusion tensor imaging (DTI) was performed on 20 autistic children and healthy controls aged 6-12 years matched for age, sex, handedness and IQ. We examined the functional and structural connectivity of key regions of the mentalizing network using DTI, fMRI and volumetric measure; in addition, DTI measures were correlated with cognitive and behavioural measures.

Results:

Results showed that there were significant differences in fractional anisotropy values between groups. Differences were less significant between individuals with higher IQ and lower symptom scores.

Conclusions:

In summary, results suggest that disruption of white matter tracts may contribute to impairments in social cognition in autistic children. Moreover, differences may be more subtle in high functioning individuals.

93 107.24 A meta-analysis of functional imaging studies in Autism Spectrum Disorders: the role of anterior cingulate cortex. A. Di Martino*, K. Ross, A. Sklar, L. Q. Uddin, F. X. Castellanos and M. P. Milham, *NYU Child Study Center*

Background: Functional imaging studies of autism spectrum disorders (ASD) have reported abnormalities in regions related to mentalizing and facial processing. A parallel line of studies has focused on the brain correlates of additional cognitive and sensory impairments related to ASD. This imaging literature is characterized by generally small sample sizes and task design differences which

impede true refutation or replication of results. Objectives: To conduct an objective, quantitative meta-analysis of published functional neuroimaging studies of ASD. Methods: We used the activation likelihood estimate (ALE) technique implemented in BrainMap. ALE were calculated voxel-wise by modeling each coordinate with an equal weighting using a 3-D Gaussian probability density function (FWHM=10 mm). The resulting ALE-map was entered into a permutation test to calculate voxel-wise activation likelihood. Statistical maps were corrected for multiple comparisons using false discovery rates ($p < 0.5$, corrected). Thirty-two functional imaging studies comparing individuals with ASD and Neurotypical Controls (NC) were divided in 18 focusing on social processes and 14 examining non-social processes. Within ASD and NC we ran meta-analyses including 1) all studies combined, 2) social studies only, and 3) non-social studies only. To compare NC and ASD, we calculated the difference between the two group ALE maps for each study-set examined. Each map was entered into permutation analyses to generate voxel-wise statistical scores. Results: Analyses including all studies combined indicated greater probabilities for activation in NC compared to ASD in ventral and dorsal anterior cingulate (ACC). Secondary analyses revealed a dissociation in the ASD with vACC hypofunction only being observed for social-task studies, and dACC hypofunction for non-social. Conclusions: Results suggest abnormalities in two ACC-regions, one commonly implicated in social cognition, and the other in executive control. These areas are key nodes of structurally and functionally distinct networks the integrity of which should be examined in individuals with ASD.

94 107.25 fMRI of Children and Adults with Autism During an Irony Comprehension Task: Developmental Implications. D. L. Williams*[1], V. Cherkassky[2], R. K. Kana[3], N. J. Minshew[4] and M. A. Just[2], (1)*Duquesne University*, (2)*Carnegie Mellon University*, (3)*University of Alabama, Birmingham; Carnegie Mellon University*, (4)*University of Pittsburgh School of Medicine*

Background: Comprehension of irony requires the integration of regions associated with language processing and social cognition. It is also a later developing language skill, leading to potential differences in processing in children and adults with autism. Objectives: The purpose of the study was to compare the brain activation and cortical synchronization in children and adults with autism during the comprehension of irony. Methods: Adult groups were 13 individuals with high-functioning autism (HFA) and 12 age/IQ-matched controls. Child groups were 17 children with HFA and 16 age/IQ-matched controls. The participants completed an event-related fMRI study consisting of two experimental conditions in which the first two sentences provided the context for the third sentence that was either literal or ironic. Results: No reliable activation differences occurred between the adults with autism and the adult controls for the ironic critical utterances. Activation differences were more prominent for the child groups with the child controls exhibiting greater activation particularly in left inferior frontal and left and right temporal areas. The adults with autism had reliably less functional connectivity than the controls for the frontal:parietal and frontal:temporal networks during the ironic critical utterance. The children with autism had reliably less functional connectivity than the control children for the temporal:occipital network during the ironic critical utterance. Conclusions: The activation pattern of the adults with autism was similar to that of the adult and child controls with the use of more right hemispheric language areas. Differences in the areas of functional underconnectivity occurred primarily because of lesser posterior connectivity and higher frontal connectivity in the control adults as compared to the control children. Although changes occurred in the areas of activation, measures of functional connectivity for the adults and children with autism were highly similar during the ironic critical utterances.

Poster Presentations Program

108 Sensory Systems Posters

95 108.1 Autism: Alterations In Auditory Perception. P. L. Nieto del Rincón*, *Universidad San Pablo-CEU; Asociación Nuevo Horizonte*

Background: The wide group of investigations made in the previous decades about irregularities in auditory perception in persons with autism is reviewed with revised clinical and theoretical implications provided.

Objectives: Emphasis is placed on the fact that these auditory perception irregularities of people with autism are very important for the understanding of the symptoms, for the search of its etiology, for the implementation of an adequate treatment program and for the formulation of an adequate theoretical explanation of the syndrome.

Methods: Bibliographical review.

Results: There are enough experimental data suggesting that perceptive alterations are common in autism.

Conclusions: Important implications must be inferred to the design of an adequate therapy for persons with autism. Their auditory alterations can interfere with the therapy and we must always consider them in our work.

96 108.2 Relationship Between Sensory Processing and Severity in Children with High Functioning Autism Spectrum Disorders. C. Hilton*[1] and P. D. LaVesser[2], (1)*Saint Louis University*, (2)*Washington University*

Background:Dunn (2001) conceptualized atypical sensory processing as four discrete patterns of atypical responses in which individual respond either passively or actively in relation to their sensory thresholds: low registration, sensation seeking, sensory sensitivity, and sensation avoiding. Correlations between severity of social responsiveness and atypical sensory processing were previously demonstrated in a group of children with high functioning autism spectrum disorders (HFASD, Hilton, Graver & LaVesser, 2007).

Objectives:In this work, we extended our findings to compare with a control group.

Methods:

A bivariate correlational design was used to compare the scores between a social severity assessment and a sensory processing assessment of children with HFASD (N = 36), and a control group (N = 26), ages 6 to 10. Participants were full-term, had an overall IQ of at least 70, and had no history of cerebral palsy, or any other diagnosed major neurological condition.

The Social Responsiveness Scale (SRS, Constantino & Gruber, 2005) was used to assess social severity. The Sensory Profile (SP, Dunn, 1999) was used to assess sensory processing.

Results:Significant differences were seen between the incidence of atypical sensory responses in the HFASD group and the control group in each of the four sensory quadrants: ($p < .001$). A high frequency of atypical sensory responses in multiple quadrants was seen in the HFASD group (66.7%), but not in the control group (3.8%). The number of quadrants with definitely atypical responses was strongly correlated with social severity (.86). Strong correlations were found between the SRS severity scores and each of the four sensory processing quadrant levels (.70 - .84).

Conclusions:The presence of multiple atypical quadrant responses in this group of HFASD children indicates that atypical sensory processing follows a more diverse pattern in children with HFASD and the diversity is related to social severity.

97 108.3 COMORBID FEATURES OF AUTISM SPECTRUM DISORDERS (ASDs) PREDICTIVE OF ASD SURVEILLANCE CASE STATUS. L. D. Wiggins, C. Rice*, J. Baio and A. Washington, *Centers for Disease Control and Prevention*

Background: Although social, communication, and behavioral deficits define ASDs, comorbid features further characterize children with the disorders.
Objectives: This study examines comorbid features that predict ASD case status in a

surveillance cohort, including eating/drinking/sleeping difficulties, mood difficulties, cognitive scatter, aggression, oppositional behaviors, delayed or unusual motor development, lack of fear or excessive fearfulness, unusual sensory response, self injurious behaviors, seizures or seizure-like behaviors, and temper tantrums.
Methods: 517 children were identified by the Centers for Disease Control and Prevention surveillance system in Atlanta as being a potential ASD surveillance case. Clinicians applied a standardized coding scheme to abstracted health and educational records to code the presence or absence of comorbid features. Based on pre-determined criteria, 285 children were defined as an ASD surveillance case. Comorbid features did not influence case status; they were recorded to further characterize children with ASDs.
Results: Results indicated 75.6% correct classification for ASD cases provided by the logistic regression model (compared to 55.1% correct classification provided by the null model). Unusual sensory response ($p = .000$), lack of fear or excessive fearfulness ($p = .13$), and delayed or unusual motor development ($p = .17$) made significant contributions to correct ASD classification. Odds of being classified as an ASD surveillance case increased 12.85 for unusual sensory response, 1.80 for lack of fear or excessive fearfulness, and 1.70 for delayed or unusual motor development.
Conclusions: Children defined as an ASD surveillance case can be predicted by the presence of unusual sensory response, lack of fear or excessive fearfulness, and delayed or unusual motor development recorded in health and educational records. Unusual sensory response contributed six times more to correct classification than other significant predictors. These results suggest that sensory abnormalities are significant comorbid features that may help further characterize and distinguish children with ASDs.

98 108.4 Oculomotor Function in Children with Autism Spectrum Disorders During a Natural Viewing Task. C. J. Zampella*, A. M. Krasno, W. Jones and A. Klin, *Yale University School of Medicine*

Background: Previous research has investigated oculomotor function in individuals with autism spectrum disorders (ASD) to determine whether these individuals exhibit normal or abnormal motor control of eye movements. Most results indicate that basic eye movement function is intact in individuals with ASD, while some abnormalities may be present when tasks require higher-order cognitive abilities. Another body of research has studied looking patterns during natural viewing, revealing that individuals with ASD look less at others' eyes and more at mouths and background objects. While this research finds differences in the content of what viewers with ASD and typical development focus on, it has not directly compared oculomotor function in these two groups during natural viewing. The current study is intended to address that question.

Objectives: To compare properties of visual fixations and saccades in children with ASD and in typically developing children during natural viewing of social scenes.

Methods: Eye-tracking data were collected while children watched film clips of social interactions. From these data, fixations and saccades were identified. Data on the frequency and duration of fixations, and on the frequency, duration, and velocity of saccades, were then compared across groups.

Results: Preliminary analyses suggest that properties of saccades and fixations do not differ between children with ASD and typically developing controls.

Conclusions: Basic oculomotor circuitry appears to be intact in children with ASD. This suggests that discrepancies in viewing patterns between individuals with ASD and their typically developing peers are not the result of oculomotor impairments, but rather reflect differences in what aspects of a scene are salient.

99 108.5 Unimpaired perceptual causality in high-functioning children with autism. S. Congiu*[1], A. Schlottmann[2] and E. Ray[2], (1)*University of Siena*, (2)*University College London*

Background:

Observers from six months are sensitive to physical and social causality in launching (Michotte 1946/63) and reaction (Kanizsa & Vicario 1968), schematic events involving movements of simple geometrical shapes. Early in development perceptual causality might support learning about mechanical interactions of material bodies and about the social interactions of intentional agents (Leslie 1988; Schlottmann & Surian, 1999).
A deficit/delay in perceptual causality fits with theories focusing on either the social or perceptual peculiarities characterising autism. Ray and Schlottmann (2007) reported a link to the latter, but not the former in low-functioning young children with autism.

Objectives:

Our study investigated perceptual causality for launch, reaction and related events in 20 high-functioning children with autism (mean CA=13, VMA=9.7) and 22 typically developing controls, to consider whether deficits in launching that appear for younger children with autism are overcome with higher age/verbal ability.

Methods:

We employed a picture choice methodology like Ray and Schlottmann (2007), but with more articulate verbal instructions. Children watched 14 animations (designed to test possible explanations of any launch deficit), choosing one of three pictures depicting physical or social causality, or non-causality for each.

Results:

Children with autism performed similar to controls, with no deficit on any event.

Conclusions:

Early problems with launch perception are overcome with age/higher verbal IQ. This suggests a perceptual causality delay rather than deficit in autism. Although this might still interfere with early causal learning, that it is overcome agrees with the general sparing of physical reasoning in autism. Deficits on social animations (Bowler & Thommen, 2000; Klin 2000) may only appear for complex stimuli requiring mental state rather than goal attributions. Thus, unimpaired perception of reaction in autism coexists with deficits in complex social attributions, suggesting a discontinuity between the two.

100 108.6 The Implications of Colour Obsessions in Autism Spectrum Disorders: The case of J.G. A. K. Ludlow*[1], E. Hill[2] and P. Heaton[3], (1)*Anglia Ruskin University*, (2)*Goldsmiths, University of London*, (3)*Goldsmiths College, University of London*

Background: Case studies of individuals diagnosed with disorders characterised by high levels of heterogeneity potentially highlight factors contributing to this. Whilst cases of "colour phobia" in ASD have been reported anecdotally (White & White, 1987; Williams, 1999), no systematic research into their effects on the individuals who experience them, or their association with other sensory abnormalities has been carried out.

Objectives: The study of colour phobic individuals may provide important insights into heterogeneity in perceptual processing in autism, as well as in cognitive organisation within the phobic domain in individuals with autism. We report the case of J.G., a boy diagnosed with an Autism Spectrum Disorder (ASD), whose early and persistent colour obsession has resulted in highly selective processing of colour information.

Methods: Here we evaluated sensory processing abnormalities (measured by the Sensory Profile test (Dunn, 1999), colour perception, memory and categorisation in a child with an extreme colour phobia. His performance was compared to a group of both chronological age and non-verbal intelligence matched children with autism and typically developing controls.

Results: The Sensory Profile revealed significant difficulties across all sensory modalities, in relation to both typical and developmentally atypical populations. Assessment with the WISC showed an uneven

cognitive profile with good performance on non-verbal sub-tests and strikingly poor verbal subtest scores. In experiments 1 & 2 we investigated the effect of J.G.'s colour aversions on memory recall and perceptual discrimination. As the findings showed that J.G.'s preferred colour was poorly discriminated in comparison to colours with negative affective associations, we tested his categorisation of colours that shared category boundaries with his preferred colour in experiment 3.

Conclusions:Taken together the findings showed an extreme reliance on colour terms in memory, hypersensitivity to colours with negative affective valence and atypical processing of blue across different experimental tasks.

101 108.7 A DETAILED EXAMINATION OF THE SENSORY SENSITIVITIES OF CHILDREN WITH AUTISM SPECTRUM AND OTHER DEVELOPMENTAL DISORDERS. A. E. Robertson* and D. R. Simmons, *University of Glasgow*

Background:

A variety of evidence, e.g. parent reports, scientific data and personal accounts, have shown that there appears to be problems processing sensory stimuli in Autism Spectrum Disorders (ASDs). We constructed a questionnaire to investigate this in children with ASD and those with developmental disorders (DD). A qualitative, open approach was emphasised, in order to encourage parents to discuss the extent to which they felt sensory sensitivities played a role in their children's lives.

Objectives:

1. Does the AS group exhibit more sensory symptoms than the DD group?
2. Clarify what parents perceived to be the most difficult situations and/or places when with their child.
3. Highlight the behaviours most commonly exhibited by the ASD group.
4. Determine whether there is any evidence of fluctuations in sensitivity within the same modality.

Methods:

A sensory questionnaire, which was distributed to parents of children with Autism Spectrum (AS) and other developmental disorders (DD), was developed for use in this study. The questionnaire consisted of both closed and open questions.

Results:

The ASD groups exhibited significantly more sensory-sensitive behaviour in16 of the 43 closed questions (when a level of 0.5 was applied). 7 were significant when a more stringent $p<0.1$ was used. 76% of the ASD sample had had their hearing medically tested at a young age. Content Analysis was utilised for the replies to the open questions. Busy, sensory-laden places often proved a problem with the ASD sample. Objects were often used for sensory-stimulation (e.g. water/sand).

Conclusions:

1. The ASD group exhibited more sensory sensitivities than the DD group.
2. The most difficult places appeared to be supermarkets, schools and leisure centres
3. Sensory self-stimulation was common, as was aversive behaviour to stimuli.
4. There was evidence of both hyper- and hypo-sensitivities within the same modality in certain participants.

102 108.8 Making sense of sensory integration: Is perceptual coherence important in ASD?. L. Grayson*[1], J. Briscoe[2] and A. O. Holcombe[3], (1)*Cardiff University*, (2)*Bristol University*, (3)*University of Sydney*

Background:

Reports of 'fragmented' multisensory perception in autism spectrum disorders (ASDs) have increased interest in this area (Iarocci & McDonald, 2006). Recent research

has produced conflicting results. Van der Smagt, van Engeland and Hemner (2006) found no difference in susceptibility to the Shams audio-visual illusion between control and high-functioning autism/AS groups. However, Smith and Bennetto (2007) suggest a 'pre-attentive crossmodal' component partially accounts for atypical audiovisual speech comprehension thresholds in adolescents with high-functioning autism.

Objectives:

Our study used an audio-visual 'launch/pass' phenomenon (Sekuler, Sekuler & Lau, 1997), in which a disk is made to appear to crash into and launch a second disk of the same colour by presenting an auditory stimulus at the point of occlusion. Such phenomena putatively reflect early perceptual integration (Bushara et al., 2003). We hypothesised that ASD children/adolescents with normal/near normal IQ would report fewer crashes in response to these stimuli than age-matched controls, as a consequence of compromised audio-visual processing.

Methods:

Age-matched participants with/without ASDs (n = 19 per group) were presented with five blocks of twenty trials in which experimental and control trials were inter-mixed. In experimental trials, an auditory signal was presented at one of three stimulus onset asynchronies (SOAs) relative to the point at which a disk passed over a stationary disk of the same colour (0ms, -250 ms and +250ms). The number of crash percepts reported in response to each condition was the dependent measure. The control trials presented unambiguous crash and miss events accompanied by auditory signals with the same SOAs.

Results:

No significant differences in the proportion of crashes reported in response to the simultaneous SOA condition, or the response pattern across SOAs, were obtained.

Conclusions:

This study found no evidence to support compromised audio-visual integration in ASD. Interim findings relating to diagnostic subgroups, IQ matching and ADHD comorbidity measures will be presented.

103 108.9 Evidence of atypical processing of biological motion in Autistic Spectrum Disorders. L. S. McKay*[1], D. R. Simmons[1], P. McAleer[1], J. Piggot[2] and F. E. Pollick[1], (1)*University of Glasgow*, (2)*University of California, Los Angeles*

Background: It is known that Autistic Spectrum Disorders (ASDs) are associated with perceptual difficulties, and it has been suggested that the perception of motion and, more specifically, biological motion may be affected.

Objectives: To determine whether the perception of biological motion is impaired in people with ASDs relative to neuro-typical individuals.

Methods: **Exp 1**-Using a two-alternative forced choice paradigm we investigated participants' ability to detect point-light walkers in noise. A walker containing varying numbers of points was presented to either the left or right of the centre of the screen within a noise mask of varying numbers of dots. Participants were asked to determine whether the walker was present in the left or right of the display. **Exp 2**-To rule out effects of divided attention between each side of the displays in experiment 1 a second task was designed in which participants judged the direction of motion of a centrally presented point light walker within a noise mask. In one condition the walker preserved varying degrees of structural information within a noise mask containing an opposing motion signal. In the second condition the walker contained no structural information but was still masked with noise points containing opposing motion signals.

Results: Results from Experiments 1 suggest that participants with ASDs required stronger biological motion signals than neuro-typical participants and that they were more sensitive to masking noise. Currently results from Experiment 2 with neurotypical participants

showed that structural information improves performance at direction discrimination. From the results of Experiment 1 we predict that the benefits of structure will be diminished among the ASD group.

Conclusions: People with ASDs have difficulties in detecting biological motion given a weak or noisy signal and we predict that the benefits of structural information will be diminished in direction discrimination tasks.

104 108.10 The Role of Chronic Neural Noise in Autism Spectrum Disorders. D. R. Simmons*, E. Toal, L. McKay, A. E. Robertson, P. McAleer and F. E. Pollick, *University of Glasgow*

Background: Few theories of the neural basis of Autism Spectrum Disorders (ASDs) adequately address the well-known and oft-reported symptoms of hyper- and hypo-sensitivities in different sensory modalities (see Robertson & Simmons, this meeting). We argue that the existence of chronic levels of internally-generated neural noise in affective pathways might provide an explanation of these phenomena. To test this theory, it is necessary to directly measure perceptual abilities of ASD participants in "noisy" backgrounds. Whilst increased internal noise levels would normally mask a signal (and therefore increase thresholds), in some circumstances thresholds can be decreased (i.e. signals enhanced) via the well-known non-linear systems phenomenon of stochastic resonance. Objectives: To demonstrate the feasibility of chronic neural noise as a factor in ASD. Methods: We measured performance of adults with ASD and typical controls on a task involving a judgement based on visual motion information. The component motion trajectories of a cloud of moving dots were perturbed by increasing amounts of directional variation, and participants were asked to judge the overall direction of the cloud. Results: Peaks and troughs in performance of the ASD group, relative to the control group, as a function of increasing directional variation were suggestive of increased levels of internal noise in visual motion pathways. Conclusions: Taken together with other data from the literature on sensory processing within ASD (e.g. McKay et al, this meeting, in which point-light walkers were harder to detect on a background of noisy dots), these results suggest that increased levels of internal noise could be a factor in ASD. Furthermore, we suggest that these resonance and masking phenomena might underlie the sensory symptoms, and possibly other classes of symptom, within ASD.

105 108.11 A controlled study of psychophysiological responses of young children with autism to sensory, social, and repetitive phenomena. C. McCormick*, C. Green, C. Zierhut, D. Hessl and S. Rogers, *UC Davis M.I.N.D. Institute*

Background: Atypical behavioral responses to sensory and object stimuli are seen in autism in infancy and discriminate those with autism from other clinical groups. Controlled psychophysiological studies of such responses are infrequently reported, have produced conflicting findings, and have not been conducted on very young children.
Objectives: To compare psychophysiological responses to sensory, object, and social stimuli of young children with autism and typical age matched peers.
Methods: Two groups of young children matched for age (40.4), ASD (45) and Typical (22) participated. Parents completed the Short Sensory Profile and Repetitive Behavior Scale. Electrodermal and electrocardiogram signals were recorded on 96% of the sample. Stimuli involved five trials of a loud auditory stimulus, a live display of happy, pain, and fear displays, and a live exposure to approach and physical contact of a familiar and unfamiliar person. EDR was coded for peak response amplitude after presentation of auditory and emotional displays. Vagal tone was analyzed for the first two-minute period of interaction with the non-familiar and familiar person.
Results: Parents of children with ASD reported more abnormal responses to sensory stimuli and repetitive behavior than did the TYP group. Psychophysiologically, there were no group mean differences between the two groups of children in any condition. Significant differences in variance between the groups were found on only two variables: during the first presentation of the auditory

probe (p=.5) and the happy emotional display (p=.1) the ASD group showed greater variability. Parental behavior reports showed no relationships with physiological data. Conclusions: The data do not support hypotheses concerning physiological hyper- or hypo-reactivity to either social or environmental stimuli in these young children. This pilot study needs replication; the method was successful in gathering such data in very young children. The field needs new hypotheses concerning the origins of sensory and repetitive behaviors in autism.

106 108.12 Release from masking in speech perception by children with Asperger's syndrome. C. Füllgrabe*, J. I. Alcántara and E. J. Weisblatt, *University of Cambridge*

Background: Although the diagnosis of autism spectrum disorder (ASD) is largely based on abnormal social communication, and restricted/repetitive activities, abnormal sensory sensitivity is also prevalent. Anecdotal and experimental evidence suggest that individuals with ASD experience difficulty in understanding speech in noisy environments, such as classrooms.
Objectives: To investigate if this finding is the consequence of impaired masking release (defined as the difference between speech identification scores obtained in steady-state and temporally fluctuating noise), due to a less-than-normal ability to take advantage of the temporal dips in the background in order to take "glimpses" of the target speech signal.
Methods: Six normal-hearing children with Asperger's syndrome (AS) and six age- and IQ-matched typically-developing control children were tested (age range = 11-15 years). Participants and their parents completed a questionnaire as a subjective measure of everyday listening difficulties. Identification scores were obtained for nonsense vowel-consonant-vowel (VCV) stimuli, containing 21 English consonants in an /a/ vowel context, presented in silence and a speech-shaped background noise that was either steady and sinusoidally amplitude modulated (SAM) at modulation frequencies from 4 to 128 Hz.
Results: Speech identification in steady noise was initially lower for participants with AS, but this difference disappeared with further practice. Relative improvement in SAM noise in terms of overall percent correct and reception of phonetic features (*i.e.*, voicing, manner, and place of articulation) showed a similar dependence on modulation frequency in both groups, but could be lower by up to 17% points in the AS group. However, these differences generally failed to reach statistical significance. Again, performance improved with practice over several test sessions. Conclusions: Participants with AS did not show abnormal levels of masking release for VCV stimuli if training was provided. This observation contrasts with the questionnaire data showing auditory aversiveness and impaired speech-in-noise perception in the AS group.

107 108.13 Synaptic causes for hyper perception in autism: A model-driven approach. Y. Bonneh*, Y. Adini and M. Tsodyks, *The Weizmann Inst. of Science*

Background: One of the often observed but poorly documented symptoms of autism is the perceptual instability across time, with intermittent episodes of hyper and hypo perception and sensitivity. The neurobiological basis of these symptoms is currently unknown. Here we report a preliminary investigation of the possible synaptic causes for these symptoms using a biologically-inspired neural-network model that may apply to different levels of cortical processing.

Objectives: To develop a functional hypothesis and a neural-network model at the synaptic level to account for the evidence for hyper-perception and perceptual instability in autism.

Methods: Inspired by the analysis of individual cases, we developed a recurrent cortical network model that consists of excitatory and inhibitory populations, interconnected with synaptic connections with slow activity-dependent modifications in the intrinsic connections of the network leading to a changing balance between excitation and inhibition.

Results: Overall, the cases we studied suggest that severe autism is characterized by stimulus driven, winner-takes-all type of

sensory processing in which a strong stimulus tends to extinguish other stimuli, leading to intermittent perceptual collapses. These collapses could be avoided by various detaching strategies such as looking to the side or covering the ears. Our preliminary investigation of the model shows that intermittent hyper states could be accounted for by abnormal synaptic homeostatic plasticity that normally regulates the balance between excitation and inhibition in cortical columns, and its failure could lead to unstable activity and intermittent runaway excitation at different levels of cortical processing, including perceptual sensitivity, attention and arousal.

Conclusions: Analysis of cases of severe autism and investigation of a simple neural-network model suggest that a local fault in homeostatic plasticity could lead to intermittent runaway cortical excitation, which may correspond to perceptual collapses. These could be reduced by detachment, thus initiating a severely abnormal developmental process.

108 108.14 NORMAL LOW-LEVEL AUDIOVISUAL INTERACTION IN ADULTS WITH AUTISM: THE DOUBLE FLASH ILLUSION. C. Cascio*[1], R. E. Sassoon[2], A. Carroll-Sharpe[2], S. Guest[2], G. T. Baranek[3] and G. K. Essick[2], (1)*Vanderbilt University*, (2)*University of North Carolina*, (3)*University of North Carolina at Chapel Hill*

Background: Some clinical interventions for people with autism target sensory processing, under the assumption that low-level sensory processing forms the foundation for higher levels required for social interaction and cognition (Ayres, 2005). Integration of vision and hearing is particularly important for social-communicative abilities, and thus a good candidate for investigation in autism. Objectives: To determine whether low-level auditory and visual stimuli are integrated similarly in adults with versus without autism. Methods: Low-level audiovisual integration was characterized in a group of eight high-functioning adults with autism and eight controls (matched for age and IQ) using a paradigm (Shams et al., 2002) in which multiple beeps presented concurrently with a single flash evoke the illusory percept of multiple flashes. In a second experiment, the temporal window of this cross-modal influence was explored by incrementally increasing the time separating the onsets of the auditory stimuli. Results: The autism group reported perceiving illusory flashes similarly to controls at short (< 80 msec) temporal windows. At longer temporal windows (> 80 msec), the illusory effect disappeared in the control group but persisted in the autism group (t= 2.68; p=0.3). Persistent illusory perception at these longer intervals was significantly correlated with autism severity on the social domain of the ADI-R (r = -0.764 (p =.27), and strongly negatively correlated with IQ in both groups (autism: r = -0.574, p =0.137; control: r = -.842, p =0.009). Conclusions: These results suggest that simple audiovisual integration is intact in autism. The group difference at longer auditory separations is likely to reflect differences in cognitive strategy or response bias rather than perception, although further experiments must be done to rule out perceptual differences completely. Our results are consistent with previous unimodal studies demonstrating normal or enhanced perception for simple but not complex stimuli (Bertone et al., 2005).

109 108.15 The Development of a Clinical Measure of Sensory Processing Behaviors for Toddlers with Autism Spectrum Disorders. A. Ben-Sasson[1] and M. B. Kadlec*[2], (1)*University of Haifa*, (2)*Boston University*

Background: Toddlers with autism spectrum disorders (ASD) exhibit a range of responses to sensory stimuli, from sensitivity to seeking behaviors, with varying degrees of impact on participation in activities. There are no assessments for toddlers that directly measure the presence of sensory behaviors in learning and play contexts.

Objectives: (1) Investigate the reliability and validity of a clinician-based measure of sensory processing behaviors. (2) Examine the concordance between parent report and clinicians' observations of sensory behaviors. Methods: This study included 48 toddlers with ASD with a mean age of 28 months, 76% boys, and a mean Mullen developmental

quotient of 62. The Sensory Processing Impact Child Evaluation (SPICE; Ben-Sasson & Kadlec), an observational measure designed for the current study, included 21 sensory behavioral responses grouped into three scales: Seeking, Under-responsivity, and Over-responsivity. The presence of behaviors was coded from videos during a battery of assessments in the laboratory. Parent data were collected from the Infant Toddler Sensory Profile (ITSP; Dunn, 2002).
Results: Inter-rater reliability $ICC_{(2,2)}$ on the SPICE was 0.83 for the Total score, 0.62 for Seeking, 0.89 for Under-responsivity, and 0.80 for Over-responsivity. For comparable items, Seeking was observed for toddlers an average of 64% on the SPICE compared with 55% on the ITSP, Under-responsivity was 26% on the SPICE compared to 60% on the ITSP, and Over-responsivity was 17% on the SPICE versus 59% on the ITSP. Although Seeking was the most frequently coded sensory behavior, a higher percentage of toddlers had extreme (>2*SD* above age norms) ITSP Under- and Over-responsivity scores (77% and 29% respectively) than extreme Seeking scores (0%).
Conclusions: Findings highlight the need for valid and reliable methods to assess sensory behaviors in multiple contexts through parent and clinician's perspectives so that interventions can match the demands required for children's participation in the various contexts.

110 108.16 Modification of the Preferential Looking Technique for use with Children with Autism. L. Hancock*[1], J. Bebko[1], K. Wells[1] and J. H. Schroeder[2], (1)*York University*, (2)*York University, Toronto*

Background: Intermodal perception describes the capacity to simultaneously process and organize sensory information that is arriving from more than one modality. One method to assess the development of auditory-visual intermodal perception is the preferential looking technique (Spelke, 1976). This involves two side-by-side visual displays, with an auditory track matched to only one display. Intermodal perception is considered to be present if the child shows a preference for one of the displays as assessed by calculating the total amount of time spent looking at either the left, or right screen. Using this technique, Bebko et al. (2006) have identified a deficit in the processing of audio-visual intermodal information in children with autism. However, typically the sizes of difference observed are small due to a chance level of 50%. In this study we modified the methodology to lower the chance level in order to significantly sharpen the effects that distinguish the groups.

Objectives: To develop a preferential looking technique that can be more sensitive to differences between autism and comparison groups.

Methods: 10 children (ages 6-10 years) with autism were shown a video with four screens, one in each quadrant of the display with an audio track that was temporally matched to only one of the screens. Preferential looking was assessed based on a) total time spent looking at each screen and b) longest look.

Results: Results are compared to data previously collected with children with autism using a 2-screen video presentation. Analysis is ongoing.

Conclusions: These findings will demonstrate which of two methodologies is more sensitive and accurate in detecting differences in intermodal processing between children with autism and typical children.

109 Tools You Can Use: Identify Early Signs with the ASD Video Glossary.

Speaker: A. M. Wetherby*Florida State University*

This lunch session will demonstrate an innovative Web-based tool designed to help professionals and parents learn more about early red flags and diagnostic features. A Collaborative effort by Autism Speaks, Florida State University, and First Signs.

Invited Educational Symposia Program

110 Linking Genes and Behaviour Using Brain Imaging: A Practical Guide to a Dark Art.

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

Autism spectrum disorder is perhaps the most highly genetic neurodevelopmental disorder. Also there is increasing understanding that the symptoms are biologically based; and that particular brain systems are implicated.
The genetic determinants of the biological differences, however, are unknown. Also there is much debate as to how the genome can, and cannot, be related to the neurobiological endophenotype.
These challenges have been confronted by researchers in fields outside autism. Hence the purpose of this program is to learn from those individuals who are experts in applying genetic approaches to behaviour and brain imaging; and to provide an overview of current work in autism.
Professor Robert Plomin will firstly discuss theoretical issues and problems in relating genes to behaviour, exploring how findings from work in the SGDP centre illuminates the genetic and environmental contributions to autism/social behaviour, and why therefore we need to be extremely careful when 'doing brain'.
Professor Mick Brammer will discuss how, if you still want to carry out a genetic imaging investigation, you should design the study and analyse the data.
Professor Gunter Schuman will then give an overview on how similar problems have been addressed, and solved, by researchers in Addictions.
Professor Joe Piven discuss how early 'genetic' imaging studies in autism are progressing; problems and solutions.

110.1 Introductory Remarks.

110.2 From genome to phenome: Autistic spectrum disorder as an example. R. Plomin*, *Institute of Psychiatry*

A complete understanding of understanding of behavioural disorders will involve connecting the dots between all of levels of analysis between genes and behaviour – from genome, transcriptome, epigenome, and proteome to the brain, mind and behaviour. In the case of autistic spectrum disorder (ASD), the behavioural level of analysis has been useful in showing not only high heritability but also genetic heterogeneity among the three components of the autistic triangle (social, non-social and communicative problems); progress towards identifying genes responsible for this high heritability has been slow, in part because it seems likely that there are many genes of small effect. The brain level of analysis can be useful in understanding ASD to the extent that it is related to the behavioural problems that we call ASD. However, I disagree with the notion that, as compared to behaviour, the brain is a simpler endophenotype, more heritable, or caused by a smaller number genes. Thus, it will not be easier to identify replicable gene associations at the brain level of analysis and if such genes are found the crucial question is whether the genes will be associated with ASD behaviours. It seems much more likely that genes will be identified for ASD at the behavioural level, and then these genes will be used as small footholds in the climb towards understanding the complexities of the brain as it relates to ASD.

110.3 An integrated approach to identify neurobiological mechanisms of addictive behaviour. G. Schumann*, *Institute of Psychiatry, King's College London*

Addiction disorders are frequent oligogenic disorder with complex inheritance patterns and interplay of genetic and environmental factors contributing to their phenotype. They are heterogenous by nature with common and distinct genes contributing to different phenotypes of substance use disorders. To identify the genetic and neurobiological basis of addiction disorders we take into account these characteristics by identifying candidate genes shown to alter drug taking behaviour in animal models and analyse them for association with analogous phenotypes of substance use disorders in humans. A recent example of this approach, the characterization of the role of a circadian rhythm gene Period 2 in human alcohol drinking behaviour will be presented (Nature Medicine, 2005; 11: 35-

42). Neuroimaging permits reduction in phenotypic heterogeneity by measuring specific brain functions implicated in the etiology of addiction disorders and link them to genetic variations and behavioural characteristics relevant to disease processes. We will provide examples demonstrating the validity of this approach by analyzing the association of 5-HTT and COMT genotypes with fMRI-response to negative emotional cues (Nature Neuroscience, 2005; 8: 20-21, J. Neuroscience, 2005; 25: 836-42, Mol. Psychiatry 2007, 12:307-17). The integration of our candidate gene approach using behavioural animal models and neuroimaging studies will be described by providing an outlook of a recently funded EU-integrated gene-neuroimaging project "IMAGEN".

110.4 Relating genetic and imaging data - current methodlogy and how we might improve it. M. Brammer*, *Institiute of Psychiatry, Kings College London*

Relating genetic and brain imaging data - current methodology and how we might improve it. Mike Brammer, Brain Image Analysis Unit, Department of Biostatistics and Computing, Institute of Psychiatry, Kings College SE5 8AF. In recent years, genetic analysis and functional and structural neuroimaging have been widely used to probe brain normal and abnormal brain function. Papers in which these approaches are combined are also becoming increasingly common. The purpose of this presentation is to review the approaches that are currently being used, to discuss their strengths and limitations and to introduce approaches that allow us deal with some statistical problems in data analysis and to exploit multivariate aspects of the data sets that are often ignored. These methods might be useful when dealing with combined effects of multiple genes on distributed changes in brain structure and function.

110.5 Imaging, Genetics and The Developing Brain in Autism. J. Piven*, *University of North Carolina*

This presentation will review the results of longitudinal MRI brain imaging studies, conducted by our research team and collaborators, focused on two year olds with autistic disorder and two year olds with Fragile X Syndrome, followed up at 4 years of age. MRI brain imaging data will be presented reviewing key findings in autism as well as Fragile X Syndrome. Results from preliminary studies of selected candidate genes and their relationship to brain volume will be reviewed. Contrasts between autistic individuals with and without Fragile X will be discussed that provide insights into the complexity of genetic mechanisms underlying autistic behavior.

110.6 Linking Genes and Behaviour Using Brain Imaging: A Practical Guide to a Dark Art. D. Murphy*[1], R. Plomin[1], M. J. Brammer[2], G. Schumann[1] and J. Piven[3], (1)*Institute of Psychiatry, King's College London*, (2)*Institute of Psychiatry, Kings College London*, (3)*University of North Carolina*

Autism spectrum disorder is perhaps the most highly genetic neurodevelopmental disorder. Also there is increasing understanding that the symptoms are biologically based; and that particular brain systems are implicated.

The genetic determinants of the biological differences, however, are unknown. Also there is much debate as to how the genome can, and cannot, be related to the neurobiological endophenotype.

These challenges have been confronted by researchers in fields outside autism. Hence the purpose of this program is to learn from those individuals who are experts in applying genetic approaches to behaviour and brain imaging; and to provide an overview of current work in autism.

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Professor Joe Piven discuss how early 'genetic' imaging studies in autism are progressing; problems and solutions.

Lifetime Achievement Award and Presentations Program

111 Lifetime Achievement Award

111.1 Student And Travel Awards.

111.2 Introductory Remarks.

111.3 Autism at age 60+: some contributions of a fascinated participant. I. Rapin*, *Albert Einstein College of Medicine*

Oral Presentations Program

112 Clinical Phenotype 1

112.1 The Autism Diagnostic Observation Schedule – Toddler module: Preliminary findings using a modified version of the ADOS. R. Luyster*[1], W. Guthrie[2], K. Gotham[2], S. Risi[2], P. DiLavore[3] and C. Lord[2], (1)*Autism Consortium*, (2)*University of Michigan Autism and Communication Disorders Center*, (3)*Division TEACCH*

Background:

The Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000) is widely accepted as a "gold standard" diagnostic instrument, but its downward limits restrict utility in research samples of very young children at risk for ASD.

Objectives:

The objective of the present investigation was to modify the ADOS for use in very young children.

Methods:
A modified ADOS, the ADOS-Toddler module (ADOS-T), was used in 272 evaluations. Participants included children 12-30 months of age with either best estimate diagnoses of ASD, non-spectrum developmental delay or typical development. A final set of protocol and algorithm items was selected based on their success in discriminating the diagnostic groups.

Results:

For all children ages 12-20 months and nonverbal children 21-30 months, a new ADOS-T algorithm yielded a sensitivity and specificity both of 95%. For verbal children 21-30 months, the revised "Some Words" Module 1 algorithm (Gotham et al., 2007) yielded a sensitivity of 93% and a specificity of 95%.

Because of the variability in early development, we proposed to use scores on the algorithm to indicate a range of concern, rather than employ the traditional cutoffs. For all children ages 12-20 months and nonverbal children 21-30 months, a score of 12-15 on the ADOS-T algorithm indicates mild concern, and scores >15 indicate significant concern. Similarly, for verbal children 21-30 months, scores of 7-10 on the "Some Words" algorithm indicate mild concern, and scores >10 indicate significant concern.

Conclusions:

The ADOS-T appears to be a useful addition to the existing ADOS. It is appropriate for use in children as young as 12 months and successfully discriminates between diagnostic groups, yielding high sensitivity and specificity. Given the variability of behavior in very young children, the proposed "range of concern" may be a more useful interpretation of algorithm results than the traditional "cutoffs" approach.

112.2 Are the three domains of autism spectrum disorders (social interaction, communication, and stereotypies and rigidity) clustering together in the general population at 18 months?. K. Beuker*[1], S. Schjolberg[2], K. Kveim Lie[2], M. Lappenschaar[1], M. Hornig[3], M. Bresnahan[3] and J. Buitelaar[1], (1)*Radboud University Nijmegen Medical Centre*, (2)*Norwegian Institute of Public Health*, (3)*Columbia University*

Background: ASD are defined by deficits in social interaction and communication, and by stereotyped behaviour. It is unclear whether

these three domains correlate in the general population at young age, and cluster together at the level of the individual.

Objectives: Insight into the underlying structure of ASD-symptoms in the general population may facilitate the development of screening-instruments and screening-procedures.

Methods: Data have been collected in the context of the ongoing prospective Autism-Birth-Cohort-Study, funded by the Norwegian Institute of Public Health, and National Institute of Health of the USA. Mothers of 13,346 18-months-old children completed a questionnaire including items about their child's socio-emotional development and behaviour. The DSM-IV three-domain classification of ASD at 18 months was tested using exploratory and confirmatory factor analyses. Latent Class Analysis (LCA) was conducted to empirically identify homogeneous groups of children.

Results: An exploratory factor analysis extracted a three-factor solution with a satisfactory fit and meaningful interpretation. Confirmatory factor analysis demonstrated further support for this three-factor structure. LCA revealed four 4 classes. Class 1 (0.7% of sample) has the highest scores of all classes on the domains of Social interaction and Communication, but moderate scores on the domain Stereotypies; Class 2 (18.6% of sample) scores in-between class 1 and 4 on Social interaction and Communication but scores low on Stereotypies; Class 3 (13.4%) scores low on the domains of Social interaction and Communication, but the highest of all classes on the domain of Stereotypies; Class 4 (67.4% of sample) represents the reference group which relatively low scores on all domains.

Conclusions: The underlying structure of ASD symptoms is generalizable to the population at 18 months. In the general population four classes can be identified with a clear distinction between the clusters Social interaction and Communication on one hand and the cluster Stereotypies on the other hand.

112.3 Predicting social competence in ASD from age 2-age 8. S. J. Rogers*[1], S. Hepburn[2], A. Philofsky[3], D. Most[4] and D. Fidler[4], (1)*UC Davis*, (2)*University of Colorado at Denver*, (3)*University of Colorado Health Sciences Center*, (4)*Colorado State University*

Background: Current developmental explanatory theories of autism include the imitation/mirror neuron theory (Rogers/Pennington,Williams), executive function theory (Russell), triadic joint attention/intersubjectivity theory (Mundy, Tomasello), sensory overarousal theory, and a dyadic social-emotional theory (Hobson and colleagues).

Objectives: to compare the predictive power of variables involving imitation, joint attention, emotional , executive function, and imitation at age 2 and social competence at age 8.

Methods: We used a longitudinal design, from age 2-3 to ages 8-10 in two groups of children, Autistic Disorder (n = 31), and other developmental difficulties (n = 33) matched on MA and CA. The test battery at age 2 included measures of intellectual function, adaptive behavior, and autism severity, as well as measures of executive function (spatial reversal), imitation (manual, oral, and object), initiating and responding to joint attention, emotional communication (directed smiles), and sensory abnormality (via parent report).

Results: At age 2-3, only three measures: emotion (directed smiles), initiating joint attention, and imitation, significantly differentiated the groups ($p<.5$). At age 8, the ASD group was significantly superior to the DD group in overall IQ (20 point advantage; $p=.2$) and nonverbal IQ (25 point advantage, $p=.002$). Regression analyses revealed that, for ASD, imitation and executive function at age 2 each accounted for a significant amount of the variance in age 8 Vineland language and social skills and Verbal IQ. IJA was significant only for communication outcomes. In the DD group, almost no variables predicted significantly to age 8 outcomes.

Conclusions: Age 2 neuropsych variables had much more influence on age 8-10 outcomes for ASD than DD group, and were more

predictive than age 2 IQ measures. The imitation variable alone carried significant weight in all outcome measures. The nature of the IQ deficits appear different in ASD, more linked to the social deficits, than in DD.

112.4 Down Syndrome, Regression, and Autism Spectrum Disorders. S. Hyman*[1], S. B. Sulkes[1], C. I. Magyar[1], E. Van Wijngaarden[1], L. Rodgers[1], S. Nagel[1], A. Diehl[1] and N. Roizen[2], (1)*University of Rochester*, (2)*Case Western Reserve*

Background: Regression or loss of language, social, or other skills occurs between 18-24 months in about 25% of children with ASD; this may not be true in children with DS with or without ASD.

Objectives: To determine the prevalence of regression in children with DS with or without ASD, and examine its relationship to medical illness and developmental level.
Methods: Children with DS (ages 3-14 years) in NY state were recruited to examine their medical and behavioral characteristics. The Autism Diagnostic Interview-Revised (ADI-R) was completed on 174 participants and responses were used to identify regression. Medical and behavioral characteristics were described in terms of means and proportions.

Results: Nineteen children (11%; 95% confidence interval (CI) = 7-17) were identified with regression; 6 with loss of language, 3 with loss of language and other skills, and 10 with loss of other skills only. Eleven of the 19 subjects (58%; CI = 34-79) related loss to medical illness, the most common being infantile spasms/seizures. The average age at regression of language and other skills was 44 (standard deviation (SD) = 19) and 27 (SD = 25) months, respectively. Eleven of 19 children with regression (58%; CI = 34-79) were positive on the ADI-R diagnostic algorithm. Regression was reported in 11 of 70 children (16%; CI = 8-27) with positive ADI-R. The Vineland ABC was 63 in children with regression as compared to 68 in those without (p-value for difference = 0.52).

Conclusions: There appears to be greater variability in age of regression in children with DS relative to what has been reported for children with ASD only. Further research is needed to understand the nature and timing of regression, potential differences in the phenotype, and medical influences on regression in children with DS with or without ASD.

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112.5 No evidence for higher rates of gastrointestinal problems in young children with ASDs versus those with other developmental delays. H. Boorstein*, M. Helt, E. Troyb, M. Barton, T. Dumont-Mathieu, S. Hodgson and D. Fein, *University of Connecticut*

Background: Parental reports and published research have suggested a possible increased incidence of gastrointestinal (GI) symptoms in children with autism spectrum disorders (ASDs).

Objectives: To investigate feeding and gastrointestinal complaints in a community-based sample of young children with ASDs and other developmental delays.

Methods: The 236 participants were given a developmental evaluation after screening positive on the M-CHAT. After evaluation at approximately age two, 134 children were diagnosed with an ASD and 102 with other developmental delays (DD).

Results: X^2 analyses revealed no significant differences between the ASD and DD groups in parentally reported spitting up/vomiting, food sensitivities or allergies, constipation, diarrhea, or other GI symptoms. Significantly higher rates of early feeding problems and gagging in infancy were found in the DD sample. Analyses comparing the characteristics of children with ASDs with and without GI symptoms found no significant differences in autism symptom profiles or severity, developmental levels, or adaptive skills. 106 children (70 with ASD and 36 with DD) were re-evaluated at approximately age four. There were no significant differences found between diagnostic groups in parentally reported diarrhea, constipation, other GI problems, or food allergies. There continued to be no significant differences between children with ASDs with and without GI complaints.

Conclusions: In this sample of young community-based children with ASDs and other developmental delays, no significant group differences in parentally reported feeding problems and gastrointestinal symptoms were found at age two or at age four. Most published research has been conducted at specialty GI or DD/ASD clinics with older children. The results of this study suggest that their findings may not be applicable to young children or to children evaluated in community settings. While GI problems may be increased in children with developmental disorders, we found no evidence that they were specific to autism spectrum disorders.

112.6 Bowel Symptoms in Children with Autism. G. Antolovich*, J. E. Walstab, A. M. McVeigh-Dowd and C. Marraffa, *Royal Children's Hospital*

Background: It is reported that children with autism have high rates of gut symptoms, resulting in the use of a range of therapies to modify gut function.

Objectives: To determine how often gut symptoms occur in children in a community based sample of children with autism (ASD), children with other developmental disabilities excluding children with a motor disability (DD) and typically developing children (TD).

Methods: Data was collected by parent completed questionnaire. Children (n=134) aged four to six years were recruited from kindergartens and early intervention programs. Results were analysed using SPSS 15.0 and Stata 10.

Results: There were no differences between the three groups demographically, or for measures of general health, uptake of immunizations, and use of complementary therapies. Report of allergy or food intolerance was common in children with ASD (ASD 47.5%, DD 33.3%, TD 13.5%, $p < 0.001$), and were more likely to have had dietary manipulation (ASD 44.4%, DD 18.2%, TD 15.6%, $p < 0.001$). Chewing or swallowing difficulties, vomiting, abdominal bloating, abdominal pain and diarrhoea were more commonly reported in the ASD and DD groups. High rates of constipation were reported in all three groups (ASD 80.0%, DD 50.0%, TD 53.8%, $p = 0.12$). A large proportion of children with ASD (57.8%) and DD (44.1%) had seen a medical doctor for the management of bowel symptoms (cf. TD 13.2%, $p<0.001$). Almost half of the parents of children with autism felt their child's bowel habit was not typical of other children of a similar age (ASD 44.4%, DD 19.2%, TD 5.1%, $p<0.001$).

Conclusions: Children with developmental disability have higher reported rates of gut symptoms and gut related problems. This raises the possibility that gut related symptoms in children with autism may be a function of their underlying developmental disability, rather than being directly related to their diagnosis of autism.

112.7 The Relationship between Adaptive Functioning and Symptom Severity in Toddlers with ASD. C. Saulnier*, K. Chawarska and A. Klin, *Yale Child Study Center*

Background:

Research has shown little relationship between adaptive functioning and symptomatology in higher functioning school-aged individuals with ASD, as well as striking deficits in adaptive skills compared to IQ.

Objectives:

The relationship between adaptive functioning (Vineland) and symptomatology (ADOS-G, Modules 1 and 2) is investigated in relation to age and IQ in a longitudinal sample of toddlers at ages 2 and 4.

Methods:

Participants included 101 toddlers with ASD with mean ages of 2.4 years at Time 1 and 4.3 years at Time 2.

Results:

Contrary to older individuals, strong negative relationships were found between Vineland and ADOS Socialization and Communication scores [Communication $r\ (100) = -.40$ and Socialization $r\ (100) = -.53$ at Time 1, and $r\ (100) = -.51$ and $r\ (100) = -.61$ at Time 2, respectively], suggesting that toddlers with

less severe social and communicative impairments have more advanced adaptive skills. Paired t-tests indicated that, over time, children made significant improvements in adaptive Communication skills ($t = 3.26, p<.1$), and their Communication ($t = 8.24, p<.1$) and Social ($t = -3.91, p<.1$) symptoms as captured by the ADOS-G improved over time. Yet, no significant change in standard scores was noted in the adaptive Socialization skills area ($t = .43, p=.67$). Despite progress, significant discrepancies were evidenced between mean Mullen and Vineland scores at Time 1 ($t = 2.37, p<.1$) and Time 2 ($t=9.20, p<.1$), with this gap widening with age.

Conclusions:

Results suggest that in very young children, level of symptomatology impacts adaptive functioning; however, minimal gains are evident in functional social skills over time regardless of symptom severity. Of further concern, despite progress in both developmental and adaptive skills, the gap between developmental skills and adaptive functioning widens with age, suggesting that the acquisition of functional skills is not keeping pace with developmental gains.

112.8 Diagnostic and Developmental Trajectories in Toddlers with ASD. S. Macari*[1], K. Chawarska[1], A. Klin[2] and F. R. Volkmar[2], (1)*Yale University School of Medicine*, (2)*Yale Child Study Center*

Background:

Increasing awareness among parents and professionals of early signs of ASD has led to a rise in the number of toddlers referred for a diagnostic evaluation in the second year of life. The question of the stability of social-communicative impairments remains to be clarified, as well as the extent to which the constellation of delays and abnormalities observed in the second year is unique to ASD.

Objectives:

To examine developmental and diagnostic trajectories of children evaluated for ASD in the second year and to identify profiles of skills that are predictive of the diagnostic outcome in the fifth year.

Methods:

Developmental and social-communication skills of 89 toddlers were assessed at Time 1 (age: M = 21.5 months, SD = 4.9) and Time 2 (age: M = 46.9 months, SD = 7.7) and clinical best estimate diagnosis (CBE) was assigned at both times. Groups with stable diagnostic presentation (e.g., AUT-AUT; DD-DD) and unstable presentation (e.g., AUT-PDD) were identified and compared on cognitive and social-communication profiles at Time 1.

Results:

Diagnostic trajectories from Time 1 to Time 2 were stable in the majority of toddlers with ASD (77%). In a minority of toddlers initially diagnosed with autism (26%), marked improvements warranted a change in diagnosis at follow-up (AUT-PDD). While their social behavior at Time 1 was similarly impaired as the AUT-AUT group, they tended to have fewer repetitive behaviors and their overall intentionality of communication was rated as more impaired by experienced clinicians. Cognitive profiles across the diagnostic trajectory groups differed significantly at Time 1.

Conclusions:

Stability of the CBE diagnosis of ASD in the 2nd year appears satisfactory. Examination of cognitive profiles can be helpful in making diagnostic distinctions. In a subgroup of children with ASD, early social dysfunction might be exacerbated by profound impairments in intentional communication.

Oral Presentations Program

113 Epidemiology 1

113.1 Autistic traits and birth problems: A study suggesting that both genes and environment play a part in their association. A. Ronald*[1], F. Happé[2], P. Bolton[3] and R. Plomin[4], (1)*Birkbeck College*, (2)*Institute of Psychiatry, Kings College London*, (3)*Institute of Psychiatry*, (4)*Institute of Psychiatry, King's College London*

Background: Autistic spectrum disorders (ASD) are thought to be caused by a combination of genetic and environmental risk factors, but identifying specific environmental triggers has proved difficult. Problems during the birth process have been shown to be associated with ASD but whether these problems are an independent cause of ASD, or a consequence of an existing liability for ASD, is unknown. Previous research has shown that many apparently environmental variables show genetic influence. Objectives: The current project aimed to explore whether perinatal problems are associated with dimensional measures of autistic behaviours, whether birth problems are themselves influenced by genetic factors, and whether there is evidence that the association between birth problems and autistic traits could be due to environmental influences. Methods: Parents of over 20,000 twin pairs from the Twins Early Development Study, a UK-based longitudinal twin cohort, reported on birth-related problems one year after the twins were born. When the twins reached middle childhood, parents and teachers of over 6000 pairs reported on the twins' autistic behaviours. Results: Weak but significant and positive correlations were observed between birth problems and dimensional measures of autistic behaviours at ages 7-9. Twin model-fitting revealed that child-specific birth problems were modestly heritable (~30%), as well as showing significant shared and nonshared environmental influences. Difference scores between identical (monozygotic, MZ) twins, on a child-specific birth problems scale correlated significantly with MZ twin difference scores on autistic traits. Conclusions: These data reveal that at least some types of birth problems may be driven by genetic influences, raising the possibility that part of the association between birth problems and autistic behaviours could be genetically influenced. The correlations between MZ differences reveal, however, that nonshared environment also plays a significant role in this association.

113.2 Obstetrical and neonatal factors and risk of autism. L. Dodds*[1], D. B. Fell[2], S. Shea[1], A. Allen[2], B. A. Armson[1] and S. E. Bryson[1], (1)*Dalhousie University*, (2)*IWK Health Centre*

Background: It remains unresolved whether obstetric or neonatal complications are independent factors in autism etiology, contribute via gene-environment interactions or reflect an epiphenomenon, (i.e., familial factors predispose to obstetric complications and to autism).
Objectives: Our objective was to identify obstetric/neonatal factors associated with the subsequent development of autism and assess whether these contribute to its etiology.

Methods: Women who gave birth between 1988 and 2002 were identified from a population-based perinatal database in Nova Scotia, Canada. Diagnoses of autism among children of women in this cohort were identified from anonymous linkages to administrative databases with relevant diagnostic information from 1992 to 2005. Information on maternal conditions, prenatal factors, obstetrical and neonatal conditions was evaluated. Cox proportional hazards regression models were used to estimate adjusted relative risks and 95% confidence intervals. Analyses controlled for factors suggestive of a strong genetic etiology (e.g., having an affected sibling or maternal psychiatric/neurologic conditions).

Results: Among 129733 children born between 1988 and 2002, there were 924 children with an autism diagnosis between 1992 and 2005. After controlling for factors suggestive of a strong genetic etiology, the following obstetric/neonatal factors were significant: pre-pregnancy weight ≥ 90 kg (RR=1.6, 95% CI 1.2-2.0), ≥ 18-kilogram pregnancy weight gain (RR=1.2, 95% CI 1.0-1.4), <18-month inter-pregnancy interval (RR=1.5, 95% CI, 1.1-2.0), maternal prescription drug use during pregnancy (RR=1.7, 95%CI 1.0-2.8), induced labour (RR=1.2, 95% CI 1.0-1.5) or no labour (RR=1.3, 95% CI 1.0-1.7) (versus spontaneous labour), male infant sex (RR=4.3, 95% CI 3.5-5.2), 5-minute Apgar score ≤ 3 (RR=3.6, 95% CI 1.2-11.3), and presence of a major congenital anomaly (RR=7.2, 95% CI 3.6-14.5).

Conclusions: Some obstetrical and neonatal factors appear to have an independent role in autism etiology. The association between pre-pregnancy obesity and excessive weight gain

during pregnancy and increased autism risk are novel findings that require further investigation.

113.3 Antenatal Ultrasound Exposure and Risk Of Autism Spectrum Disorders. J. K. Grether*[1], X. Li[1], C. Yoshida[2] and L. A. Croen[2], (1)*California Department of Public Health*, (2)*Kaiser Permanente*

Background: Frequency of exposure to antenatal ultrasound (U/S) has increased since it's introduction in the 1970's, and U/S protocols and techniques have also changed, leading to concerns that antenatal U/S exposure may contribute to autism spectrum disorders (ASDs). Although prior studies have not evaluated an association with ASDs, some studies have suggested an association with dyslexia or left-handedness.

Objectives: To evaluate antenatal B-mode U/S exposure and risk of ASDs in a case-control study within a large integrated health care delivery system.

Methods: Singleton children enrolled in Kaiser Permanente (KP) and born 1995-1999 were included. Cases were identified from diagnostic codes and controls were randomly sampled within gender and birth month strata. Primary analyses were limited to simplex cases (N=361) and controls without siblings with ASD (N=393). Information on U/S scans and other clinical data were obtained from multiple electronic files and medical records and demographic data were obtained from birth certificates. *Chi-square* tests and multivariable logistic regression models were used to evaluate case-control differences.

Results: Demographic characteristics of cases were similar to those of controls, but cases had slightly lower gestational age at birth ($p=0.54$) and higher maternal education ($p<0.001$). Thirteen percent of both cases and controls had no U/S scans, 29% of cases and 28% of controls were exposed in the 1st trimester, 78% of cases and 79% of controls in the 2nd trimester, and 28% of both cases and controls in the 3rd trimester. Cases were statistically similar to controls in adjusted analyses with regard to the number and type (complete OB, limited OB, transvaginal) of U/S scans performed throughout pregnancy and for each trimester.

Conclusions: Children with autism and control children born 1995-1999 were similar with regard to antennal U/S exposure, indicating that fetal exposure to B-mode ultrasound is unlikely to increase the risk of ASD.

113.4 Household Pesticide Use in Relation to Autism. I. Hertz-Picciotto*[1], I. N. Pessah[2], R. Hansen[1] and P. Krakowiak[1], (1)*University of California at Davis*, (2)*University of California at Davis, M.I.N.D. Institute*

Background: Pesticides affect a number of targets in the CNS, and cross the placenta. One previous report suggests a link between maternal residential proximity to commercial organochlorine pesticide exposure during early prenatal life and the risk of autism. That study did not evaluate individual exposures to household pesticides.

Objectives: To examine household pesticide use during the prenatal period or early postnatal period in relation to autism.

Methods: Participants were from the CHARGE (Childhood Autism Risks from Genetics and the Environment study, a large population-based case-control study in California. Autism spectrum disorders were confirmed using the ADI and ADOS. Mothers were extensively interviewed regarding demographics, lifestyle, and prenatal and early postnatal exposures of the child. Questions addressed use of numerous household products, including insecticides for flies and ants, pet shampoos, and weed control products. Interview data were available for 333 ASD cases and 198 confirmed typically developing controls. Logistic regression models were adjusted for family socioeconomic status. An index exposure period was defined as three months prior to conception through the child's first year of life.

Results: Mothers of ASD children were twice as likely to report using pet shampoos for fleas or ticks during the index period as compared with control mothers: adjusted Odds Ratio (aOR) = 2.0, 95% Confidence Interval (CI) = [1.2, 3.6]. When examined by trimester, the

strongest association was during the second trimester: aOR = 2.6, 95% CI = [1.3, 6.0].

Conclusions: The higher prevalence of self-reported use of pet shampoos by CHARGE study mothers of children with ASD could be due to reporting bias, although many other products did not show differences. Pyrethrins have largely replaced organophosphates for flea control, but early life exposure to pyrethrins has been shown to compromise the blood-brain barrier in rodents, raising concern about prenatal and early postnatal exposures.

113.5 PRENATAL HORMONE MARKERS AND AUTSIM SPECTRUM DISORDERS. G. Windham*[1], M. Anderson[2] and J. Grether[1], (1)*CA Department of Public Health*, (2)*Impact Assessment, Inc.*

Background: Hormonal etiologies have been proposed to explain some of the observed patterns of autism occurrence.

Objectives: To explore direction for further studies, we linked hormonal data from routine prenatal screening to autism prevalence data in California.

Methods: Our statewide autism surveillance links data from the Department of Developmental Services to birth certificates. This surveillance data was linked to maternal serum triple marker screening data for two birth years, 1996 and 2002. Over 50% of pregnancies were screened, yielding nearly 600,000 singleton births and 2,500 autism cases for analysis. The three markers are 1) maternal serum alpha-fetoprotein (MSAFP), a glycoprotein that may also bind estrogen, 2) unconjugated estriol (uE3), the principal estrogen metabolite found in blood during pregnancy, and 3) human chorionic gonadotropin (hCG), important for the maintenance of pregnancy and steroid regulation. Analyte concentration is measured and also converted to multiples of the median (MoM) for reporting risk of various fetal conditions. We examined the marker levels as continuous and categorical variables, comparing autism cases to remaining births, and will adjust for additional factors in multi-variate models.
Results: For 1996 and 2002 combined, mean and median MSAFP levels were slightly, but statistically significantly, higher in mothers of autistic children. In contrast, uE3 mean levels were significantly lower among case mothers. The pattern persisted when markers were treated as categorical variables, with significant odds ratios around 1.2 for the highest decile of MSAFP and the lowest decile of uE3, compared to the mid quartile range (25th-75th percentiles). Risks of similar magnitude were noted for both the high and low deciles of hCG.
Conclusions: Low and high levels of these markers are associated with adverse fetal outcomes. Should the differences we observe persist after further analyses, it would suggest these hormone markers may also be related to autism, warranting further study.

113.6 Induction and Augmentation of Labor and Autism. C. K. Walker*[1], P. Krakowiak[1], R. L. Hansen[2] and I. Hertz-Picciotto[2], (1)*University of California, Davis*, (2)*University of California at Davis*

Background: Fetal life and birth represent key periods of developmental vulnerability during which environmental influences may have considerable impact. In this study, we explore whether induction and augmentation of labor are associated with autism.

Objectives: We hypothesize that prostaglandins and oxytocin administered during the perinatal period to initiate or enhance labor alter fetal neurobehavioral development.

Methods: The CHARGE (Childhood Autism Risk from Genetics and the Environment) Study is an ongoing case-control study of the environmental etiology of autism. The study population consists of 232 children with autism and 129 population-based controls for which we have medical records documenting their mother's labor. Demographic data, use of drugs to induce or augment labor, and covariates related to the labor and delivery process were abstracted in a systematic fashion. Logistic regression was used to examine the relationships between use of such drugs and autism status.

Results: After adjustment for mother's education, preeclampsia, cesarean delivery, and date of delivery, use of oxytocin was less

common among mothers whose children developed autism compared with those whose babies developed typically (30% vs 40%, AOR 0.46, 95% CI 0.27, 0.80). After controlling for oxytocin administration, use of vaginal prostaglandins was more common among mothers of children with autism compared with controls, although this association failed to achieve statistical significance (13% vs 9%, AOR 2.10, 95% CI 0.93, 5.00).

Conclusions: Oxytocin is released in the hypothalamus and amygdala in response to stimuli including stress, and modulates pro-social, anxiolytic and antistress actions. Fetal exposure to exogenous oxytocin during the perinatal period may enhance or protect neurodevelopment. Prostaglandins regulate many immunological processes, including cytokines IL-1, IL-4, IL-6 and TNFa & ß, which critically influence brain development and function. It is plausible that perinatal exposure to exogenous prostaglandins may result in abnormal brain development, possibly via disruption of normal immune function.

113.7 Risk of autism spectrum disorder in children with unprovoked seizures in the first year of life – A population-based study. E. Saemundsen*[1], P. Ludvigsson[2] and V. Rafnsson[3], (1)*State Diagnostic and Counseling Center*, (2)*Landspitali, University Hospital*, (3)*University of Iceland*

Background: A subgroup of children diagnosed with autism spectrum disorder (ASD) has a history of unprovoked seizures in the first year of life.

Objectives: To study the association between unprovoked seizures in the first year of life and ASD.

Methods: Children diagnosed with seizures in the first year of life during the period 1982-1998 were identified in hospital records of all the pediatric in-patient facilities in Iceland. Of 121 children five had died and one lived abroad. The parents of 115 children were invited into a study of possible ASD. The Social Communication Questionnaire was used as an initial test of autistic behaviors, followed by the ADI-R and the ADOS and/or the CARS. Prevalence of ASD as the percentage of cases and exact 95% confidence intervals (CI) were calculated. Logistic regression was used to calculate odds ratio (OR) and 95% CI.

Results: Ninety-five children participated (82.6%). Of these, 17 (17.9%) had infantile spasms (IS) and 78 (81.1%) had other types of seizures. Thirteen children or 13.7% (95% CI, 7.5-22.3) had ASD, eight females and five males. Six of the children with ASD had IS, and seven had other types of epilepsy. All but one had intellectual disability (ID), and six had profound ID (IQ<20). The OR was 1.55 (95% CI, 0.33-7.37) for children with IS compared to those without IS, adjusted for symptomatic origin of seizures. The OR was 8.73 (95% CI, 1.88-40.54) for children with symptomatic origin of seizures compared to those with non-symptomatic seizures, adjusted for IS.

Conclusions: High prevalence of ASD was found in children with a history of unprovoked seizures in the first year of life. There was an overrepresentation of the female gender and ID in the ASD group. The symptomatic origin of seizures increased the risk of ASD, rather than IS.

113.8 AUTISM SPECTRUM DISORDERS IN PRESCHOOL CHILDREN: EFFECT OF CHANGES IN DIAGNOSTIC PRACTICES. N. Nassar, G. Dixon, J. Bourke, C. Bower, E. Glasson, N. De Klerk and H. Leonard*, *Telethon Institute for Child Health Research*

Background: It is unclear whether the increase in autism prevalence over the past two decades is a real increase or due to changes in diagnosis and ascertainment of autism spectrum disorders (ASD). Objectives: The aim of this study was to examine the trend of ASD over time and the possible effects of diagnostic substitution, changes in diagnostic criteria and eligibility for service provision. Methods: A population based study was conducted among a birth cohort of children born in Western Australia between 1983 and 1999 and diagnosed with an ASD up to 2004. The trend in the birth prevalence of ASD and corresponding diagnosis of intellectual disability (ID) during the study period was investigated. Sub-group analysis of children aged five years and under where complete data were available was also conducted to examine the incidence and trend

of ASD diagnoses over time. Results: Prevalence of all ASD increased by 29.6% per annum, with autism rising by 20.8% each year. Up to 1992, diagnosis of ID was more common but it was then surpassed by ASD and with the prevalence of severe ID decreasing by 6.2% each year. From 1992, for children aged five years or less the incidence of autism increased significantly with an annual increase of 27.4% as did PDD-NOS with an annual increase of 35.1%. In the corresponding years the incidence of severe ID fell annually by 6% and mild-moderate ID continued to increase by 6.6% per annum. Conclusions: The rise in birth prevalence of ASD and autism by birth year in WA can be partly, but not fully, explained by a diagnostic substitution of ID to autism. Introduction of ASD assessment in WA and iincreased government funding and availability of services at the time of the increase in ASD is likely to have contributed to the rise.

Poster Presentations Program

114 Treatment Posters 1

1 114.1 526481Family support programs for parents of adults with High-functioning Autism and Asperger syndrome in Japan. M. Tsujii*, *Chukyo University*

Background: In Japan, there are many autistic people who have secondary mental disease, and they had been improperly treated based on cultural problems. In Japan, usually single adults live with their families and have been close relationship between parents and autistic adults even in adulthood.

Objectives: The purpose of this study was to reveal an effect on the program for parents of adults with High-functioning Autism(HFA) and Asperger syndrome(AS) in Japan. The programs were focused on treatments for Secondary mental, emotional and behavioral problems for adults with HFA and AS.

Methods: The participants were 10 mothers for adults with HFA and AS. We organized two groups for them, and the program was composed with 5 sessions; understanding traits of Autistic people, understanding Secondary mental emotional and behavioral problems for them, understand interaction between mothers – adults with HFA and AS, understanding belief of mothers themselves, and how mothers response positively for their children's behavior. Mothers discussed each other in group settings. Their behaviors in daily-life and belief of mothers were evaluated each session and after programs using self-reports of mothers.

Results: In the program, mothers could notice their parenting styles depending on Japanese traditional ways and that style could not match their children's autistic traits. Also they could understand their negative response for their children's behaviors, because of difference from standard Japanese way of behaviors. Mothers could learn how to response positively for behaviors of their children and Children's behaviors gradually changed, especially anger expression decreased.

Conclusions: This program encouraged parent's understanding of belief and behaviors for themselves. It is important to notice mothers' traditional beliefs that every adult should do "Normal" behaviors and autistic behaviors should response negatively. It is also important to treat cultural problems for support parents of adults with HFA and AS.

2 114.2 Sleep Education Classes for Parents of Children with Autism Spectrum Disorders. B. A. Malow*, S. G. McGrew, K. Artibee, H. Reed, S. E. Goldman and K. Frank, *Vanderbilt University*

Background: Children with autism spectrum disorders (ASD) have a high prevalence of insomnia, which has both biological and behavioral causes.
Objectives: Our hypothesis is that parents of children with autism and insomnia, through participation in a sleep education program, can teach their children to become better sleepers. Furthermore, enhanced sleep in children with ASD may result in improved daytime behavior.
Methods: We provided a structured setting in which small groups of parents learned about establishing effective sleep habits for their children with ASD. All children had a clinical

diagnosis of ASD, confirmed by the Autism Diagnostic Observation Schedule, and did not have a history of epilepsy. A series of three two-hour workshops were conducted on-site at our Children's Hospital. Workshops were led by two physicians with presentations as well as breakout sessions, homework, and question-and-answer periods focused on bedtime routine and night wakings. Sleep and behavior questionnaires, in addition to one week of actigraphy, were collected prior to the workshop and one month after the workshop. Data were analyzed using paired t-tests to detect change.
Results: To date, we have analyzed data obtained from 12 children, ages 3-10 years, whose parents have completed the workshop. Improvements after treatment were seen in the total scale as well as several insomnia-related subscales of the Child Sleep Habits Questionnaire (CSHQ), including bedtime resistance, sleep onset delay, sleep duration, and sleep anxiety ($p \leq 0.3$), but not subscales related to sleep-disordered breathing and parasomnias ($p > 0.1$). Significant improvements were also noted in the affective ($p = 0.007$) and attention-deficit hyperactivity ($p = 0.27$) domains of the Child Behavior Checklist (CBCL). Review of individual actigraphy records showed improvements after treatment in sleep latency and night wakings.
Conclusions: Sleep education classes improve sleep parameters and aspects of daytime behavior in children with ASD.

3 114.3 What Happens Next? Outcomes from the Children's Toddler School. N. Akshoomoff*[1], A. Stahmer[2] and C. Corsello[1], (1)*University of California, San Diego*, (2)*Rady Children's Hospital*

Background:Previous research indicates toddlers with ASD who attend an inclusive early intervention program (the Children's Toddler School; CTS) demonstrate significant gains in functional communication social and play behaviors at program exit.

Objectives:To examine the relationship between child characteristics at exit from CTS and later IQ, adaptive behaviors, diagnosis, school placement, utilization of services, and parental stress.

Methods:Twenty-nine primary caregivers of children who exited CTS completed the Parenting Stress Index (PSI) and a school placement and services questionnaire. Twenty of these families participated in follow-up diagnostic testing; children ranged in age from 4 to 12 years.

Results:The majority of children attended non-inclusive special education upon exit from CTS. Among the 15 children currently in elementary school, a majority were in typical classrooms. As expected, scores at follow-up were significantly correlated with scores at program exit more often than the scores at program entry. Although the largest gains in IQ were seen between the time of program entry and exit, IQ gains were typically maintained or increased at follow-up. Similar gains were found on the Vineland, excepting Socialization scores which remained low. Diagnosis was generally stable. Parents continued to report clinically significant stress associated with child behaviors. The PSI Child Domain scores in the areas of Distractibility/Hyperactivity and Demandingness at follow-up were significantly correlated with the number of services currently received by the children.

Conclusions:Children enrolled in early intervention make gains in many domains, including IQ, which are stable over time. Diagnosis remained stable as were behavioral issues. Socialization is a particularly difficult area to affect change and should continue to be an area of research and treatment focus. Parent stress over child behaviors may need to be more directly addressed.

4 114.4 INDIVIDUAL DIFFERENCES IN LONG-TERM PROGRESS AND OUTCOMES FOLLOWING INTENSIVE EARLY INTERVENTION. P. Howlin*[1], I. Magiati[2], J. Moss[2] and T. Charman[3], (1)*Institute of Psychiatry, King's College, London.*, (2)*Institute of Psychiatry, King's College, London*, (3)*ICH*

Background: Recent research has demonstrated the short-term effectiveness of early, intensive, behaviourally based interventions for children with ASD, but very few studies have examined longer term

outcomes.
Objectives: The aim of this prospective UK study was to assess children's outcomes immediately following a 2-year early intensive intervention (either home- or school-based) and to assess progress 7 years later.
Methods: 36 children with ASD participated (22 originally enrolled in an early intensive behavioural intervention (EIBI) home-based programmes in the community and 14 in intensive specialist preschool provisions). Participants were initially assessed at a mean age of 3 years; followed up after 2 years (mean age 5 years) and again at mean age of 10 years. Standardised assessments of cognitive, language and adaptive behaviour abilities and severity of autism-related difficulties were available at each time point.
Results: There was a significant increase in mental age over time (MA T1= 28.6, T2: 42.5, T3: 66.3) but a *decline* in IQ scores over this period (IQ T1= 70.5, T2: 64.4, T3: 49.7). ADI-R scores showed a slight improvement (ADI-R total mean T1= 36.4, T2: 31.0, T3: 31.8). However, individual children showed very different trajectories of change. Based on an overall composite change score, 28% showed little or no improvement; 32% showed small but continued improvements and 22% made significant and steady improvement over time. Four children (12%) made large gains in the first 2 years which then plateaued; one child showed little improvement during intensive intervention but much greater change thereafter. Variables associated with these different patterns of change will be analysed.
Conclusions: Changes in mean scores following intervention do not provide information on outcome in individual children, which can vary widely over time. There is a need to attend more to individual trajectories following intervention and to the variables that may be associated with different degrees and patterns of change.

5 114.5 Behavioral and Physiological Effects of Weighted Vests for Children with Autism. S. Hodgetts*, J. Magill-Evans, J. Misiaszek and D. Sobsey, *University of Alberta*

Background: Sensory dysfunction is frequently reported in children with autism, and can impact their ability to participate in classroom activities. Weighted vests are commonly used to improve classroom participation. Somatosensory stimulation provided through a weighted vest is thought to mitigate sensory dysfunction through effects on the autonomic nervous system.
Objectives: This study investigated behavioral and physiological effects of weighted vests for children with autism. We hypothesized that: (1) wearing a weighted vest would result in decreased off-task and stereotypic behaviors, (2) improved behavioral outcomes would correlate with changes in heart rate, and (3) teachers and educational assistants would find weighted vests acceptable.
Methods: A single-case, randomized and blinded, ABAB/BABA design (A=vest with 5% body weight, B=unweighted vest) was used to assess the effects of weighted vests for 4 children with autism (ages 5 to 10) in the classroom. Participants were videotaped during a structured table-top activity, part of the daily classroom routine. Heart rate was collected when participants wore the vest using Polar Vantage XL chest monitors.
Results: Preliminary analysis suggests that the weighted vest was associated with decreased off-task behavior in 3 of 4 participants based on percent of non-overlapping data points (PND = 70-89%), and decreased stereotypic behavior in 1 participant (PND = 60%). Only 1 participant had a change in heart rate, with an increased heart rate with the weighted vest. Teachers and educational assistants reported that weighted vests were beneficial for the participants, and that they will continue using weighted vests in the classroom.
Conclusions: Weighted vests may be an effective and acceptable strategy to help decrease off-task behaviors in the classroom for some, but not all, children with autism. It remains unclear whether behavioral changes are related to changes in autonomic nervous system functioning. Additional children are being recruited to provide further data.

6 114.6 A Robotic Therapist For Positive, Affective Prosody in High-Functioning Autistic Children. E. S. Kim*[1], E. Newland[1], R. Paul[2]

and B. Scassellati[1], (1)*Yale*, (2)*Southern Connecticut State University*

Background: Deficits in prosody have been considered an identifying characteristic of ASD since Kanner (1943). Prosodic abilities have been shown to be related to attributions of social competence (Paul et al., 2005) and to success in vocational placements (Shriberg and Widder, 1990). Prosody has been found to remain impaired in speakers with ASD, even when other aspects of language improve (Kanner, 1971; DeMyer et al., 1973). The known preference of children with ASD for mechanical objects (Baron-Cohen and Belmonte, 2005) suggests that intervention with a robotic agent may increase efficacy in prosodic therapy.

Objectives:

1. To assess the accuracy of a robotic agent in classifying child prosody.
2. To compare the effectiveness of prosodic therapy delivered by a human therapist and by a robotic agent, measured by change in blind listeners' pre- and post-therapy judgments of participants' positive prosodic production.

Methods: Six speakers with ASD (ages 7-12), demonstrating deficits in positive prosody production, are randomly assigned to one of two treatment conditions: script-based (McClannahan and Krantz, 2005) training provided by a speech-language pathologist or provided by a robotic agent. The robotic agent has an expressive face, "speaks" prerecorded scripted conversations, and utilizes a signal processor that classifies child prosodic responses as inappropriate or appropriately positive. Both human and robotic therapists provide reinforcement only to appropriate prosody in these scripted conversational contexts.

Results: Preliminary data demonstrate that the robotic therapist is capable of correctly classifying over 70% of utterances produced by children in this age range as positive or not. Pilot testing of the robotic therapist revealed that participants readily engage with the robot, and that participants significantly modified their prosodic production during therapy.

Conclusions: Preliminary data support the hypothesis of the efficacy of a robotic agent for prosody intervention. Results of the randomized controlled trial will be presented.

7 114.7 Good Practice Guidelines for the treatment of autistic spectrum disorders. L. Boada Muñoz*[1], J. Fuentes Biggi[2], M. J. Ferrari Arroyo[3], G. (Study Group of Autistic Spectrum Disorders)[4] and M. Posada de la Paz[4], (1)*Instituto de Salud Carlos III de Madrid*, (2)*Psiquiatría Infanto-Juvenil.Policlínica Guipúzcoa*, (3)*Health Institute Carlos III.*, (4)*Getea Grupo de Estudio de los Trastornos del Espectro Autista*

Background:

Due to the inexistence of an aetiology-based intervention for Autistic Spectrum Disorders (ASD) families and professionals are exposed to diverse and sometimes conflictive recommendations when they have to decide the most adequate alternative for treatment.

Objectives:

For the first time in Spanish and updated to 2007 the ASD Study Group of the (National) Institute of Health Carlos III has reviewed (1995-2007) more than 20 different interventions following the clasification principles of Evidence Based Medicine (EBM) and has summarized treatment guidelines for this population analyzing efficacy and effectiveness.

Methods:

All data in this work is extracted firstly by 1) the available evidence based medical and psychological databases trough Tripdatabase- 2) Practice Parameters published by World Government Organizations (NY, California, Maine-Manchester, Ontario, and Sydney) 3) Reports from International Institutions and Scientific Societies like the American Academy of Neurology or A.A. of Pediatrics and finally 4) the opinion and

experience of a multidisciplinary expertise panel of 16 Spanish proffesionals.

Results:

In general, based recommendations are in the weaker degrees of EBM classifications. Nevertheless, there is widespread agreement to stress that education with special incidence in the development of communication and social competence, with the addition of community support are nowdays the main means of treatment. This can be complemented, depending on individual needs, with medication, behavioural approaches and cognitive behavioural therapy for associated psychological problems in persons with higher cognitive level.

Conclusions: No simple treatment algorithm can be produced at this time at the level of available evidence.

8 114.8 A comparison of home based and centre based early intervention for young children with autism: A randomised control study. J. M. A. Roberts*[1], T. R. Clark[2] and D. Evans[1], (1)*University of Sydney*, (2)*Autism Spectrum Australia (Aspect)*

Background:

Consistent with international trends there is increasing demand for early intervention (EI) for autism across Australia. This demand is adversely influenced by a lack of empirically based evidence about program quality and effectiveness. This paper reports on an empirical study examining the effectiveness of Autism Spectrum Australia (Aspect)'s Building Blocks Program (2007 = 165 children/families) by a team of researchers at the University of Sydney. This study specifically examined the effectiveness of the Building Blocks centre based (CB) and home based (HB) programs. 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.

Objectives:

This project seeks to compare outcomes for three groups: 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.

Methods: Three participant groups were recruited in 2006-7 - HB (n=30), CB (n=30), waitlist/control (n=30). 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 preliminary analyses of child/family outcome measures. Dependent variables included: Child; autism (ADOS), cognition (Griffiths), communication, (Reynell & Pragmatics Profile), independent functioning (Vineland), educational evaluation: Parent/family: stress (PSI), Quality of life (Beach), and perception of competence. Strengths of the project included: random assignment of participants to treatment groups, a non-treatment comparison group, verification of diagnosis of autism (ADOS), pre and post measures by staff blind to participant status, verification of treatment fidelity, recording information about additional interventions throughout the study.

Conclusions:data analysis being completed

9 114.9 PEERS, School, and Me. J. Davies*[1], E. Rastall[1], G. Stobbe[2], A. Mulloy[2], E. Laugeson[3] and F. Frankel[3], (1)*Seattle Pacific University*, (2)*ASTAR Center*, (3)*UCLA Semel Institute for Neuroscience & Human Behavior*

Background: Previous research indicates that the Program for the Education and Enrichment of Relational Skills (P.E.E.R.S.) is an effective intervention for adolescents with developmental delays. This 12-week, parent-supported, social skills training program is

aimed at increasing social skills repertoires for teenagers with Autism spectrum disorders.

Objectives: The purpose of the current study is to effectively implement the P.E.E.R.S. program in a school setting. More specifically, while providing intervention for high school students on the Autism spectrum, this research is aimed at enhancing the school system's ability to independently provide empirically-validated social skills training to their students. Thus, teachers will be trained to both instruct and coach students during the P.E.E.R.S. training.

Methods: Approximately six to nine ASD high school students will be recruited via teacher referrals. Students will be between the ages of 13 and 17, will have an ASD diagnosis, and will have an I.Q. of 70 or above. Students will attend twelve 90-minute social skills training groups, while parents will attend twelve 90-minute social skills support sessions. The student group will be facilitated by a group leader, two coaches, and a teacher coach. The parent group will be facilitated by a group leader and one teacher coach.

Results: Screening measures will be used to determine program eligibility. In addition, comprehensive assessments of the student's social and adaptive functioning will be conducted both before and after P.E.E.R.S. training to determine clinical efficacy of the program.

Conclusions: The P.E.E.R.S. program is expected to meaningfully enhance its student participants' social competency, increase the ability of participants' parents to coach and support students during social interactions, and ensure teachers' competency in providing social skills intervention in a schools setting. Strengths and weaknesses of the methodology and implications for future research will be discussed.

10 114.10 Joint and social attention behaviours in ASD children attending a "IAES" developmental intervention. S. De Falco*[1], S. Cainelli[1], G. Esposito[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: Joint attention and social attention deficits are specific to Autism Spectrum Disorders (ASD). Furthermore, these skills are considered pivotal to many different dimensions of cognitive and affective development in typical children and in children with ASD (Mundy, Neal, 2001).
Objectives: The aim of this study is to assess joint and social attention of ASD children within a specific developmental intervention focused on Intersubjectivity Activation and Emotional Sharing (IAES; Venuti, 2003).
Methods: A group of 9 children with ASD (clinical diagnosis by DSM, confirmed by ADOS), aged 7 to 13 years, were videorecorded during weekly music therapy sessions. One session at the beginning of the intervention and one session occurring 12 months later were coded.
A joint attention coding system measured the occurrence and duration of both simple joint attention behaviours (showing, pointing, etc.) and a more complex level of shared activity (active joint engagement). The observation coding system for social attention measured the direction of subject gaze (toward the therapist, toward a shared object or an object held by therapist, non-shared focus).
Results: Data analyses document substantial improvement of joint and social attention skills. Significant increases were found in the duration of joint engagement and in the amount of time during which children's gaze was directed towards objects of shared activity or towards objects held by the therapist.
Conclusions: Within the IAES developmental intervention, ASD children improved their joint and social attention skills. As these abilities are considered essential to many other dimensions of child social and communication development, we hypothesize that this intervention can lead to improvements in social adjustment.

11 114.11 THE PAIRS PROJECT: PARTNERS IN AUTISM INTERVENTION RESEARCH STUDIES: A UNIVERSITY COMMUNITY ALLIANCE PROGRAM. L. A.

Vismara and S. J. Rogers*, *UC Davis M.I.N.D. Institute*

Background: Although knowledge about the efficacy of behavioral interventions for children with autism is increasing, there is little research on the effectiveness and transportability of empirically supported models in diverse community settings.

Objectives: The current study examined the effectiveness of the telehealth training approach in terms of therapist and child behavior changes. The participants involved 16 therapists in four community agencies across two states and 21 families of young children with autism. Therapists were taught the conceptual framework and teaching principles of the Early Start Denver Model (ESDM), a model that fuses development, relationship, and behavioral methods specifically developed for use with infants and toddlers with autism spectrum disorder (ASD) aged 12-36 months.

Methods: Three different methods of learning were used to teach the ESDM: (a) self-instruction in which therapists reviewed the written and video materials and implemented the model without direct training or instruction; (b) group instruction in which direct training was provided on the assessment and intervention procedures via distance education technology; and (3) individual instruction in which further training, supervision and feedback was provided independently to each site via distance education technology.

Results: Preliminary data indicate that group and individual instruction (via distance education technology) resulted in therapists' acquisition of the intervention techniques and in improvements in child social communicative behaviors. Data are currently being analyzed to examine whether therapists may also learn the ESDM parent coaching practices via distance education technology.

Conclusions: Family characteristics, therapist variables, and contextual factors will be examined to determine whether modifications from the original efficacious intervention model are needed for the generalization of positive treatment effects to large community populations. Findings are also discussed in terms of the circumstances under which the ESDM is effective and for whom.

12 114.12 A PLACEBO-CONTROLLED TRIAL OF ORAL HUMAN IMMUNOGLOBULIN FOR GASTROINTESTINAL DYSFUNCTION IN CHILDREN WITH AUTISTIC DISORDER. R. Melmed*[1], B. Handen[2], R. Hansen[3], M. Aman[4], J. Bruss[5], D. Burnham[5], C. McDougle[6], S. Ober-Reynolds[1], J. Jones[1], J. Kirwan[1], S. E. Brautigam[1], S. M. Stephens[1] and C. J. Smith[1], (1)*Southwest Autism Research & Resource Center*, (2)*Univ of Pittsburgh*, (3)*University of California at Davis*, (4)*Nisonger Center*, (5)*Consultant*, (6)*Indiana University School of Medicine*

Background: Persistent gastrointestinal (GI) symptoms have been reported in subgroups of children with autistic disorder (AD), although it is unknown if a causal relationship exists between GI dysfunction and the expression of symptoms of autism. Currently, there is no specific treatment for these patients. Intravenous immunoglobulin (IVIG) is already approved in the US for the treatment of a range of immune-mediated conditions based on its anti-inflammatory and immunological properties. In an open-label prospective study of the use of oral human immunoglobulin (IGOH), GI symptoms along with behavioral symptoms in children with AD improved. Those results supported the need for a controlled study.

Objectives: We investigated whether a 12-week treatment with IGOH would improve GI symptoms in children aged 2–18 years with AD.

Methods: A randomized, double-blind, placebo-controlled, parallel-group, dose-ranging study (IGOH 140, 420, or 840 mg/day) was conducted with 100 subjects completing the study.

Results: Analysis of primary and secondary endpoints revealed no difference across treatment groups in GI symptoms (p =.52),

parent ratings of problem behaviors (p >.20), or parent or physician-assessments of global improvements. IGOH was well-tolerated and there were no treatment-emergent serious adverse events.

Conclusions: This study challenges some assertions regarding the etiology of autism and emphasizes the need for rigorous scientific investigation.

13 114.13 A NEW METHOD OF SPEECH INSTRUCTION FOR CHILDREN WITH AUTISM. A. Kotsopoulou*[1], A. Gasteratos[2], M. Gyftogianni[3] and M. Troupou[3], (1)*Technological Institute of Education*, (2)*Day Centre for Children with Develpmental Disorders*, (3)*Day Centre for Children with developmental Disorders, Messolonghi*

A NEW METHOD OF SPEECH INSTRUCTION FOR CHILDREN WITH AUTISM
Kotsopoulou A, Gasteratos A, Gyftogianni M, Troupou A
Day Centre for Children with Developmental Disorders, Messolonghi, Greece

Background: A new method by the name 'Phoneme Touch and Say' is currently being tried at the above Day Centre for children with autism without speech.

Objectives:To assess the effectiveness in therapy of 'Phoneme Touch and Say' on a sample of young children with autism who have had no functional speech. Impetus for the initiation of the present study was the success with an 11.6 yrs old autistic child who with treatment over a 13 month period, developed communicative speech (55 words), and has during the following year with further speech therapy developed a vocabulary of more than 500 words.

Methods: The method consists of a system of hand cues, which represent speech sounds, and show how and where the sounds are made by manipulating the articulators by touching the lips, chicks, nose. The method adds visual, tactile and kinesthetic information to help distinguish speech sounds.It helps both comprehension and expression. In comprehension the method requires minimum effort by the child (joint attention), and in expression it requires the ability to imitate. Three children with autism (fulfilling the DSM-IV criteria) without speech were selected for treatment. They were all males of age ranging from 3.9 to 5.0 years. All three children have had therapy sessions twice a week.

Results: With improving joint attention and imitation of hand cues all three children have responded well (number of sessions 16 to 18). Up till now they recognise most phonemes of the Greek language, they make syllables with them and name pictures starting with consonants they have already learned.

Conclusions: The effectiveness and usefulness of this method are worth exploring further.

14 114.14 The Effects of a Parents Training Program on Joint Attention Intervention for Preschool Children with Autism. Y. Y. Wang*[1] and T. R. Yang[2], (1)*Ren-Yu Company*, (2)*National Taipei University of Education*

Background: The joint attention (JA) is supposed to be one of the core deficits of autism. If JA deficit could be treated for children with autism in early intervention programs, the prospective effect will be optimistic. However, most JA intervention programs only pinpoint to children with autism only. Therefore, the effect size of JA intervention was not optimistic based on the follow-up studies. If the therapy roles could be transferred to parents, parents can intervene for their children anytime and anywhere.

Objectives: This study developed a parents training program on JA intervention for young children with autism and examined the effect of parent training program.

Methods: A single subject research method with multiple probes across behaviors design was adopted. Three parents of children with autism who were under four-year olds participated in this study. The independence variable was parent training program on joint attention intervention. The dependent variables were three target behaviors for parents, including nonverbal interactions, using nonverbal communicative gestures, and

sharing with gaze which were important for promoting JA behaviors for children with autism.

Results: The results indicate that the parents' performance of three target behaviors was improved a lot. Furthermore, the frequency of joint attention of the preschool children with autism is highly correlated with parents' three target behaviors.

Conclusions:The results implicate that parents' training on joint attention intervention is effective and very promising for future studies.

15 114.15 RISPERIDONE FOR PDD CHILDREN AND ADOLESCENTS. PREDICTORS OF LONG TERM USE (36 MONTHS): A PILOT STUDY. L. Anchisi*, G. Melis, A. Fois, P. Atzori and A. Zuddas, *University of Cagliari*

Background: Among atypical antipsychotics, Risperidone has now been identified as the only evidence-based pharmacological treatment for autism. Very few studies, however can be used to plan the length of the pharmacological treatment.

Objectives: To describe efficacy of risperidone in young people with PDD and to identify predictive parameters for prolonged use (36 months).

Methods: PDD children and adolescent according to the DSM-IV R criteria, 3 to 18 years of age, taking risperidone for at least 8 months and 36-month follow-up were retrospectively studied. Outcome measures included the Children's Psychiatric Rating Scale (CPRS) and Child Autism Rating Scale (CARS). Subjects were stratified in three groups: still on risperidone, shifted to other medication (SSRI, mood stabilizers, other antipsychotics), or drug-free. Clinical / demographic variables and efficacy of treatments were compared within the groups by mean of chi square and paired t-test.

Results: 29 children and adolescents (average age of 10.9 year; risperidone average dose 2,43 ± 1.45 mg, range 1-6 mg/day) were studied: after 36 months, 9 were still on risperidone, and 10 have replaced risperidone with other psychopharmacological treatments. 10 were free of medications. All showed a significant improvement after 2 and 8 months of treatment CPRS ($p=0.22$ and $p=0.14$ respectively) and CARS ($p=0.0001$ and $p=0.14$) and improvement persists for 36 months in all three groups of patients. The group on treatment with risperidone at 36 months had a significant lower IQ ($p= 0.16$) and more associated disorders ($p=0.16$). Within the subjects who have discontinued risperidone at 36 months, lower IQ (<50) and comorbidity for psychiatric and neurological diseaseas were associated with the use of others medication at 36 months.

Conclusions: These results suggest that in patients with higher IQ and without associated disorders, the improvement observed with risperidone can be maintained also after discontinuation.

16 114.16 Social Skill training for autistic children with Family. W. Rattanasatien*, *Yuwaprasart child and adolescent psychiatric hospital*

Background: One of the most significant problems for people on the autism spectrum is difficulty in social interaction because of problems with speech, language and mind reading. Not only a group for social skills training has been established for autistic children and adults, but social skills teaching should also be implemented for parents to support them to "do it by themselves". Objectives: This preliminary project is a qualitative study aimed to train caregivers to counter and independently establish social skills methods which support their children to have individually reinforced and learned social skills at their home and communities.

Methods: This project was designed by including the activities that promoted **basic social skills,** asking for help, asking questions, joining in, turn taking and initiating play, as well as the **conversation skills,** friendship skills, greeting, apologizing, and handing disappointment. The activities consisted of gaming, physical and music therapy, respite camping, psychological

support, joy and hope. This half year program was free of charge to all families, and also included an 24-hour care onsite. Parental supporting group were offered to families as well. The workshops were held three times for bolstering, reinforcing and evaluating improvement of the social skills.

Results: Ten autistic families attended this workshop. After finishing the program, the parents gained a better understanding of autistic symptoms, behavioral interventions, and social skill building strategies. They established a self-help group for sharing good practices, individually adapting and utilizing in their communities. Additionally, the children have gradually gained social and communicative skills.

Conclusions: This practical project could serve as a strategy for developing social skills for autism and parental training. Further researches are warranted for developing the higher level social skills in high functioning group, such as expressing feelings and recognizing others feelings, dealing with teasing, negotiating, problem solving and emotion regulation techniques.

17 114.17 Retrospective Analysis of Clinical Records in 34 Cases of Recovery from Autism. D. Granpeesheh*[1], M. Herbert[2], J. Tarbox[1] and D. R. Dixon[1], (1)*Center for Autism and Related Disorders*, (2)*Mass Gen Hosp/Harvard Med School*

Background: 20 years of research on early intensive applied behavior analytic (ABA) treatment for children with autism has consistently produced robust treatment effects. However, there appears to be a subset of children who respond best to intensive ABA treatments, including achieving a level of functioning that is indistinguishable from typically developing peers.

Objectives: The purpose of this study was to describe a subset of children who recovered from autism following intensive ABA interventions.

Methods: We reviewed the clinical files of 34 children with autism who achieved an optimal outcome after receiving intensive ABA services. The data were analyzed in regards to the age at onset of treatment, cognitive and adaptive abilities, average intensity of treatment, and overall duration of intensive ABA treatment.

Results: Overall, children who recovered from autism began services prior to 40 months of age. Average treatment intensity gradually decreased from 32 hours per week in the first year to 18 hours per week in year three. The average duration of intensive services was 39 months. Average IQ was 80 at intake and 107 at discharge. Average adaptive skills were 70 at intake and 93 at discharge. Subscales of IQ and adaptive behavior assessments demonstrated similar patterns and are discussed in greater detail.

Conclusions: Our review corroborates the finding that some portion of children with autism who receive early intensive behavioral intervention achieve functioning in the average range. Children who demonstrate optimal response to early intensive behavioral intervention may constitute a unique phenotype of autism. Finally, it should be noted that most children with autism receive one or more biomedical interventions for autism. Future analyses should be conducted regarding complementary and alternative medical treatments for autism, particularly in regard to identifying those individuals who respond to particular biomedical interventions, both in isolation and when combined with behavioral intervention.

18 114.18 Theory of Mind training in children with autism: preliminary results of a large scale, randomized controlled trial. S. Begeer*[1], C. Gevers[2], P. Clifford[2], M. Mager[2], M. Verhoeve[2], K. Kat[2] and F. Boer[2], (1)*VU University Amsterdam*, (2)*De Bascule*

Background:

Poor empathy or 'Theory of Mind' is a central feature of autism spectrum disorders (ASS). Treatments of children with ASS often involve attempts to train their Theory of Mind skills. However, international research on Theory of Mind training in children with ASS is hampered by small samples, absence of randomized

control trials, poorly designed outcome measures.

Objectives:

We aim to study the treatment effect of a Theory of Mind training in children with ASS aged 8 to 12 years old in a large scale randomized cross-over clinical trial with measures of conceptual and practical skills and background factors.

Methods:

The Theory of Mind training is provided group wise to 5 or 6 children simultaneously, in 16 weekly 60 min sessions. 100 children with ASS will be assigned to training or waiting list conditions, in two cohorts of 50 children with ASS each. Both cohorts will be measured three times with intervals of about four months. The first group receives the Theory of Mind training during the first interval, and no intervention during the second interval. The second group receives the training during the second interval, and will be on a waiting list during the first interval.

Results:

The preliminary results of the study show evidence for improvement in the conceptual Theory of Mind skills, but little evidence for increased practical skills. Age and symptom severity had little impact, but intelligence increased treatment effect on conceptual skills.

Conclusions:

The effects of the Theory of Mind training seem confined to conceptual skills. However, children with ASS and normal IQs are generally less impaired on conceptual levels. This raises the question about how interventions should be designed in order to improve practical Theory of Mind skills.

19 114.19 MATERNAL CORRELATES IN EARLY INTERVENTION PROGRAMS FOR YOUNG CHILDREN WITH AUTISM. D. Thompson*, A. Oakley and A. M. Mastergeorge, *UC Davis, M.I.N.D. Institute*

Background: Parents' understanding of their children's diagnoses of autism influences the ways they interact with their children. Maternal synchrony has been associated with gains in developmental milestones in preschool aged children with autism and is related to early interventions implemented with their children. Empirical evidence of dyadic interactions of young children with autism and their mothers' supports the idea that repeated opportunities of maternal interactions impact the outcome of their child's developmental and socio-emotional skills.
Objectives: The purpose of this study is to investigate the trajectories of maternal behavioral ratings (including directiveness, sensitivity, and responsivity) across an intervention program and the relationship of maternal interactions to ratings of maternal stress in an early intervention program.
Methods: Participants included fifteen mothers who have children diagnosed with autism (child ages range from 24 to 38 months). The mother-child dyads participated in daily in-home play interactions over a 16 weeks period. Mothers' completed the Parenting Stress Index and structured intervention play was coded throughout the joint attention intervention using the Maternal Behavior Rating Scale.
Results: Correlational analyses were conducted to examine the relationship reported between maternal stress on maternal behavior and child joint attention. Findings revealed a strong relationship between increased maternal stress and a decrease in child joint attention ($r = -.827$, $p < .1$). Additionally, maternal responsivity was correlated with reported stress with their child's adaptability ($r = .874$, $p < .1$). Paired sample t-tests results indicated that mothers demonstrated increased sensitivity toward their children over the course of the intervention with moderate decreases in reported stress.
Conclusions: With more intervention programs focusing on mothers' role in therapeutic strategies, it is critical to understand maternal perceptions and behavioral correlates. Further research is warranted to more fully explicate the relationship between maternal parenting behaviors and children's levels of joint attention.

20 114.20 efficacy of vocal imitation training for children with autism: preliminary data. H. Seung*[1] and J. Farrar[2], (1)*California State University*, (2)*University of Florida*

Background:

Children with autism have been noted to present with deficits in imitation skills (Rogers & Pennington, 1991), which appears to be associated with their deficits in orienting to social stimuli. Imitation has been examined as one of the predictors of later language development though the primary focus in the research to date has been on imitation of actions (McDuffie, Yoder, & Stone, 2005). Vocal imitation has not been examined in this population. Thus, examining both vocal imitation itself and its impact of imitation training for children with autism would be an important contribution.

Objectives:

It was hypothesized that vocal imitation training will bootstrap social interaction for children with autism who are almost nonverbal. Research questions included: 1) Can children with autism learn vocal imitation? 2) Does vocal imitation training increase dyadic eye gaze as a measure of social connectivity? 3) Is vocal imitation training associated with subsequent increases in word production?

Methods:

Four children age between 2 and 5 years, who were diagnosed with autism spectrum disorders based on DSM-IV criteria by professionals in the community, and producing less than 50 words were recruited for this study. Vocal imitation training was provided within a play context by the first author three times weekly for ten weeks at our laboratory. Each training session was videotaped behind a one-way mirror. Data were collected at baseline, during training, and post training.

Results:

The four children presented with highly variable profiles on the measures of vocal imitation, eye gaze, and caregiver reported word production.

Conclusions:

Data from this preliminary study suggest that vocal imitation training could be beneficial for children with autism who are almost nonverbal. The results of this study indicate the need for further examination of the efficacy of vocal imitation training.

21 114.21 Outcome of a Social Initiation Training for Nonverbal Children with Autism. M. Rocha* and L. Schreibman, *University of California, San Diego*

Background: Spontaneous social initiations are important social communication skills critical to initiating and maintaining reciprocal social interactions. The literature and our preliminary studies have identified marked deficits in social initiations in young children with autism. Thus far, the majority of interventions targeting social initiations have focused on teaching children with well-established verbal abilities to initiate using speech. Little is known about intervention techniques specifically designed to teach young nonverbal children to initiate using nonverbal communication skills or about the effect of this early training on response to other treatment.
Objectives: (1) develop and evaluate a social initiation training (SIT) for nonverbal children with autism, (2) assess individual differences in the types of social initiations that increase after SIT, (3) assess the relationship between individual behavior profiles prior to SIT and the acquisition of social initiations during SIT, and (4) assess the generalization of social initiations learned during SIT.
Methods: A single subject multiple baseline design across subjects was used to examine treatment efficacy and to evaluate individual differences in treatment response. Baseline and treatment sessions were evaluated for changes in social initiation behaviors, the development of verbal and nonverbal communication, and changes in other social interaction skills. Results: Increases in social initiations skills were evidenced for all participants in the SIT program. Differences in

individual behavior profiles prior to SIT were related to the individual response patterns in social initiation acquisition during SIT. Social initiations learned with experimenters in the laboratory generalized to parents in the home environment.

Conclusions: SIT appears to be an effective intervention to teach appropriate social initiations to nonverbal children with autism.

22 114.22 Changes in Stress Levels of Participants in a Behavioral Intervention Parent Education Program for Children with Autism Spectrum Disorders (ASD). R. Gutierrez[1], S. Dufek*[1], L. Schreibman[1], A. Stahmer[2], R. Koegel[3] and L. K. Koegel[3], (1)*University of California, San Diego*, (2)*Rady Children's Hospital*, (3)*University of California, Santa Barbara*

Background:
Parents of children with ASD have been shown to have higher stress levels than parents of children without disabilities (Baker-Ericzen et al., 2005). These studies also show that child-related stress may be mediated by parent education (e.g. Koegel, Bimbela, & Schreibman, 1996).
Objectives:
To examine the effect of a behavioral intervention parent education program on various areas of parent stress as measured by the Parenting Stress Index (PSI; Abidin, 1995).
Methods:
Parents of children (aged 2-4 years) with ASD were trained in one of two naturalistic teaching strategies, Pivotal Response Training (PRT, N=20) or the Picture Exchange Communication System (PECS, N = 19) participated. Families completed the PSI and an Expectations Questionnaire before and after intervention, and at a 3 month follow-up period.
Results:
Parents fell into three groups at intake: low, moderate and high levels of stress. Changes in child-related stress over time varied by group and by specific subscales. The *Child Reinforces Parent* subscale showed the greatest decrease overall, while *Demandingness* showed an increase over time. Changes in some child-related stress subscales were not maintained at follow-up. Parent-related stress did not change substantially over time. Parents with low levels of stress at intake showed a trend toward increased stress over time. Low levels of intake stress were highly correlated with higher levels of expectations for positive child outcomes.
Conclusions:
Although some aspects of child-related stress are positively affected by parent education, parents may need additional support to mediate parent-related stress and maintain child-related stress changes after intervention ends. Parents of very young children with ASD with low intake stress levels that subsequently increase may not have a full understanding of the impact of the disorder until they begin a parent education program.

23 114.23 Individualization of Treatment for Young Children with Autism: A Randomized Comparison of Verbal and Pictorial Communication Training Strategies. A. B. Cunningham*[1], L. Schreibman[1], A. C. Stahmer[2], R. L. Koegel[3] and L. K. Koegel[3], (1)*University of California, San Diego*, (2)*Rady Children's Hospital*, (3)*University of California, Santa Barbara*

Background: Both Pivotal Response Training (PRT) and the Picture Exchange Communication System (PECS) are empirically-based approaches for teaching functional communication skills to young children with autism. No systematic data address the relative effectiveness of PRT and PECS for targeting spoken language. Also, little is known about variables that may influence whether verbal or pictorial training methods are more likely to benefit individual children.
Objectives: To examine the relative effects of PRT and PECS on spoken and augmentative communication skills in nonverbal and minimally verbal young children with autism, and to identify pre-treatment child characteristics that may guide treatment choices for individual children.
Methods: Thirty-nine children with autism (age 2-4), who had 10 or fewer functional words at intake, were randomly assigned to PRT or PECS. Children were matched on pre-

treatment age, word use, and developmental level. Families received 258 hours of in-home intervention and parent training across 23 weeks. Spoken and augmentative communication skills were assessed at pre- and post-treatment, and at 3-month follow-up. Results: Both treatments resulted in substantial spoken language gains for approximately 50% of children. Children with some words at intake made substantial spoken language gains in both PRT and PECS, while children with no words at intake made minimal or no gains in spoken language. There were no significant differences in spoken language gains between treatment conditions. Over 80% of PECS participants acquired augmentative communication skills. Conclusions: For young children entering treatment with some words, both PRT and PECS are likely to facilitate spoken language acquisition. Early word use appears to be a general predictor of more rapid acquisition of communication in young children with autism. For young children who enter treatment with no words, methods for deciding between verbal or pictorial training strategies for immediate functional communication skills will be discussed.

24 114.24 Early diagnosis and intervention: the Abruzzo experience. R. Cerbo[1], M. De Caris[2], M. Valenti*[2], V. De Laurenzi[2] and G. Sorge[2], (1)*ASL 04 L'AQUILA*, (2)*Il Cireneo*

Background: Autistic spectrum disorders determine in children that don't receive an appropriate treatment a sequel of consequences that in the most severe cases determine long and expensive institutional interventions. An effective treatment requires: a) early diagnosis that involves general pediatricians and specialized diagnostic centers; b) an adequate functional evaluation; c) an involvement of all subjects working with the child. Most early diagnosed children, properly treated reach an acceptable level of social interaction. Objectives: a) Verify the effect of early screening using CHAT. b) Set up and evaluation of a diagnostic protocol that accounts for the different age and functional level of children. c) Test and evaluate a model of total, continuous and intensive take in charge, involving both the hospital and the families. d) Evaluation of the cost of diagnosis and treatment Methods: This approach was promoted by parents of children with autism, and has been financially supported by the Regione Abruzzo – Assessorato alla Sanita'. The early screening has involved 190 general paediatricians while early rehabilitation intervention has been performed by the Foundation il Cireneo in the centre located in Vasto. Intervention has been performed in natural environments with the goal of improving social interaction and communication skills. Results: During the 3 years of this study we have observed a reduction of the average age at diagnosis from 5 to 3 years. Moreover in order to evaluate the efficacy of intervention we performed a longitudinal phase II study on a group of 48 clients ranging from 5 to 18 years, stratified by age and sex, and have observed a significant improvement in all groups using different evaluation scales. Conclusions: In conclusion we believe that the current model of intervention we have adopted gives an adequate treatment to children with ASD.

25 114.25 Capturing Parents' Experience: Online Treatment Survey for Families of Children with Autism Spectrum Disorder (ASD). P. Law*, A. Marvin, J. Nestle, C. Anderson, C. Cohen, C. Foster, K. Law and G. Lund, *Kennedy Krieger Institute*

Background: Families of children with ASD choose from a vast array of possible interventions - with various levels of empirical support - to treat core deficits, behaviors, and related symptoms of autism.

Objectives: To determine which treatments/interventions families of children with ASD are using.

Methods: Families of children with ASD registered to participate in a web-based U.S. national research registry and database. Parents reported on current treatments by selecting from a list of 348 interventions and adding any unlisted interventions.

Results: Treatment data was reported for 4470 affected children. 66% of children were receiving speech therapy, 53% occupational therapy, and 41% ABA or ABA-based

therapies. 18% attended social skill groups, 17% used PECS, 15% used Visual Schedules, 15% received physical therapy, and 13% used Social Stories. 40% of children were reported to be using at least one medication. The most commonly used medications were Risperdal/risperidone and Ritalin (and equivalents), each used by 9% of children. 17% of children were reported to be on at least one special diet, the most common being casein-/dairy-free and/or gluten-free. 30% were taking at least one dietary supplement, the most popular of which were melatonin (9% of children), probiotics (9%), vitamin B12/methyl-cobalamin (7%), multivitamins (6%), magnesium (5%), zinc (5%), and calcium(5%). Parents specifically indicated that 23% of children were receiving some form of sensory integration dysfunction therapy; however, the majority of these children were also listed as receiving occupational therapy, reflecting a natural overlap. 8% of parents engaged in prayer/spiritual practices.

Conclusions: Although many families are using autism interventions with strong empirical support (e.g. ABA, Risperdal), many are also using interventions for which such support is weak or nonexistent. The need to evaluate treatments that are in wide use despite a lack of support for their efficacy may help guide research priority setting.

28 114.26 PSYCHOTROPIC MEDICATION USE BY CHILDREN WITH AUTISM IN A LARGE HMO IN CALIFORNIA. M. P. Bernal*[1], L. A. Croen[2] and C. Yoshida[3], (1)*Kaiser Permanente Northern California*, (2)*Disvision of Research*, (3)*Division of REsearch*

Background: There is a dearth of empirical information on how the use of psychotropic medications changes over time in community samples of children with ASD.
Objectives: To examine changes in the use of psychotropic medications from 2006 to 2007 in a large community sample of children with ASD.
Methods: Children between the ages of 2-18 with a diagnosis of ASD who were members of Kaiser Permanente (KP) in Northern California in 2006 (N=5,636) and 2007 (N=7,076) were compared in terms of psychotropic medication use dispensed at any KP pharmacy. Medication use by each cohort was examined using an electronic prescription system.
Results: Approximately 36% of the children with ASD in the 2006 cohort were prescribed psychotropic medications. The most commonly prescribed medications were stimulants (22%), antidepressants (14%), and antipsychotics (9%). Fourty six percent of patients receiving psychotropic medication were prescribed one single agent. These data will be compared with data from the 2007 cohort to inform about changes over time within a health care system.
Conclusions: A significant percentage of children with ASD receive prescriptions for psychotropic medications, with a surprisingly large proportion receiving stimulants and antidepressants. Changes in psychotropic medication use over a one-year period will be discussed in light of expansion of services for ASD in this health care system.

29 114.27 TREATMENT AND REHABILITATION OF THE CHILDREN WITH PERVASIVE DEVELOPMENT DISODER AND SCHIZOPHRENIA. M. Igor*[1], B. Yana[1], M. Vladimir[2] and M. Inna[1], (1)*Ukrainian Research Institute of Social and Forensic Psychiatry and Drug Abuse*, (2)*National Medical Academy Postgraduated Education named by P.L.Shupik*

Background: Pervasive development disorder (PDD) and schizophrenia (SCH) is a neurodevelopment disorder that is associated with deficits in cognition, affect and social functioning. Research aim to study influence of risperidon therapy and medical - social rehabilitation on cognition and social functioning of the children. **Objectives:** We observed 93 patients in the age from 3 to18 years (253 - with the PDD, 80 - SCH-spectrum disorders). Children were divided into 3 (variants / therapeutic) groups: a) on risperidon monotherapy, b) receiving sensory integration and cognitive-behavioural and social skills trainings, c) complex therapy: risperidon and rehabilitation. Methods: The efficacy of treatment in randomizate groop were analyzed using $CGI_{SS,}$ PANSS, PEP-R, CARS, CANTAB, COGTEST and ILK test

systems.
Results: Parameters of cognition in-group of children with PDD, receiving risperidon on a background of active rehabilitation were on the higher level, than in groups of comparison (P < 0,05). Cognition in the greater degree influence to the level of social functioning at the PDD and early SCH, than negative symptoms of disorder. Long terminal therapy by risperidon raises efficiency of sensory integration and cognitive trainings for the children with PDD and severe cognition and social reintegration at early demonstrating SCH. At long-term therapy of risperidon patients with SCH on a background of active social rehabilitation with participation of family productive infringements, duration of disease and number of psychotic episodes in anamnesis, practically, did not influence a level of social functioning. **Conclusions:** Early intervention may help prevent the often significant biological, social and psychological deterioration that can occur in the early years following onset of a psychotic disorder. Significant delays before effective treatment is initiated, or secondary morbidity resulting from aspects of management, can hamper preventive efforts. Potential benefits of early intervention include: reduced morbidity; more rapid recovery; better prognosis; preservation of psychosocial skills; preservation of family and social supports; decreased need for hospitalisation.

30 114.28 Valproate for the treatment of irritability/aggression in child autism. E. Anagnostou*[1], L. Soorya[1], J. Rusoff[1], W. Chaplin[2], S. Wasserman[1] and E. Hollander[1], (1)*Mount Sinai School of Medicine*, (2)*St John's University*

Background:

Aggression, both self- and other-directed, is a common associated feature of autism, as is irritability. Several atypical antipsychotics, particularly risperidone**,** have demonstrated efficacy for the treatment of irritability / aggression in children with autism. However, the use of such medications has been associated with side effects such as weight gain that may increase the likelihood of diabetes and cardiovascular disease, sedation and movement disorders.

Objectives: This study examines the effect of valproate in the treatment of irritability/ aggression in children with autism via a 12 week, double-blind placebo-controlled trial.

Methods:

Twenty seven children ages 5-17 were randomized to valproate vs placebo. Diagnosis was confirmed by ADI-R and ADOS-G. Inclusion criteria included evidence of significant irritability (ABC irritability score >17 or OAS-M score >12). Subjects were followed biweekly and safety blood work was performed at weeks 0, 2, 4, and 12.

Results:

Ten of the 16 active treatment subjects (62.5%) showed a response on impulsive aggression/irritability, whereas only 1 of the placebo subjects (9.9%) showed a response (odds ratio =16.66). This effect is significant by Fisher's exact test (p = .008). There is a significant weeks x condition interaction (p = .48) suggesting that there is an additional drop of .53 points/week on the ABC Parent Irritability Ratings in the treatment condition compared to the placebo condition. The significant condition x weeks interaction remains significant after controlling for the IQ differences (t=-2.28, df=20.38, p=0.33). Exploratory analysis suggests that children with epileptiform baseline EEGs are more likely to be categorized as responders. The medication was well tolerated.

Conclusions:

This data supports the use of valproate for the treatment of irritability/aggression in children with autism. Further larger trials are necessary to confirm this early finding and to further examine the relationship of baseline epileptiform abnormalities and response to treatment.

Poster Presentations Program

115 Cognition Posters 1

31 115.1 Enhanced Performance on the Embedded Figures Test in Autism is not Linked to Cognitive Effort: A Pupil Dilation Study. M. T. DiNino*[1], B. M. Keehn[2], L. A. Brenner[3], S. P. Marshall[1], A. J. Lincoln[4] and R. A. Müller[1], (1)*San Diego State University*, (2)*San Diego State University and University of California, San Diego*, (3)*University of California, Los Angeles*, (4)*Alliant International University*

Background: Previous research has shown that individuals with autism spectrum disorder (ASD) excel at the embedded figures test (EFT), but the causes of this superiority are not well understood. Eye-tracking provides a tool for investigating cognitive effort by measuring the pupillary response, which has been previously shown to reflect cognitive workload during a variety of behavioral tasks (SP Marshall, Aviation, Space, & Environmental Medicine 78: B165-75). The present study utilized changes in pupil dilation to determine whether enhanced performance in individuals with ASD is associated with level of cognitive effort.

Objectives: To examine pupil response (reflecting cognitive workload) and its association with EFT for both children with ASD and typically developing (TD) children.

Methods: Participants were 10 high-ability adolescents with ASD and 10 age- and IQ-matched TD individuals. The EFT was composed of 40 test and 30 baseline trials and a complex geometric figure was displayed on each trial. In the test condition a target shape was hidden within a complex figure, while in the control condition the target shape was highlighted. Binocular eye-tracking data were collected for the duration of the experiment.

Results: There was a significant group by condition interaction for the median response time (RT). Individuals with ASD had significantly faster RTs in the test condition, but equivalent RTs in the baseline condition relative to TD individuals. For measures of pupil dilation, there was no main effect of group, or interaction between group and any factor.

Conclusions: While ASD participants demonstrated accelerated RT in the EFT, there was no difference between ASD and TD groups for pupil dilation. This suggests that cognitive effort and perceived task difficulty for the EFT do not differ substantially between ASD and TD children. Superior performance by individuals with ASD may be instead related to differences in early perceptual processes.

32 115.2 Implicit Learning and ASD. J. Brown* and K. C. Plaisted, *University of Cambridge*

Background: ASD is a disorder characterized by social and communicative impairments. It has been proposed that these may arise from an impaired ability to learn implicitly about complex social information (Mostofsky et al., 2000; Klinger et al., 2007). However, the evidence concerning the performance of individuals with ASD on implicit learning tasks is equivocal. Where deficits have been evidenced, it has been unclear whether they stemmed from a general impairment in the ability to learn implicitly. The possibility has existed that the poor performances have arisen from other deficits (such as motor dexterity), which are actually not directly related to implicit learning ability.

Objectives: The purpose of this research is to determine the extent to which implicit learning processes are preserved or impaired in individuals with ASD, and how they contrast with explicit processes.

Methods: The performance of children with ASD (n = 27) on a range of implicit and explicit learning tasks was compared to that of typically developing children matched for chronological age and IQ. The tasks were Serial Reaction Time, Contextual Cueing, Artificial Grammar Learning, Invariant Feature Learning, Probabilistic Classification Learning and Paired Associates Learning.

Results: At the time of writing, the data-collection and analysis were not quite complete. However, tentative analyses indicate that learning performance on implicit learning tasks is preserved, in contrast to impaired performance on measures of explicit learning.

Conclusions: Therefore, the tentative conclusion would be that implicit learning is preserved in individuals with ASD, and does not account for the social and communicative impairments associated with ASD.

33 115.3 Prefrontal cortical activation by switching stimuli in autism spectrum disorder and healthy controls assessed by near-infrared spectroscopy. N. Narita*[1], A. Saotome[1], M. Tazoe[2], M. Narita[3] and K. Sakatani[4], (1)*Bunkyo University*, (2)*JAPAN LUTHERAN COLLEGE*, (3)*Mie University*, (4)*Nihon University School of Medicine*

Background: It is known that patients with autism spectrum disorder (ASD) often slow at switching between stimuli, which causes their lack in the appropriate behavior expected in the schoolroom activities.

Objectives: To investigate the activation of prefrontal cortex (PFC) in relation with switching stimuli in ASD patients, we measured the changes in brain oxygenation using near-infrared spectroscopy (NIRS), during a set of two tasks performed consecutive order .

Methods: Preliminary 11 high-functioning (IQ>70 by WISC III) autism spectrum disorder (ASD) patients (ages of 7-44) and 15 healthy controls (ages of 7-38) were studied. PFC oxygenation was continuously measured by NIRS while the subjects were undergone two different tasks, i.e., a picture book reading task, followed by working memory task, in this order. Change in parameters of NIRS (oxygenated [oxy-], deoxygenated [deoxy-], and total hemoglobin [total-Hb]) in PFC during each task were examined between control and ASD subjects.

Results: In the control group, the most common NIRS parameter change observed in the PFC was a relative decrease or no change in oxy-Hb and total-Hb level, with a slight increase or no change in deoxy- Hb level during the reading task in both side of PFC. Interestingly, it is rapidly converted into an activated PFC status immediately after the task was switched to the working memory task, typically was accompanied with an increase in oxy- and total-Hb, with a decrease in deoxy-Hb level in control subjects. In contrast, most ASD patients lack this PFC activation, and the oxy-Hb consistently showed relatively low level compared to the control subjects. The mean oxy-Hb during each task was calculated, which showed a significant difference ($p<0.1$, by 2-way anova) between the control and the ASD subjects.

Conclusions: The delayed oxygenation of PFC by switching stimuli was characteristic in the high-functioning ASD patients which suggest their core defect in complex information processing.

34 115.4 Emotional Processing in High-Functioning Autism-Physiological Reactivity and Affective Report. S. Bölte*, S. Feineis-Matthews and F. Poustka, *J.W.Goethe-University*

Background: Research has demonstrated impairments in expressing and recognizing emotions in autism. Data on autonomic reactivity and subjective experience during emotion processing are still scarce.
Objectives: This study sought to obtain more detailed insights into the nature of altered emotional processing on the levels of autonomic reactivity and subjective experience in autism.
Methods: Physiological response and affective report was examined in 10 adult individuals with autism and 10 typically developing controls. An emotion induction paradigm using stimuli from the International Affective Picture System was applied. Blood pressure, heart and self-ratings of experienced valence (pleasure), arousal and dominance (control) were assessed during the experiment.
Results: Physiological response profiles correlated low to significantly negative between groups. Individuals with autism experienced less arousal when viewing sad pictures but higher arousal while processing neutral stimuli. In addition, they reported more control than the normative group when viewing fearful and sad stimuli.
Conclusions: Generally, emotion processing differences regarding autonomic reactivity and subjective experience were not extreme in our study. Still, findings indicate some altered autonomic reactions and affective experiences

in autism, which may be related to more general impairments in socio-emotional functioning.

35 115.5 Verbal Fluency and Underlying Cognitive Processes in Adults with HFA or Asperger Syndrome. A. A. Spek*[1], T. Schatorjé[1], I. A. Van Berckelaer-Onnes[2] and E. M. Scholte[3], (1)*Mental Health Institution Eindhoven*, (2)*Leiden University*, (3)*Leiden University, Social and Behavioral Sciences*

Background: Research showed evidence for impaired verbal fluency functioning in children with autism. However, verbal fluency functioning in adults with HFA or Asperger syndrome is still unclear. Besides, not much is known about the cognitive processes underlying verbal fluency performance in these individuals.

Objectives: To examine if late diagnosed adults with HFA or Asperger syndrome show impaired verbal fluency functioning compared to a matched control group of neurotypical individuals and to examine the cognitive processes underlying the verbal fluency results.

Methods: Thirty-one (31) adults with high functioning autism, thirty-one (31) adults with Asperger syndrome and thirty (30) control participants participated in the study. The groups were matched according to age, sex and verbal abilities. ADI-R was used in the diagnostic process and differentiation between HFA and Asperger was based on criteria of ICD-10 and Gillberg & Gillberg. Two semantic and two phonemic fluency tasks were used. The verbatim reports were analyzed and the relation between verbal fluency and performance on the WAIS III factor scales was also studied.

Results: The participants with HFA were significantly impaired on both semantic fluency tasks and on one phonemic fluency task. No significant differences appeared between the HFA group and the Asperger syndrome group. The Asperger group was only impaired in the semantic fluency tasks 'professions'. The fluency deficits could not be attributed to a lack of strategy use or to difficulties in switching between strategies. Processing speed appeared to be a cognitive factor influencing verbal fluency performance.

Conclusions: Adults with HFA show impaired verbal fluency functioning, while the Asperger syndrome group may be unimpaired in their verbal fluency. Both groups show normal use of strategies and normal switching abilities compared to a neurotypical group. The relatively low processing speed in the HFA group negatively influenced their verbal fluency performance.

36 115.6 A Distinction Between Verbal and Nonverbal Working Memory in Children with Asperger Syndrome. V. N. Salimpoor*[1] and M. E. Desrocher[2], (1)*McGill University*, (2)*York University*

Background: The term working memory (WM) refers to a mental workspace, or a temporary form of memory that involves the ability to maintain and manage novel information long enough to accomplish a task. WM capacity is thought to be an important predictor of an individual's learning potential. Difficulty with this ability can lead to a wide range of encoding and retrieval deficits. Previous studies have demonstrated that individuals with autism show some deficits with WM capacity, particularly in the verbal domain. Since individuals with Asperger Syndrome typically demonstrate greater strengths in the verbal domain relative to the nonverbal domain, we predicted that they would show a reversed trend with respect to WM capacity than individuals with autism.
Objectives: To examine verbal and nonverbal WM in children with Asperger Syndrome.
Methods: Participants included 13 children diagnosed with Asperger Syndrome, and 13 age-, gender- and IQ-matched control participants. Verbal WM was assessed using the Digit Span test and nonverbal WM using the Self-Ordered Pointing Task.
Results: Consistent with previous studies of autism, children with Asperger Syndrome showed impaired performance on verbal, but not the nonverbal WM task.
Conclusions: Although this finding contradicted our hypothesis, qualitative observations and post-task interview revealed greater use of verbal strategies during the nonverbal task by

children with Asperger Syndrome. Thus, verbal reasoning abilities may have masked possible deficits in nonverbal WM capacity. Future studies should apply more sensitive spatial working memory tasks. Results are discussed with respect to compensatory techniques applied by individuals with Asperger Syndrome and implications for development of remediation techniques.

37 115.7 Reading the Mind in the Eyes: test-retest reliability of a Swedish version. M. Hallerbäck*[1], T. Lugnegård[1], F. Hjärthag[2] and C. Gillberg[3], (1)*County Council of Värmland*, (2)*Karlstad University*, (3)*Göteborg University*

Background: The "Reading the Mind in the Eyes Test" revised version (Eyes Test), was developed by Simon Baron-Cohen and his group. It is considered to be an advanced theory of mind test, sensitive to "mind reading" ability in adults with normal intelligence. The Eyes Test has been used in studying theory of mind difficulties in autism spectrum disorders. Although the Eyes Test has been translated to several languages and is widely spread, no study of test-retest reliability has yet been published.

Objectives:

Examine test-retest reliability of a Swedish version of the Eyes Test.

Methods: A Swedish translation of the child version of the Eyes Test consisting of 24 items was used. Participants were 58 students (33 female and 25 male) at the University of Karlstad. The test was given twice at an interval of three weeks. To examine the test-retest reliability we used the Bland Altman method to measure the limits of agreement. This is a statistical method designed to examine the agreement between two test methods or the repeatability of a method. Using this statistical method it is possible to both visualize and calculate the agreement between two test times.

Results: The limits of agreement was ± 4.3

Conclusions:When the Eyes Test is used, either in research or clinical practice, one has to take into account that an obtained test score must be regarded as an approximation. A test score variation in the range of ±4 (out of 24 possible) is to be expected for the same individual. However, there was no indication of learning effects when the test was repeated.

38 115.8 Creativity, Evolutionary Psychology, Psychiatry with Particular Reference to Autism and Asperger's Syndrome. M. F. Fitzgerald*, *Trinity College Dublin*

Background: Child and Adolescent Psychiatry quite rightly puts major emphasis on psychopathology and the functional impairments caused by psychopathology. Nevertheless it has been very long recognised that certain psychopathological states can have positive benefits for the individual and indeed can be adaptive.

Objectives: Peter Jensen et al. (1997) showed that in ancestral environments ADHD symptoms could be adaptive and enhance survival.

Methods: Study of case histories. This poster will discuss creative aspects of Attention Deficit Hyperactivity Disorder and Autism. It will focus on the extreme male brain and its relation to great creativity in the areas of science, engineering, mathematics, etc..

Results: This poster will show that personality traits associated with great creativity including persistence, capacity to hyperfocus, capacity for narrow focussing on detail, as well as a certain reduced interest in the wider social world.

Conclusions: Autism can lead to great originality and breakthroughs. It will examine a hypothesis that multiple genes of small effect that may be significantly responsible for psychiatric conditions can also have other effects in the areas of creativity and indeed in the areas of adaptation.

References:

(1) Fitzgerald M. (2000). Is the cognitive style of persons with Asperger's syndrome also a

"mathematical style"? Journal of Autism and Developmental Disorders, 30, 2, 175 – 176.

(2) Jensen P. (et al, 1997). Evolution and Revolution in Child Psychiatry: ADHD as a Disorder of Adaptation. Journal of the American Academy of Child and Adolescent Psychiatry, 36, 12, 1672 – 1679.

39 115.9 Visual perspective taking impairment in children with ASD. A. Hamilton*[1], R. Brindley[2] and U. Frith[2], (1)*University of Nottingham*, (2)*University College London*

Background: Evidence from typical development and neuroimaging studies suggests that level 2 visual perspective taking – the knowledge that different people may see the same thing differently – is a mentalising task. Thus, we would expect children with autism, who fail typical mentalising tasks like false belief, to perform poorly on level 2 visual perspective taking as well. However, prior data on this issue is mixed, with some reports of success in autism.
Objectives: The aim of the study was to determine if children with autism have specific difficulties with level 2 visual perspective taking, in relation to their verbal and spatial abilities.
Methods: We tested a group of 23 young autistic children and three groups of typical children on a simple level 2 visual perspective task and a closely matched mental rotation task. Groups were matched on either verbal or spatial abilities.
Results: The data show that autistic children have difficulty with visual perspective taking but not mental rotation, relative to typical children. Furthermore, performance on the level 2 visual perspective taking task correlated with theory of mind performance.
Conclusions: These results support the hypothesis that children with autism have specific difficulties with mentalising tasks, and demonstrate the value of using visual perspective taking tasks, which have low verbal requirements and close control conditions, to assess mentalising abilities.

40 115.10 Variation in the human cannabinoid receptor gene (CNR1) modulates gaze duration for happy faces. B. Chakrabarti* and S. Baron-Cohen, *University of Cambridge*

Background:
Humans look longer at preferred stimuli. This is also true for facial expressions of emotion. Here, we probed variations in the *CNR1* gene for how it influences gaze duration to facial expressions of five basic emotions (happy, sad, angry, disgust, fear). The cannabinoid receptor 1 (*CNR1*) gene is a key component of the endocannabinoid system, which works with the mesolimbic dopaminergic pathways involved in processing rewards. In a previous fMRI study (Chakrabarti et al., 2006), we found that happy (but not disgust) faces trigger different degrees of reward-related neural activity, depending on the variant of *CNR1* SNPs. We presume this is because brains differ genetically in the extent to which happy faces are treated as social rewards.

Objectives:
Variation (SNPs) in the *CNR1* gene was predicted to be significantly associated with individual variability in gaze duration for happy faces.

Methods:
30 typical volunteers (13 males, 17 females, mean age 24.1 years) were genotyped for 4 SNPs (reported earlier) in *CNR1*, and tested on an emotion recognition paradigm (16 videoclips of 3s each for each of the 5 emotions, from Mindreading™), while their gaze fixation time was recorded using ERICA (www.eyeresponse.com). Total gaze duration was measured for each stimulus.

Results:
Separate analyses of variance were performed for each SNP, with gaze duration as the dependent variable. This revealed two SNPs (rs806377 and rs806380) associated with differential gaze duration for happy (but not disgust) faces.

Conclusions:
The results converge with our earlier fMRI finding in suggesting that *CNR1* is a key element in the molecular architecture of social reward perception. Our recent genetic association study of autistic traits and empathy in a typical sample found a

significant association with *CNR1*. Together, this suggests an important role for CNR1 in social reward perception. This may implicate a role for it in underlying autistic traits.

41 115.11 Selective Attention and Perceptual Load in Autism. A. Remington*, M. Coleman, R. Campbell and J. Swettenham, *University College London*

Background: When we focus our attention on an aspect of the environment it is important to be able to ignore potentially interfering distractors (selective attention). Ignoring distractors though is not always something that can be done at will, and it does seem that under some circumstances we process distractor information whether we like it or not (e.g. we hear our own name mentioned in a conversation we are not focusing on at a cocktail party). Recent research by Lavie (1995) has shown that the degree to which distractors are processed depends on how much of our finite attentional resource is allocated to the task we are focussing on (perceptual load theory).

Objectives:This study examined the effect of perceptual load on selective attention within Autistic Spectrum Disorders (ASD). Previous studies suggest that individuals with ASD might find it difficult to ignore distractors (Burack et al 1994), although no studies have yet taken into account the perceptual load of the focus task. The issue of the special status of social stimuli when they are the distractors was also addressed. Typical individuals find these hard to ignore whatever the perceptual load of the task they are focussing on.

Methods:Young adults with ASD and typically developing adults performed visual attention tasks with varying perceptual load and distractor types.

Results:Preliminary results suggest that individuals with ASD continue to be affected by distractors at higher levels of perceptual load than typically developing controls. With social stimuli, a different pattern is seen: typical adults are distracted irrespective of perceptual load while ASD adults show no such 'special case' for faces.

Conclusions: The results obtained appear to suggest increased perceptual capacity in individuals with ASD.

42 115.12 Nonverbal Sensitivity in Individuals with Autism Spectrum Disorders. R. L. Pohlig*[1], L. Klinger[2], M. Klinger[2], C. Klein[2] and J. Mussey[2], (1)*College of Saint Benedict & Saint John's University*, (2)*University of Alabama*

Background: Differences in face processing have been identified in individuals with autism spectrum disorders (ASD; Jemel et al., 2006), but little ASD research has examined the broader concept of *nonverbal sensitivity*, which includes processing of facial expressions, body language, and vocal prosody, and has been implicated as important for social interaction in individuals with typical development (TD; Burgoon & Bacue, 2003).

Objectives: The current study investigated understanding of facial expressions and body postures/gestures in individuals with ASD in order to expand our understanding of the nonverbal basis for their social deficits.
Methods: Participants included 19 males with high-functioning ASD and 19 males with TD, matched on age and verbal ability. Participants watched a series of 3-second video clips of women's faces and women's bodies (with the faces covered) and were asked to identify the corresponding emotion.
Results: All participants performed more accurately with face, rather than body, stimuli. The group with ASD was significantly less accurate in responding to face stimuli than the group with TD ($d = .84$). There was not a significant difference between diagnostic groups in accuracy of response to body stimuli ($d = .36$). However, for the group with ASD only, there were significant correlations between accuracy on face and body stimuli and verbal reasoning skill ($r = +.78$ and $+.79$), as well as between accuracy on face stimuli and lifetime social deficits ($r = -.44$).
Conclusions: Results replicated findings of face processing impairments in ASD. Relative impairment in a broader range of nonverbal sensitivity in ASD was not supported by the current methodology. However, the strong relation between nonverbal sensitivity and

verbal reasoning in participants with ASD suggests that they may be able to use verbal reasoning to compensate for weak nonverbal sensitivity. Weak nonverbal sensitivity may also underlie social skills impairments.

43 115.13 Recognizing emotions in music: A strength in ASD. E. M. Quintin*[1], A. K. Bhatara[2], H. Poissant[3], E. Fombonne[4] and D. J. Levitin[2], (1)*Université du Québec à Montréal & Centre for Interdisciplinary Research in Music Media and Technology*, (2)*McGill University, Centre for Interdisciplinary Research in Music Media and Technology*, (3)*Université du Québec à Montréal*, (4)*Montreal Children's Hospital*

Background: Individuals with autism spectrum disorders (ASD) exhibit a heightened interest in music and above average auditory processing abilities (Heaton, 2005). Baron-Cohen et al. (2000) suggest that hypo-functioning of the amygdala may explain the social and emotional deficits in ASD such as a diminished sensitivity to fear.
Objectives: Given the amygdala theory of autism and given that recognition of frightening and peaceful music is impaired in patients with damage to the amygdala (Gosselin et al., 2005), it is expected that individuals with ASD should not recognize frightening music as such. However, happy and sad music should be correctly identified by individuals with ASD (Heaton et al., 1999).
Methods: Teenagers with ASD (N=26; age: Mean±SD= 13.6±1.9 years, FSIQ: Mean±SD= 97±15) and typically developing (TD) teenagers (N=26, age: Mean±SD= 13.5±2.2 years, FSIQ: Mean±SD= 108±12) with comparable verbal and performance IQ and musical knowledge and ability participated in the study. Participants described musical excerpts using one of the 4 following emotions: happy, sad, scared or peaceful.
Results: Significant main effects were found for "intended emotion", $F(3,150)= 28.6$, $p<.001$, and diagnostic group, $F(1,50)= 5.28$, $p = .3$, with the ASD group being less accurate than the TD group, but there was no interaction between the factors. Emotion recognition was significantly correlated with VIQ, $r=.44$, $p=.1$, one-tailed, for participants with ASD but not for TD participants. Post-hoc analyses failed to find a diagnosis group difference when the four emotions were considered separately.
Conclusions: Our results replicate Heaton and colleagues' (1999) observations that individuals with ASD can identify happy and sad music. However, our results fail to support Baron-Cohen and colleagues' (2000) amygdala theory of autism, which states that individuals with ASD exhibit impaired fear recognition. It is possible that music represents a specific domain where the amygdala theory of autism does not hold.

44 115.14 ADMINISTRATION OF A COMPLETELY NON-VERBAL FALSE BELIEF TEST FOR CHILDREN WITH ASD. A. Senju*[1], V. Southgate[1], Y. Miura[2], T. Matsui[2], T. Hasegawa[3], Y. Tojo[4], H. Osanai[5] and G. Csibra[1], (1)*Birkbeck, University of London*, (2)*Kyoto University*, (3)*University of Tokyo*, (4)*Ibaraki University*, (5)*Musashino Higashi Gakuen*

Background: Recent studies adopted completely non-verbal false belief tasks to the preverbal infants, using children's looking behaviour as a dependant measurement. These studies have revealed that children younger than 3 years of age, who consistently fail the standard verbal false belief test, can anticipate others' action based on their attributed false beliefs. These tests would be beneficial for children with limited linguistic abilities. However, so far these studies have been limited to the typically developing children and it is still unknown whether children with ASD, who are known to have difficulties in the standard verbal false belief test, would also fail in a non-verbal false belief test.

Objectives: The current study examined whether children with ASD show action anticipation in a non-verbal false belief test.

Methods: We presented video stimuli of an actor watching an object hidden in a box. The object was then displaced while the actor was looking away. We recorded children's eye movement with an eye-tracking device while they watched the subsequent action and coded whether they spontaneously anticipated the

model's behaviour that could only have been predicted based on her false belief. We also administered a standard verbal false belief task and examined the relation between verbal and non-verbal false belief tasks both in typically developing children and in children with ASD.

Results: In the non-verbal false belief task, although typically developing children correctly anticipated the action, children with ASD failed to show such action anticipation. The performance in the non-verbal false belief task positively correlated with that of the standard false belief task in typically developing children. In contrast, these two tasks were not correlated with each other in children with ASD.

Conclusions: The results suggest that children with ASD have an inherent impairment in false belief attribution, which is independent of their verbal ability.

45 115.15 Exploring the Construct of Social Attention. S. Fletcher-Watson*[1] and S. Leekam[2], (1)*University of Newcastle*, (2)*University of Durham*

Background: Autism spectrum disorders often entail atypicalities in attention directed to social stimuli in the real world. However 'social attention' is a poorly defined term, used differently in various areas of psychology. If we are to understand the crucial role of social attentional impairments in the development of autism we must examine this construct in more detail. This examination should incorporate multiple measures of attention and types of social information and must also acknowledge individual differences within a diagnostic group.
Objectives: To examine the nature of social attention in people with and without autism, using cross-task analyses to investigate both an underlying social attention construct and individual and group differences in its manifestation.
Methods: Three experiments employing different methods (content analysis, change detection and eye-tracking), all produced measures of attention to social information (e.g. people, and particularly eyes). Comparable measures were incorporated into an analysis of group and individual response patterns across all three tasks, assessing attention to social information in the visual domain.
Results: Though sample sizes were small, statistical techniques including principal components analysis, cluster analysis and a case study revealed an absence of relationships between different measures of social attention.

Conclusions: This report presents an important first step in investigating the complex nature of social attention. The assumption of a single social attention construct should continue to be questioned; social information varies across tasks just as attentional processes do. In future, it may be useful to consider a hierarchy of social information, each level demanding different degrees of attention. This hierarchy is likely to be flexible, varying between individuals and across situations. This conclusion has significant consequences for our understanding of social impairments in autism.

46 115.16 The Level and Nature of Autistic Intelligence Revisited. F. Poustka*[1], I. Dziobek[2] and S. Bölte[1], (1)*J.W.Goethe-University*, (2)*Max-Planck Institute for Human Development*

Background: Owing to higher performance on the Raven's Progressive Matrices (RPM) than on the Wechsler Intelligence Scales (WIS), it has recently been argued that intelligence is underestimated in autism. Objectives: This study sought to replicate and elaborate the findings on RPM versus WIS performance in autism. Methods: RPM and WIS IQs were studied in a clinical sample of $N = 48$ individuals with autism (36 males and 12 females) aged 7.5 to 28.3 years ($M = 15.3$; $SD = 6.4$). Results: Average RPM IQ was higher than WIS IQ, albeit to a much lesser degree than previously reported. While the discrepancy between tests was substantial for participants with WIS IQs < 70, it was negligible for those with IQs ≥ 70.
Conclusions: Giving the importance of reliable multidimensional IQ estimates in autism, the WIS should continue to be regarded as the first choice IQ measure in high functioning individuals. Additional testing with the RPM

might be indicated in the lower end of the spectrum.

47 115.17 Facial emotion recognition in high-functioning Autism - a new sensitive test of subtle deficits using dynamic stimuli. M. J. Law Smith*[1], B. Montagne[2], M. Gill[1] and L. Gallagher[1], (1)*Trinity College Dublin*, (2)*UMC St. Radboud*

Background: The ability to recognise the emotional expressions of others forms an essential part of successful social functioning. Autism Spectrum Disorders (ASD) are characterised by social and communication impairment, yet evidence for deficits in the ability to recognise facial emotions is equivocal. Some studies have shown individuals with ASD show deficits on interpreting emotions from facial expressions compared to the general population (e.g. Bolte & Poustka 2003). Other studies, however, have reported that individuals with ASD do not show deficits in recognition of the basic emotions (e.g. Grossman et al. 2000). This discrepancy in results may be due to differing methodologies. Studies reporting no deficits have used stimuli that may be too simple (with associated ceiling effects), for example, 'full-blown' expressions.

Objectives: The study aims to test individuals with high-functioning Autism (HFA) on a new sensitive test of facial emotion recognition using varying intensities of expression (Montagne et al. 2007) in order to investigate subtle deficits in recognition of the basic emotions.

Methods: 10 males with HFA, diagnosed using research diagnostic criteria aged 15-17 are undergoing testing on the Emotion Recognition Test (Montagne et al. 2007) which uses dynamic stimuli of facial expressions in varying intensities of the 6 basic emotions (happy, sad, anger, fear, surprise, disgust). 10 age and IQ matched controls are undergoing testing on the ERT. IQ was measured using the Leiter-R.

Results: Data is currently being collected.

Conclusions: Results will be discussed in relation to previous findings and theory.

48 115.18 SELF-PERCEPTION AND SOCIAL ORIENTING IN YOUNG CHILDREN WITH AUTISM. L. E. Bahrick*[1], I. Castellanos[1], M. Shuman[1], M. Vaillant-Molina[1], L. C. Newell[2] and B. M. Sorondo[1], (1)*Florida International University*, (2)*Indiana University of Pennsylvania*

Background: Children with autism show self-awareness and social orienting deficits (e.g., Dawson, Meltzoff, Osterling, Rinaldi, & Brown, 1998; Gergely, 2001). Self-perception and social orienting develop in infancy, partly from detecting contingent relations between visual and proprioceptive feedback from self-produced body motion (Bahrick, 1995). By five months, infants demonstrate social orienting and prefer to watch the noncontingent video display of a peer's leg motions over the perfectly contingent display of their own leg motions (Bahrick & Watson, 1985).

Objectives: We assessed self-perception and social orienting in young children with autism (ASD) and typically developing (TD) children.

Methods: Nine ASD (M = 3.60 yrs) and nine TD children (M = 2.55 yrs), matched for functional age on the ABAS (TD: M = 2.30 yrs; SD = .54; ASD: M = 2.23, SD = .84), participated in a task identical to Bahrick & Watson's (1985) visual paired-comparison procedure. A perfectly contingent, live video of the child's own leg motions was shown alongside a pre-recorded noncontingent video of a peer's leg motions, both wearing white socks.

Results: TD, but not ASD, children discriminated between the contingent display of their own leg motions and the noncontingent display of a peer's leg motions. TD children showed social orienting by looking preferentially to the noncontingent peer display $t(8) = 2.82$, $p < .5$; ASD children showed no preference ($p > .5$), and their looking to the peer was significantly lower than that of TD children $t(16) = 2.35$, $p < .5$.

Conclusions: In contrast with TD infants and children, ASD children showed no evidence of detecting the intermodal proprioceptive-visual contingency generated by self motion, and no

discrimination of contingent self motion from noncontingent peer motion. Future research will assess whether these findings are attributable to impaired social orienting, impaired detection of intermodal proprioceptive-visual contingency, or both.

49 115.19 Do children with autism spectrum disorder (ASD) recognize and describe his/her own emotions appropriately? A survey of school-aged children with ASD in Japan (I). M. Kamiya*, Y. Yoshihashi, T. Miyachi, K. Tsuchiya and M. Tsujii, *Osaka-hamamatsu Joint Center for Child Mental Development*

Background: Studies have revealed that children with autism spectrum disorder (ASD) have an impairment in identifying other's emotion. However, few studies have ever addressed whether they are also limited in recognizing and describing the emotions elicited inside themselves.

Objectives: The present study aimed at elucidating whether children with ASD recognize and describe his/her own emotions differently from age-matched typically developed children using a questionnaire we developed.

Methods: We recruited 41 children with ASD and 205 age-matched control children (8 to 12 years). The participants were asked to complete a questionnaire, where six situations were prepared to elicit specific emotions (e.g. delight, anger, sadness). Then, the participants were asked to describe in a free text form how they feel when facing with each of the 6 situations. Two children with ASD and 14 control children were excluded from the analyses because no texts were provided. We analyzed the texts from three viewpoints: a) whether any kind of emotions appropriate for the situation are included (an examination of appropriateness), b) whether any words identifying a specific emotion are included (an examination of appropriate use of words conveying emotional contents), c) whether any colloquial expressions are included (an examination of emotional involvement).

Results:We found that children with ASD and typically developed children both provided emotionally appropriate expressions with an equal frequency. However, children with ASD were more likely to use colloquial expressions in some situations (e.g. "You got a birthday present"), and less likely to in other situations (e.g. "A friend of yours teased you").

Conclusions:The results implied that, although children with ASD are not limited in recognizing his/her own emotions appropriately, they may describe his/her own emotion differently from typically developed children.

50 115.20 Do children with autism spectrum disorder (ASD) recognize his/her own facial expression appropriately? A survey of school-aged children with ASD in Japan (II). Y. Yoshihashi*[1], M. Kamiya[1], T. Miyachi[1], M. Tsujii[1] and K. J. Tsuchiya[2], (1)*Osaka-Hamamatsu Joint Center for Child Mental Development*, (2)*Hamamatsu University School of Medicine*

Background: Studies have revealed that children with autism spectrum disorder (ASD) are limited in face-reading, i.e. not good at relating other's facial expression to a specific emotion. However, few studies have ever explored whether they are also limited in relating his/her own facial expression to a specific emotion elicited inside themselves.Objectives:The present study aimed at examining whether children with ASD show a different pattern of recognition of his/her own facial expressions under situations designed to elicit a specific emotion in comparison with age-matched typically developed children.

Methods: We recruited 41 children with ASD and 205 age-matched control children (8 to 12 years). The participants were asked to complete a questionnaire, where six situations were prepared to elicit specific emotions (e.g. delight, anger, sadness). For each of the 6 situations, the participants were asked to choose one picture that most closely resembled his/her elicited emotion out of 6 cartoon pictures of facial expressions (e.g. astonishment, anger, neutral, confusion, delight, sadness). Two children with ASD and 14 control children were excluded from the

analyses because no choices were provided. We analyzed the frequency of chosen pictures for each of the 6 situations.

Results:The proportion of participants who chose pictures suitable for each situation did not differ between the two groups. However, in two situations where the participants are expected to choose a sad face, and in one situation where they were expected to choose an angry face, children with ASD were more likely to choose an astonished face than were typically developed children.

Conclusions:The results implied that most children with ASD can recognize his/her own facial expression appropriately, whereas a few children who could not recognize it appropriately although they tended to recognize it uniformly as astonishment.

51 115.21 Theory of Mind Precursor Deficit in Young Children with Autism. D. Rakison[1], C. Johnson*[2], J. Cicchino[1] and K. Sacco[3], (1)*Carnegie Mellon University*, (2)*University of Pittsburgh*, (3)*Children's Hospital of Pittsburgh*

Background: According to one well-known perspective, the characteristic social and communication deficits in autism result from a lack of *theory of mind* (Baron-Cohen, 1995). This deficit means that individuals with autism cannot make inferences about what others know, believe, think, and feel. However, it remains to be seen whether this inability to mentalize results from a more basic deficit in interpreting action as goal-directed. That is, if an individual cannot understand that objects' motion is targeted at another referent they will not be able to understand that intentions and desires are also directed at a referent.

Objectives: The objective of our work is to examine whether young children with autism (AD) interpret the actions of animals and vehicles as goal-directed and compared this behavior to typically developing (TD) infants and young children

Methods: We used a version of Woodward's (1998) task. Participants were shown a toy animal or a toy vehicle moving to one of two objects (e.g., food, toys) on the left or right side of a board. The locations of the two objects were then switched, and participants were encouraged to imitate the action they observed with the same toy used by the experimenter. If participants interpret the action as goal-directed they should move animals – but not vehicles – to the old object in the new location

Results: Current data with children with AD (N = 14, mean age 38 months) suggests that they may not generalize goal-directed action appropriately to animals; in other words, they do not move animals to the same object to which the experimenter did. This pattern of behavior differs from younger TD children who generalize goal-directed action to animals by 22 months of age. Conclusions:The data will be discussed in regard to cognitive deficits in autism and the ability of AD children to imitate.

52 115.22 COMPARISON OF THE MULLEN SCALES OF EARLY LEARNING AND THE BAYLEY COGNITIVE SCALE, 3RD EDITION, IN ASSESSING NONVERBAL IQ IN TODDLERS WITH AUTISM SPECTRUM DISORDERS. A. Esler*, S. Stronach, S. E. Weismer and M. A. Gernsbacher, *University of Wisconsin-Madison*

Background: The Bayley and Mullen scales are commonly used measures of cognitive skills in toddlers, with the Mullen used frequently in research involving children with autism spectrum disorders (ASD). The Mullen and Bayley-III are the only standardized measures of nonverbal cognitive functioning for children under age 2. Convergent validity was examined for the Mullen and original Bayley Scales of Infant Development, with small to moderate correlations (Mullen, 1995). Neither measure has been investigated with regard to convergent validity in young children with ASD. Validity of nonverbal cognitive scores is particularly relevant for young toddlers with ASD, who are likely preverbal, as they provide information on overall development.

Objectives: Examine the convergent validity of Mullen nonverbal scales with Bayley-III cognitive scales in a sample of toddlers age 2 years with ASD.

Methods: Participants were over 50 children in the Toddler Talk Project, a longitudinal study on language development of children with ASD. Children are seen yearly, starting at age 2 until age 5. ASD diagnoses were determined using full diagnostic evaluations that included the ADI-R and ADOS. The Mullen and Bayley-III were given at the same appointment at the 2-year-old visit.

Results: Preliminary results indicated strong correlations between the measures for nonverbal mental age; standard scores were not correlated. A significant number of children had differences in standard scores greater than 1 SD, putting them into a different qualitative score range on each measure. In almost all cases, standard scores on the Mullen were lower.

Conclusions: Nonverbal IQ has been identified as an important predictor of later functioning (Lord et al., 2006). It has important implications for research, as it often is used as a primary variable. Caution should be taken in interpreting nonverbal standard scores for toddlers with ASD using the Mullen or Bayley-III. Age equivalent scores showed good agreement.

53 115.23 Future Thinking in Children with Autism Spectrum Disorders. L. K. Jackson* and C. M. Atance, *University of Ottawa*

Background: All typically-developing humans can direct their thinking away from the present and towards the future. Future thinking ability lies at the root of our ability to delay gratification, plan ahead, and anticipate future events. Without this ability, our behavior in the present would appear unusually restricted, inflexible, and seemingly unreasonable. We propose that difficulties in future thinking ability may characterize children with Autism Spectrum Disorders (CWAs), thus accounting for some of the inflexibility in their thinking.

Objectives: This study examined future thinking skills in CWAs, using two types of future thinking tasks that we termed *self-based* and *mechanical-based*. We argue that *self-based* tasks require a projection of the *self* into the future to pre-experience an event, whereas *mechanical-based* tasks require reasoning about future *physical* transformations. We predicted that CWAs would perform better on *mechanical-based* tasks than on *self-based* tasks, since the latter rely heavily on a concept of a future self, and hence on theory of mind skills, which are frequently impaired in CWAs.

Methods: Fourteen children, diagnosed with Autistic Disorder, Asperger's Syndrome, or Pervasive Developmental Disorder-Not Otherwise Specified by independent clinicians, completed 10 tasks; 5 of each of the two types described above. They also completed the Peabody Picture Vocabulary Test, 3rd edition (Dunn & Dunn, 1997).

Results: CWAs passed significantly more of the mechanical tasks (M = 2.7) than the self tasks (1.14), z = -2.59, p = .1.

Conclusions: Although the results must be considered preliminary due to the small sample size, this study is an important addition to the body of autism literature which, to date, has not targeted future thinking skills. Our next step is to examine future thinking skills in a larger, more representative, sample of children with Autism Spectrum Disorders.

54 115.24 Children with Autism Show Perceptual Bias Consistent with Altered Ventral Visual Pathway Processing. C. T. Fuentes*[1], C. E. Connor[2], S. H. Mostofsky[1] and A. J. Bastian[1], (1)*Johns Hopkins School of Medicine, Kennedy Krieger Institute*, (2)*Johns Hopkins University, Johns Hopkins School of Medicine*

Background: Previous studies have demonstrated a visual perceptual bias in autism that results in a focus on details, or 'local' features, often at the expense of the whole, or 'global' features. This pattern is opposite to that usually observed in typically developing populations. It is possible that this bias reflects changes along the ventral visual pathway, which assembles local image features into representations of whole shapes.

Objectives: We asked whether children with high-functioning autism (HFA) are more perceptually sensitive to local rather than

global geometric features known to be explicitly represented in ventral pathway visual areas (e.g., areas V4, IT). If so, this would suggest altered processing in regions responsible for assembling object parts into whole shapes.

Methods: We studied children with and without HFA on a two-alternative forced choice task that asked which shape was most different from a sample shape. We generated shapes using Bezier splines and locally or globally manipulated parameters (curvature, orientation, relative position) that neurophysiological studies have shown to be explicitly represented in higher-level ventral visual cortex. An algorithm was developed to quantitatively compare differences between shapes on local and global scales.

Results: First, we confirmed that our algorithm quantitatively discerns local and global manipulations of the abstract shape stimuli. Second, our preliminary data show that children with HFA select local manipulations as having a greater effect on altering shape than global manipulations.

Conclusions: We have quantitatively manipulated local and global geometric characteristics that are explicitly represented in higher-level ventral visual cortex. Relative to controls, children with HFA perceive local geometric differences to be more salient than global differences, implying altered processing in the ventral visual pathway. This study provides an objective measure of the local visual bias in autism and establishes a link between this bias and the neural basis of object perception.

55 115.25 Shared Affective Instability in Autism Spectrum Disorder and Bipolar Disorder. K. C. Bertoglio*[1], G. T. Voelbel[2], M. E. Bates[3], G. J. Pandina[4] and R. L. Hendren[1], (1)*UC Davis MIND Institute*, (2)*Kessler Medical Rehabilitation Research and Education Center*, (3)*Rutgers State University*, (4)*Ortho-McNeil Janssen Scientific Affairs*

Background: A subset of children with autism spectrum disorder (ASD) present with emotional dysregulation that resembles the affective instability (AI) symptoms observed in bipolar disorder (BD). A growing literature suggests co-occurring disorders and possible morbidity or etiologic overlap between ASD and BD. However, this overlap has not been well defined. A better description of AI may help elucidate symptom and etiological similarities between BD and ASD and facilitate the identification of potential biomarkers and treatment targets.

Objectives: To use K-SADS variables to study AI symptoms in children with ASD and children with BD thus delineating a domain of affective instability.

Methods: Children between 7 and 13 years with either DSM-IV ASD or BD, recruited for separate studies, received assessments including: Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS), the Autism Diagnostic Interview (ADI-R), and the DSM-IV Asperger's/Autism Checklist. Nineteen symptoms from the K-SADS were selected as representative of AI based on face validity. The ASD and BD groups were compared for the frequency of these AI symptoms.

Results: As expected, K-SADS symptoms of AI were more prevalent in the BD group. However, a subset of the ASD group also demonstrated a high frequency of AI symptoms. A cluster of eight symptoms displaying the greatest overlap between the two groups including acts before thinking, distractibility, depressed affect, grandiosity, inappropriate affect, decreased sleep, elated mood, and flight of ideas had an average frequency of 47% in the BD group, 26% in the ASD group, and 3% in the control group. Symptoms of AI were extreme enough in 13% of children with ASD to warrant a secondary lifetime diagnosis of BD.

Conclusions: A subset of children with ASD has significant AI resembling BD. Biomarker research may help identify overlapping etiopathogenesis of AI across DSM disorders.

56 115.26 Theory of Mind (ToM), Social Skills, Syntax and Vocabulary in Children with Autism Spectrum Disorder. J. M. Paynter* and C. C. Peterson, *The University of Queensland*

Background: Previous research suggesting false belief (FB) understanding is related to social maturity for children with ASD supports the ToM hypothesis of autism. There are however inconsistencies in this research with not all individuals passing FB scoring higher than failers on social skills (Frith, Happe' & Siddons, 1994). It has been hypothesised (preserving this theory) that compensatory verbal strategies may be used by some individuals to "hack out" solutions which do not translate into everyday social skills (e.g. Happé, 1995). Supporting this hypothesis receptive vocabulary and syntax have been found to be more highly correlated with FB for individuals with ASD than for those without (Fisher et al., 2005). Research however has not investigated how syntax relates to social skills nor how language and social skills interconnect in relation to broad ToM (e.g. Wellman & Liu, 2004).

Objectives: The current research aimed to fill this gap.

Methods: 22 Australian children (ASD=14, typical= 8) aged 4 through to 13 years took a standard FB battery, a broad ToM scale (Wellman & Liu, 2004), PPVT-III, Raven's Matrices and TROG-R. Parents and teachers rated the children on two social skills tests previously shown to relate to ToM (Frith et al., 1994; Peterson, Slaughter & Paynter, 2007).

Results: Both the parent's and teacher's ratings of social skills correlated with both the broad ToM and standard FB battery for children with ASD but not typical children. In addition vocabulary and syntax were found to be related to both ToM measures for ASD children only.

Conclusions: Vocabulary and syntax appear to be more influential on ToM and social skills for children with ASD. In addition previous findings with FB were replicated and shown to generalise to broad ToM.

57 115.27 Individuals with autistic spectrum disorders are impaired in time-based prospective memory tasks. M. Altgassen*[1], M. Kliegel[1] and T. I. Williams[2], (1)*Technische Universitaet Dresden*, (2)*University of Reading*

Background: Prospective memory is defined as the ability to execute previously formed intentions. Individuals with autistic spectrum disorders (ASD) often have difficulties to organize and coordinate everyday activities as a result of poor time management, poor preparation and sequencing of actions. Thus, they show deficits with planning ahead and possibly with prospective remembering.

Objectives: Investigate, for the first time, time-based prospective memory performance in children with ASD in comparison to controls.

Methods: Eleven children with ASD and 11 age- and ability- matched typically developing controls participated in the current study. The prospective memory test was embedded in a visuo-spatial working memory test and asked participants to respond to certain target times.

Results: Analyses of variance (ANOVA) revealed that controls had significantly more correct prospective memory responses than individuals with ASD. Moreover, controls checked the time more often and increased time-monitoring more steeply as the target times approached.

Conclusions: Individuals with ASD showed a reduced time-based prospective memory performance in comparison to controls. Time-checking data implies that this performance difference may result from impaired self-initiated processing skills as indicated by reduced task monitoring.

58 115.28 What Cognitive Factors Predict Emotion Recognition in Children with Autism?. S. Garib-Penna*, D. G. Moore and R. George, *University of East London*

Background: There is an ongoing debate as to whether the deficits shown by children with autism in emotion recognition stem from a specific and widespread affective disorder (Hobson et al., 1986, 1988, 1989) or are a consequence of other cognitive problems. Objectives: Our studies extended the work of Gepner et al. (2001) and systematically investigated the extent to which problems in emotion recognition in faces and bodies in children with autism are predicted by cognitive factors including motion perception abilities,

biological motion sensitivity and capacities for featural and configural processing of faces and non-faces. We wished to establish whether, once these factors are accounted for, children with autism continue to show impairments in emotion recognition in faces and bodies. Methods: Children with autism aged 8 to 14 years and verbally-matched typically developing children aged 4 to 7 years took part in this series of experiments. Children were asked to undertake three emotion recognition tasks, in which they had to match photographs or dynamic videos of emotions with corresponding photographs. In the first task, target stimuli consisted of static images or dynamic videos of facial emotions in which the *speed of presentation* was manipulated; in the second task, the *amount and type of movement* presented in dynamic facial stimuli was manipulated; the third task tested emotion recognition abilities in moving silhouettes of whole bodies. Children's capacities for general motion processing; face perception and processing style were assessed using a motion coherence threshold task (based on Reiss et al., 2005), a biological motion processing task (based on Blake et al., 2003), a modified 'Ann' face-processing task (based on Yovel & Duchaine, 2006), and a Navon task (based on Plaisted et al., 1999). Results: and Conclusions: Analyses are currently being conducted and will be ready for presentation and discussion at the IMFAR conference.

59 115.29 Development and test of a method of discriminating between the contributions of recollection and familiarity to declarative memory in young or learning disabled individuals with ASDs. S. Bigham*[1], S. Anns[1], A. Mayes[2] and J. Boucher[3], (1)*Thames Valley University*, (2)*University of Manchester UK*, (3)*City University*

Background:

We have hypothesised that whereas recollection is selectively impaired in individuals with HFA/AS, both recollection and familiarity are impaired in individuals with LFA, and that this pervasive impairment of declarative memory contributes to impaired language and intellectual disability in LFA. To test this hypothesis the contributions to declarative memory of recollection and familiarity must be measured separately. However no method exists suitable for use with young children or older learning-disabled individuals.

Objectives:

Our objective was to develop and test such a method.

Methods:

Two groups of 15 young children took part: an HFA/AS group and an age- and language ability-matched TD group. Children were seen individually for a single session.

A forced-choice recognition test was administered first, using 16 non-meaningful 2-dimensional shape stimuli, each paired with 3 similar foils at test. This specific test is known to provide a relatively pure measure of familiarity in amnesic adults.

A cued recall test was administered next, using as cues the last 10 shapes successfully recognised by each child in the previous test, each paired with a stimulus-directed action (e.g., turning the stimulus over; placing a fist on it). At test, shape-recognition was checked in a forced-choice recognition pre-test using a single novel foil, correct recognition being immediately followed by a test of shape-cued action recall. This constitutes a relatively pure measure of recollection.

Results:

The groups performed similarly on the difficult shape-recognition test, with no floor or ceiling effects. All but one child performed at ceiling on the easy shape-recognition pre-test. The HFA/AS group was significantly impaired on the action-recall task.

Conclusions:

Children with HFA/AS have a selective impairment of recollection, as predicted. The predominantly nonverbal method we developed is suitable for use with young children and should transfer to the study of memory in older individuals with LFA.

60 115.30 Source Memory and Social Functioning in Children with High Functioning ASD- A Pilot Study. 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: Social deficits are central in autism spectrum disorder (ASD). Evidence from relatively few studies in ASD population may suggest that episodic memory could be associated to the level of social functioning (Goddard & al.,2006; Liss & al., 2001,Shapiro,1997). Findings from the literature suggest that children with ASD experience deficits especially with the source monitoring in episodic memory. However, the nature of these deficits remains unclear and to this date no study has investigated precisely if source memory may be linked to social difficulties in ASD.

Objectives: To better understand source memory functioning and its relation with social skills in children with ASD .

Methods: A preliminary sample of 13 high functioning boys with ASD aged 8 to 17 years old and matched control were assessed. Groups were match on age, sex and global IQ. Social skills were assessed with the Vineland Adaptive Behavior Scale-2nd edition (Sparrow & al., 2006). Children's memory was assessed using a theory driven experimental task designed to measure memory for source and temporal context of studied words (Doré & al., 2007).

Results: Preliminary findings revealed that children with ASD were not different from the control group in recognition of target words nor in identification of their source and temporal context. However, qualitative data revealed that the ASD group had a different pattern of responses bias. Furthermore, results showed that the ASD children who significantly recognized more target words also displayed a lower level of global adaptive functioning on the VABS. Analyses on the subscales are yet to come.

Conclusions:These preliminary findings suggest that episodic source memory seems to be associated to the adaptive functioning in children with high functioning ASD. Recruitment for this project is still in process and results from further assessment will be discussed.

61 115.31 Executive Dysfunction in Autism Spectrum Disorders; are siblings affected?. J. Sanders*[1], K. Johnson[2], H. Garavan[2], M. Gill[1] and L. Gallagher[1], (1)*Trinity College Dublin*, (2)*Trinity College Institute of Neuroscience*

Background: People with high functioning autism (HFA) have difficulties in social interaction, communication and behaviour, but normal intelligence. In HFA, deficits in the executive function of response-inhibition (eg. inability to suppress context-inappropriate behaviour) lead to conduct that is unsuitable and socially embarrassing[Kana et al, 2007]. Recent research from our laboratory suggests a specific deficit in response-inhibition in children with HFA using the Sustained Attention to Response Task (SART)[Johnson et al, 2007]. Executive dysfunction (held to account for the defining behavioural features of autism[Turner, 1999]) has been reported both in probands with HFA and their close relatives, suggesting that executive function may play a central role in the aetiology of autism[Wong et al, 2006]. However, there are a very limited number of studies investigating executive function in relatives of individuals with HFA. This is surprising as this strategy is important in determining which cognitive deficits are potential endophenotypes for autism [Hughes et al, 1999]. We hypothesise that there will be response-inhibition deficits in probands with ASD and partial deficits in their unaffected siblings suggesting that this executive function is familial and heritable and may be a useful cognitive endophenotype for use in future studies attempting to localise susceptibility genes for autism.

Objectives:

1. To characterise the performance of children with and without HFA on a task testing response inhibition.

2. To determine the familiality/heritability of response-inhibition, by comparing the performance of children with HFA, their unaffected siblings, and control

participants on a task of response inhibition.

Methods:

Neuropsychological testing will be carried out in HFA probands, unaffected siblings, and controls using the SART to assess response-inhibition, and Wechsler Intelligence Scale for Children (WISC-IV) to assess IQ. Neuropsychological data will be analysed using ANOVA and regression analyses.

Results:

Data is currently being collected. Results will be discussed in relation to current theory.

Conclusions:

To be discussed.

62 115.32 Generalised emotion recognition deficits in adults with ASD. R. C. M. Philip*[1], H. C. Whalley[1], A. C. Stanfield[1], R. Sprengelmeyer[2], A. P. Atkinson[3], W. H. Dittrich[4], A. J. Calder[5], E. C. Johnstone[1], S. M. Lawrie[1] and J. Hall[1], (1)*University of Edinburgh*, (2)*University of St Andrews*, (3)*University of Durham*, (4)*University of Hertfordshire*, (5)*MRC Cognition and Brain Sciences Unit*

Background: The debilitating social dysfunction integral to autism has been shown to relate to deficits in processing emotional information from human stimuli. The majority of investigations into emotion processing in autism have used static images of emotional faces[1]. There is however increasing evidence to suggest that those with autism may also display deficits in other stimulus domains and sensory modalities[2,3].

Objectives: We sought to address this by investigating basic emotion recognition across a range of stimulus types and across sensory modalities within a group of people with ASD, using tasks of comparable format.

Methods: 23 AS/HFA participants [mean age 32.5 years (s.d. 10.9 years), 16 males, 7 females] and 23 age and gender matched controls were recruited. ASD participants had previously received a clinical diagnosis of an ASD and were further assessed using the ADOS and AQ. There were three emotion label tasks; faces[4], body movements[5] and voices[6]. Participants selected a text label from a choice of five to describe the emotion expressed in the stimulus. Ten trials of happiness, sadness, anger, fear and disgust were presented in random order in the body movement and voices tasks. Seven trials of each emotion were used in the faces task. A t-test was used to assess differences in group performance for each task.
Results: The ASD group was significantly impaired in labelling emotion in each of the tasks. In the Faces task; control accuracy = 92%, ASD =80%, $t=3.6$, $p=0.003$. In the Body Movement task; control accuracy =86%, ASD 71%, $t=4.17$, $p<0.001$. In the Voice task; control accuracy =79%, ASD 61%, $t=5.5$, $p<0.001$.

Conclusions: Results are indicative of a cross-modal emotion processing deficit in autism. This implicates a neurobiological substrate that is part of an extended network involved in emotion processing, rather than structures specific to face processing.

1.Baron-Cohen,S.*etal*.*JChildPsycholPsychiatry***42**,241-251(2001).
2.Hubert,B.*etal*.*JAutismDevDisorders***37**(7):1386-92(2007).
3.Rutherford,M.D.*etal*.*JAutismDevDisorders***32**,189-194(2002).
4.Matsumoto,D.&Ekman,P.*JACFEEandJACNeuF,*(DeptPsychol,SanFranciscoStateUni,1988).
5.Atkinson,A.P.*etal*.*Perception***33**,717-746(2004).
6.Calder,A.J.*etal*.*Brain***127**,1958-1969(2004).

63 115.33 Features discrimination in real vs. cartoon faces: Do children with autism make the difference?. D. Rosset*[1], A. Santos[2], D. Da Fonseca[1], F. Poinso[3] and C. Deruelle[2], (1)*INCM, CNRS; Autism Resource Center*, (2)*INCM, CNRS*, (3)*Autism Resource Center*

Background:

It is now widely accepted that atypical face processing is a hallmark feature of autistic

spectrum disorders (ASD). However, recent studies suggest that atypical face processing in children with ASD, though present for human real faces, does not extend to cartoon faces, that can be considered as less socially relevant stimuli (e.g., Rosset et al., in press).

Objectives:

The aim of the present study was to determine whether facial perceptual skills in children with ASD differ as a function of the social nature of a face. To this aim, children with ASD were presented with a facial features-discrimination task including pictures of real and cartoon faces, and their performance was compared to that of typically developing controls.

Methods:

17 high-functioning children with ASD and 17 chronological matched controls were presented with 96 pairs of real or cartoon faces. Half of pairs was composed of two identical faces (Same trials), while the remaining pairs included faces differing in terms of the eyes' or the mouth's brightness level (Different trials). Each pair of faces was displayed either upright or inverted. Children were asked to decide whether the two faces of each pair were same or different.

Results:

For controls, a higher performance on upright than inverted trials was found for real but not for cartoon faces. By contrast, children with ASD showed higher performance on upright than inverted trials for both types of faces.

Conclusions:

Contrary to typically developing children, children with ASD fail to show processing differences between real and cartoon faces. Results of this study provide further support to the idea that human faces do not have a special status for children with ASD.

64 115.34 Can children with autism respond appropriately to mental states from dynamic faces?. E. Back*, S. Brown and E. Beecham, *University of Birmingham*

Background: Recent evidence has emerged that children and adolescents with autistic spectrum disorders (ASD) can successfully attribute mental states to facial expressions (e.g., Back, Ropar, & Mitchell, 2007). However, identifying that someone is giving you a *disapproving* look does not necessarily mean that an individual will adjust their behaviour accordingly, this may reveal more profound differences between people with and without ASD with respect to effective social interactions.

Objectives: To investigate whether children / adolescents with ASD can respond appropriately to dynamic facial depictions of mental states.

Methods: 14 participants with ASD and 14 matched typically developing participants (11-14 year olds) took part. A paradigm was developed that had been previously validated with over 60 adults and children. 16 dynamic facial expressions were presented depicting various mental states. After each facial expression was shown, 4 different ways of responding to the face appeared on the screen and participants were asked to choose the option that was the most appropriate way to respond (e.g., ask her what you have done wrong was the correct response for the *disapproving* face).

Results: Overall, participants with ASD (58% correct) were poorer than typically developing participants (69% correct) at choosing the most appropriate response, yet this difference was not quite significant, $F(1, 26)= 3.479$, $p= .73$.

Conclusions: Children with ASD were able to choose an appropriate way to respond to a variety of facial expressions depicting mental states. However there was a trend for poorer performance compared to controls. This provides evidence that the difficulties they have in their everyday social interactions could be related to not knowing the appropriate way to respond, rather than with identification.

65 116.1 In Home Training for Fathers of Children with Autism: A Summary of Year 3 Findings. J. Elder*[1], S. Donaldson[1], G. Valcante[2], R. Bendixen[2] and R. Ferdig[2], (1)*College of Nursing*, (2)*University of Florida*

Background: Literature regarding fathers of children with autism remains sparse, and because mothers are the more common intervening parent, few training methods have been tested with fathers. This presentation summarizes the first three year findings of a NINR/NIH funded study aimed at the development and implementation of novel father-directed training methods.
Objectives: (a) evaluating the effects of training fathers of autistic children with an expanded training module, (b) evaluating the effects of the expanded father training on skill acquisition by mothers, (c) evaluating the effects of the in-home training on parental stress and family cohesion, and (d) developing an Internet-based investigator-father feedback system and evaluating its feasibility during the training protocol and maintenance phases.
Methods: Fathers are taught four components of an in-home training intervention (following the child's lead, imitation, commenting, and expectant waiting). Implementation of these strategies is evaluated via twice weekly, in-home videotaping and father-child and mother-child sessions. Parent and child behaviors have been operationalized and data are analyzed using the Observer Program. Training is enhanced by feedback that fathers receive in person and via a newly developed interactive website.
Results: Data analyzed during the first three years of this R01 (N=18 families) support earlier findings where children responded with increased social initiations, responses, and vocalizations. Newly emerging is the finding that children who benefit most are younger with <50 intelligible words. In addition, we now have preliminary data from five fathers who have used our newly developed interactive website to boost their own training and to train mothers.
Conclusions: These Year 3 data suggest that younger, less verbal children may benefit most from the intervention. Also, pilot work with the new website demonstrates that fathers can successfully use computerized platforms to enhance their family's knowledge. This information will help design parent training interventions that can be remotely delivered interactively over the internet.

66 116.2 Manual Preference and Motor Coordination Levels in Individuals with Autism Spectrum Disorders. N. M. M. Correia*[1], M. A. M. Silva[2] and M. O. F. Vasconcelos[2], (1)*Faculdade de Desporto da Universidade do Porto / Associação Portuguesa para as Perturbações do Desenvolvimento e Autismo Norte*, (2)*Faculdade de Desporto da Universidade do Porto*

Background: The Autism Spectrum Disorder (ASD) is a global development disorder (Marques, 2000). Usually, subjects with ASD present disturbances in gait pattern, global and fine motor coordination and motor stereotypes (Adams et al., 2004; Milne et al., 2006). Left-handedness or an ambiguous manual preference reveals a higher incidence in people with ASD than in general population (McManus and Cornish, 1997; Hauck and Dewey, 2001).

Objectives: The aim of this study was (i) to assess manual preference in each group (ASD and non clinical); (ii) to compare motor coordination levels between groups, according to sex, age (16-30 yrs old and 30-46 yrs old) and handedness (right-handers and left-handers).

Methods: The sample was composed by 130 subjects of both sexes, between 16 and 46 years old, divided in 2 groups. The ASD group had 65 subjects, and the nonclinical group had 65 impaired normal subjects. Subjects' manual preference and motor coordination were assessed. This last comprises (i) dynamic balance; (ii) general coordination; (iii) eye-hand coordination; (iv) eye-foot coordination.

Results: Results showed that the nonclinical group, when compared with the ASD group, presented a statistically significant higher performance in the dynamic balance, general coordination, eye-hand and eye-foot coordination. In the manual preference, the ASD group presented a higher percentage of

left-handers when compared with their counterparts.

Conclusions: The results of our study presented, as we expected, significant differences between the ASD subjects and non clinical subjects in the motor coordination levels. The more important differences appeared in global motor coordination tests when compared to the fine ones, presenting the ASD subjects more variation in relation to the non clinical subjects. The ASD subjects' left-handed percentage is significantly higher when compared with that of the non clinical group.

67 116.3 The Sequential Relationship Between Parent Attentional Cues and Sustained Attention to Objects in Young Children with Autism. N. B. Brigham*[1], P. J. Yoder[1], M. A. Jarzynka[2] and J. Tapp[1], (1)*Vanderbilt University*, (2)*Willowbrook Health & Home Services, Inc.*

Background: Sustaining attention to objects may be particularly challenging for young children with autism. When a child has difficulty sustaining attention to an object or activity, the parent's opportunity to provide developmentally facilitating input may be limited. Determining the types of attentional cues that parents use successfully to orient their child with autism to objects may help us understand how we can extend these developmentally enriching opportunities.

Objectives: To determine if there is a stronger sequential association between child sustained object attention and parent attentional cues when the parent (a) matches the child's focus of attention than when s/he redirects the child or introduces a new focus of attention and (b) coordinates multiple behaviors in the attentional cue than when the s/he uses fewer behaviors. Methods: Twenty-five parent-child dyads were observed during one 20-minute free-play interaction session in a university laboratory setting. Sequential analysis was used to examine the extent to which child sustained object attention occurred after different types of parent attentional cues. Results: The strength of the sequential association between child object attention and parent cues which maintained the child's focus of attention was significantly greater than the strength of the sequential association between child object attention and parent cues which either redirected the child or introduced a new focus of attention. The strength of the sequential association between child object attention and parent cues which included a combination of three or more behaviors was significantly greater than the strength of the sequential association between child object attention and parent cues which included one or two behaviors.
Conclusions: Based on the results of this study, we can recommend that most parents match their child's focus of attention and coordinate multiple behaviors in their attentional cues when attempting to sustain the object attention of their young child with autism.

68 116.4 Comparison of sensory-motor and daily living skills in preschool children with and without autism spectrum disorders. M. Couture*[1], E. Jasmin[2], E. Gisel[2], G. Reid[2] and E. Fombonne[2], (1)*Laval University*, (2)*McGill University*

***Background*:**
While there is controversy in the literature with respect to the nature and extent of sensory-motor difficulties in children with Autism Spectrum Disorders (ASD), very few studies have compared the performance of sensory-motor skills and their impact on daily living skills in different groups of preschool children.

Objectives:
The proposed research will compare the performance of children with ASD to typically developing children (TD), children with intellectual disability (ID) or with speech-language impairment (SLI) on measures of gross and fine-motor skills, sensory processing and daily living skills.

***Methods*:**
This is a clinical descriptive study of children 3 to 6 years of age. Currently, 60 children with ASD, 17 with TD, and 15 with ID or SLI have been recruited. Recruitment for control groups is still in progress. Children were tested with the Peabody Developmental Motor Scales-

PDMS-2, Sensory Profile, the Wee-FIM and the Vineland Adaptive Behavior Scales-VABS-2.

***Results*:**
Based on preliminary analyses most children with ASD (90%) presented sensory symptoms. Their total motor quotient on the PDMS-2 was 69 (fine motor = 75, gross motor = 69). Mean quotients on daily living skills were 55 on self-care (Wee-FIM), and 75 on the daily living skills of the VABS-2. Data of the control groups are currently being processed. Performance of the children with ASD will be compared to the control groups.

Conclusions:
A high percentage of children with ASD present sensory symptoms and have poor motor skills as well as poor daily living skills, which presents an increased burden of care for the parents. In order to be effective, interventions fostering functional independence will need to address the sensory-motor deficits that children with ASD exhibit.

69 116.5 Imitation performance in preschoolers referred for autism spectrum disorders (ASD): A comparison between true cases and false positives. M. Vanvuchelen*[1], H. Roeyers[2] and W. De Weerdt[3], (1)*Katholieke Universiteit Leuven - University College of the Province of Limburg, Belgium*, (2)*Ghent University*, (3)*Katholieke Universiteit Leuven*

Background:
Over the last 35 years, researchers consistently reported imitation impairments in young children with ASD. Nevertheless, differential diagnostic aspects of imitation have not yet been studied with a multidimensional imitation test.

Objectives:
To explore imitation abilities in young children suspected of ASD, using the Preschool Imitation and Praxis Scale (PIPS) and to compare imitation to other developmental domains.
Methods:
Seventy-one preschoolers (CA: M=40.5m, range 23-54m, IQ above 70) suspected of ASD and referred to University Autism Clinics (Belgium) were divided in two groups according to their ADOS-G classification: 48 children with ASD (19 with autistic disorder AD and 29 with PDD-NOS) and 23 children without ASD. Children were age-matched and assessed on five developmental domains: cognition (Bayley, SON-R), gross motor (PDMS2-locomotion), fine motor (PDMS2-visuomotor), language reception (RTOS, CDI) and imitation (PIPS). The PIPS is a newly developed instrument to measure meaningful and non-meaningful procedural and single and sequential bodily imitation. Age norms were derived from PIPS scores of 498 typically developing children. Results:
Within-group analyses revealed that both groups performed less well than expected for their chronological age on all developmental domains, with the exception of language reception in children without ASD and mental age in children with ASD. Between-group analyses revealed that children with ASD performed significantly poorer compared to children without ASD on imitation ($p<0.5$), gross motor ($p<0.5$) and receptive language tasks ($p<0.5$). Sub analysis revealed that children with PDD-NOS and AD did not differ from each other on the five developmental domains, with the exception of sequential bodily imitation ($p<0.5$).

Conclusions: This study is the first to investigate imitation abilities in young children suspected of ASD with a standardised multidimensional imitation test: The Preschool Imitation and Praxis Scale (PIPS). Findings of this study indicate that the investigation of imitation can contribute to the diagnosis of ASD.

70 116.6 IMITATION OF MEANINGFUL GESTURES IN INDIVIDUALS WITH HIGH-FUNCTIONING AUTISM AND ASPERGER SYNDROME. H. Stieglitz Ham*[1], M. Corley[1], T. Rajendran[2], A. Bartolo[3], J. Carletta[1] and S. Swanson[4], (1)*University of Edinburgh*, (2)*University of Strathclyde*, (3)*Université Charles-de-Gaulle Lille III*, (4)*Medical College of Wisconsin*

Background: Although imitation deficits have been widely-reported in autism, the cognitive

mechanisms affecting the processing of meaningful gestures are not well established. We investigated the role of visuomotor integration (VMI), working memory (WM), and visuoperceptual processing (VP) in praxis processing in a group of individuals with in HFA/AS.
Objectives: To investigate the underlying cognitive mechanisms recruited in performing meaningful gesture imitation in autism, specifically, in tasks of elicited imitation; and to analyze the error types and explore the relationship between imitation performance and dyspraxia in meaningful gesture imitation.
Methods: 19 individuals with HFA/AS and 23 TD controls (mean age of 12.0 and 12.1 respectively) were tested in 3 tasks of meaningful gesture imitation at the Medical College of Wisconsin. The study included tasks for both recognition and imitation of meaningful gestures. Productions were videotaped, coded, and analyzed.
Results: A significant between-group difference was found in all 3 tasks: transitive gestures [$F(1, 40) = 51.6$, $p<.001$]; intransitive gestures [$F(1, 40) = 65.21$, $p<.001$]; and pantomimes [$F(1,40) = 72.82$, $p<.001$]. A significant interaction revealed that although the AS/HFA group performed all of the imitation tasks poorly compared to the controls, they appeared to demonstrate the greatest impairment in pantomime imitation. The HFA/AS group made more errors of hand postures in pantomime imitation than they did during transitive and intransitive gesture imitation and associations between recognition and production of pantomimes were revealed that were similar to patterns observed in adults with limb apraxia.
Conclusions: Our findings revealed imitation deficits in all 3 tasks of meaningful gestures in the AS/HFA group, but this was more pronounced in pantomime imitation. Analyses of the errors suggest that individuals with AS/HFA not only demonstrate imitation deficits but also present with deficits in praxis processing.

71 116.7 Decreased Feedback Sensitivity During a Motor Decision-Making Task in Autism. M. McWhirr*, M. Mon-Williams, S. Kent, M. Plumb, A. Wilson and J. H. G. Williams, *University of Aberdeen*

Background: Impairment of movement skills is a well-known feature of autism and deficits in motor cognition may possibly be related to later impairment in social cognition.
One hypothesis is that the feedback loop that serves to develop motor control in the reach-to-grasp action is important for the development of theory-of-mind.
Objectives: To explore feedback sensitivity during a repetitive incrementally modified task.
Methods: In a motor decision-making task, participants (68 adults, 74 control children and 20 children with autism) were required to reach-and-grasp a 4cm length of doweling positioned at a variable angle in the transverse plane and use a pincer grip to grasp the ends of the dowel. The doweling was positioned at different orientations either randomly or systematically (orientation changed by 30° every five reaches either clockwise or counter-clockwise). This required a variable rotation of the lower arm, either clockwise or anticlockwise. In one group of participants, the angle changed randomly. In another group it changed incrementally. Participants could choose either to rotate the lower arm to gain maximum economy of movement or to use the same direction of lower arm movement as used in the previous trial.
Results: When the angle changed incrementally, control participants continued to select the previous direction of movement, even when the opposite direction would have been more economical and comfortable, as indicated by movements selected during random trials. Participants with autism showed a reduced influence of prior movement history. Thus, movements selected during trials when the angle changed incrementally were more similar to those choices made when the angle changed randomly.
Conclusions: Among control participants, successful prior actions bias decision-making to favour repetition of movement strategies in subsequent tasks. In autism, this influence appears to be significantly weaker, perhaps resulting in a diminished capacity for motor learning that could impact upon social cognitive development.

72 116.8 Visually driven postural reactivity in autism: A fully immersive virtual reality study. S. Greffou*[1], E. M. Hahler[1], A. Bertone[2], L.

Mottron[1] and J. Faubert[1], (1)*University of Montreal*, (2)*Mc.Gill University*

Background:
In addition to manifesting social difficulties, persons with autism often manifest other anomalies such as atypical sensori-motor integration.

Objectives:
We investigated visuo-motor integration in autism by assessing the development of postural regulation for children with and without high-functioning autism (HFA) between the ages of 12 through 25 years.

Methods:
Postural reactivity was assessed for 12 children with HFA and 19 typically developing children (TDC) whose ages ranged from 12-25 years. They stood within a virtual tunnel that oscillated in an anterior-posterior fashion at 0.125Hz, 0.25Hz and 0.5 Hz. The tunnel was presented using a fully immersive virtual environment system. Body sway and instability index were measured.

Results:
For Instability Index, a significant difference between children with HFA and TDC was found for the 0.5Hz frequency with increased instability for the HFA. We also found significant differences for body sway for 0.5 Hz showing a reduced postural response to this frequency. Other temporal frequencies did not show significant differences between groups for either dependent measure.

Conclusions:
Persons with HFA seem to perceive and integrate certain visual stimuli as well as TDC (0.125Hz and 0.25Hz) but have difficulties integrating other types of stimuli (0.50 Hz). This is likely to be due to dysfunctions of multimodal brain areas but not of primary receiving areas for processing this type of information because the stimuli used were composed of very salient and high contrast moving checkerboard patterns. There is clear evidence that the HFA have sensitivity levels for luminance defined motion stimuli similar to that of TDC . Furthermore, the condition showing significant effects between groups (0.5 Hz) generated higher levels of instability meaning that the stimulus was indeed visually perceived; otherwise we would expect a null or reduced visually driven postural reactivity. We emphasize the importance of visual parameters to determine the influence of vision on postural control in HFA.

Poster Presentations Program

117 Services Posters 1

73 117.1 Networks surrounding families with children having ASD. K. A. K. Valkama*, *University of Vaasa*

Background:

The Finnish welfare system has encountered radical changes, for example the central government transfer system was rearranged; the legislation regulating municipalities and the work distribution between basic and specialized services was altered. Economic difficulties have challenged the system to develop. Simultaneously the emphasis towards a client centered approach has aroused. These changes are affecting the supply and availability of all welfare services. Autism spectrum disorders are a relatively new diagnosis, hence the service and support system providing care for autism spectrum disorder is fairly unorganized.

Objectives: The aim was to map out and analyze the experiences of the families with ASD children under 16 yrs of the welfare and support network functioning around the family. The main question is: What is the network like and how is the network functioning according to the family.

Methods: The material consists of 13 narrative interviews and egocentric networks. The families described their experiences with the help of child's lifeline, placing in the line their encounters with the service and support system in certain area of Finland. The interview was completed with an egocentric network map drawn by the family describing the network surrounding the family at that moment.

Results: Support and service are highly dependent on the family's own strengths and

informal social network, and also on isolated professionals. This makes the system very vulnerable. Problems were experienced for example with delayed diagnosis, lack of expertise and understanding of the complexity of ASD in the local official support system.

Conclusions: The results indicate a need to improve the support system and the work division in the area. The results are being used to create a functioning support and service system that takes into consideration the needs of the child and the family, but also the local resources.

75 117.2 The Experiences and Percepions of Siblings of Children with Autism. M. A. Petalas*[1], R. Hastings[1], S. Nash[1], A. Dowey[2] and D. Reilly[1], (1)*Bangor University*, (2)*North East Wales NHS Trust*

Background:

Studies investigating the adjustment and wellbeing of children who have a brother or sister with autism spectrum disorder (ASD) report mixed findings. At present there is limited empirical, exploratory research on the experiences and perceptions of siblings of children with special needs, much less with siblings of children with autism. Moreover there is a distinct lack of qualitative exploratory research with siblings of children with autism during middle-childhood.

Objectives:

The aim of this study was to explore the experiences and perceptions of siblings living and growing up with a brother with ASD.

Methods:

Semi-structured interviews were conducted with nine typically developing siblings in middle-childhood (ages 8 to 12) who had a brother with ASD. The interviews were transcribed and analysed using Interpretative Phenomenological Analysis (IPA).

Results:

The analysis yielded five main themes: siblings' perceptions of the impact of their brother's condition on their lives, siblings' perceptions of the attitudes of others and the influence these attitudes have on them, siblings' tolerance and acceptance towards their brothers with ASD, positive attitudes and experiences of the sibling participants' lives with their brothers, and sources of support for siblings.

Conclusions:

Implications for future research and practice with siblings of children with ASD will be discussed, including the importance of these exploratory findings in informing future experimental research and the development of supports for siblings of children with ASD.

76 117.3 Effectiveness of a Computer-Assisted Instructional Model for ASD. C. Whalen*, L. Liden and K. MacDonald, *TeachTown*

Background: Computer-Assisted Instruction (CAI) has increased substantially in popularity due to the increasing prevalence of ASD and shortages in available services. There is also a growing body of research in this area looking at the efficacy and potential of CAI. *TeachTown Basics* is a program that teaches language, social skills, life skills, academic and cognitive skills (4 domains) through an ABA-based computer program. The program includes computer learning for the child along with automatic data collection. A system for keeping session notes and communicating among the child's team is also included, as well as over 100 off-computer generalization activities for working on skills in the natural environment.

Objectives: The purpose of this study was to pilot the effectiveness, as well as common uses of the software, with 417 children.

Methods: Automatic data has been collected on more than 600 children using the *TeachTown Basics* software over the past 2 years. Children were selected who demonstrated at least 3 months of regular use (minimum of 1 hour/week on average over at least 3 months). Average scores on pre and post tests were analyzed, along with an analysis of the frequency of use, usage patterns (e.g. number and frequency of notes entered, average session length, etc.).

Results: Significant changes from pre to post tests were shown for all 4 learning domains, average session time was 15 minutes, average use was 6 times/week, children had average of 1.5 facilitators, average age of user was 6 years old (range 2-21 years), average notes use was 3 per week.

Conclusions: Initial results show promise for the use of this program to teach children with ASD and track their progress remotely. Future directions include a randomized clinical trial and development of a product for older children, supported by a recent Department of Education grant.

77 117.4 Sexuality, Puberty, and Growing Up... Evaluating the Effectiveness of a Group Psycho-Education Curriculum for Parents of Youth with ASDs. S. Pulver Tetenbaum[1], S. Nichols*[1], A. Blakeley-Smith[2], S. Hepburn[3] and J. A. Reaven[4], (1)*NSLIJ Health System*, (2)*JFK Partners*, (3)*University of Colorado at Denver*, (4)*University of Colorado Health Sciences Center*

Background: To understand sexual development, the emergence of sexual behavior problems, and how best to educate youth with ASDs about sexuality, evidence-based services best suited for families' needs must be developed and evaluated.
Objectives: The aim of the current study is to expand on prior work (focus groups, questionnaire completion, pilot group programming) and evaluate the effectiveness of a group-based parent curriculum designed to (a) increase parents' sense of competence in teaching their children, (b) reduce stress reported by parents regarding issues related to puberty and growing up, and (c) facilitate implementation of teaching goals and behavior management approaches.
Methods: Parents (N = 18) of high-functioning youth (13 male, 5 female; VIQ > 70) ages 12-18 (m = 15; SD = 1.65) participated in one of three 10-week parent groups. Measures include parent report of youth sexual development, parent perspectives, and pre- and post-group measures of comfort level, perceived competence, and goal attainment.
Results: Analyses support the findings from our prior pilot work, and demonstrate increased comfort with the topic for parents within group ($p < .004$), in discussions with their family ($p < .004$) and in discussions with their child ($p < .4$). Goal attainment ratings (0-5 scale) were high for all parents post-group and at 3-month follow-up (for families who have completed the follow-up phase; $t(10) = 10.37$, $p < .0001$), though specific goals varied greatly across families. Common themes arose for issues facing youth with ASDs (e.g., difficulties with privacy and hygiene, anxiety, and intensity of sexual interests).
Conclusions: Preliminary findings demonstrate the appropriateness of group-based parent psycho-education for addressing sexuality and issues related to growing up for youth with ASDs. Limitations and recommendations for future research directions in sexuality will be discussed.

78 117.5 Are Toddlers with Autism Spectrum Disorders Receiving the Recommended Hours of Early Intervention Services?. E. Caronna*[1], M. B. Kadlec[2] and A. S. Carter[3], (1)*Boston University School of Medicine*, (2)*Boston University*, (3)*University of Massachusetts Boston*

Background: The United States' (U.S.) National Research Council (2001) and American Academy of Pediatrics (2007) recommend that children diagnosed with ASD receive 25 hours of intensive services per week. Treatment recommendations and delivery of early intervention (EI) services for toddlers with ASD vary regionally. Few studies have examined whether the services children receive are consistent with recommendations.

Objectives: To describe the age of diagnosis and the amount of intensive EI services in toddlers with ASD.

Methods: A cohort of 162 toddlers with ASD and their parents participated in a longitudinal study of developmental outcomes and service delivery. Diagnosis was confirmed with the Autism Diagnostic Observation Scales (ADOS) and Autism Diagnostic Interview (ADI). Assessments of child development and

parental well-being were conducted annually. Detailed information about service delivery was collected through interviews bi-annually.

Results: The cohort consisted of 36 girls and 126 boys in a region of the U.S. that is well-funded to provide services for toddlers with ASD. At initial assessment, mean age was 28 months, with an average age of diagnosis 24 months. Average age of initiation of services was 18 months while intensive, autism-specific services began at 24 months. At initial assessment, children received an average of 11.83 hours/week of combined EI and intensive services (range: 0-32.5 hours per week). Six months later, children who were under 36 months received an average of 19.56 hours/week through EI services while children over 36 months received an average of 25.85 hours/week through preschool programming.

Conclusions: On average, children under 36 months of age were not receiving the recommended hours of services for ASD. However, by the time they entered preschool, the average child was receiving the recommended hours of services. Even in a well-funded region of the U.S., children were not receiving adequate services through the EI system.

79 117.6 Rewards and Challenges Experienced by Behavior Interventionists Working in Homes of Children with ASD. M. Elfert* and P. Mirenda, *University of British Columbia*

Background: Behavior interventionists (BIs) often provide 1:1 early intensive behavioral intervention (EIBI) to young children with autism in their homes. With the exception of a report by Elfert and Mirenda (2006), little published research exists on the experiences of this emerging professional group.

Objectives: The qualitative study explored the perspectives of BIs with regard to occupational stressors and rewards.

Methods: As part of a larger study, 65 BIs from two Canadian provinces were asked to describe the most and least rewarding aspects of their jobs, using open-ended questions. A content analysis was conducted to sort and code the responses into categories that emerged from the data. Inter-rater reliability ranged from 95%-99%.

Results: BIs reported that the most challenging aspects of their jobs were related to workplace (38%), family (27%), team (22%) and child variables (13%). In particular, BIs identified stressors such as feeling responsible for children's progress; working in families' private living spaces; experiencing conflicts, inconsistences, and lack of support from families and team members; and dealing with child problem behavior as their greatest challenges. The most rewarding job aspects were related to child (55%), family (17%), team (11%), workplace (9%) and other variables (8%). In particular, positive job aspects included seeing children make progress, helping families, and working as part of well-functioning teams.

Conclusions: These descriptive data provide important information to service agencies providing EIBI in family homes. Typically, BIs work alone and intensively with children with autism for low wages, and job turnover is often high. Service providers need to be aware of the challenges BIs face so that they can provide appropriate supports and training.

80 117.7 Serving Children with ASD in Outpatient Community-Based Mental Health Services. L. Brookmn-Frazee* and A. F. Garland, *University of California, San Diego*

Background: Children with ASD may be served in a number of different community service systems, including those that do not specialize in treatment for this population. Little is known, for example, about the characteristics of the treatment provided in outpatient community-based mental health (CMH) services.
Objectives: To characterize CMH ASD treatment and outcome.
Methods: The current study includes secondary data analyses of a sub-sample of children ages 4-12 with ASD (n=20), drawn from a large-scale observational study characterizing CMH psychotherapy for children with disruptive behavior problems. 91 randomly selected videotaped psychotherapy sessions were coded using a modified Therapy

Process Observational Coding System (TPOCS: McLeod & Weisz, 2005) yielding ratings for 27 psychotherapeutic strategies.
Results: The following strategies were observed frequently with children with ASD: *Using Positive Reinforcement* (86% of sessions), *Using Punishment/ Limit-Setting* (61%), *Affect Education* (75%), *Problem-Solving Skills* (58%). *Psychoeducation* was frequently observed with parents (78%), however, discussing behavioral principles was observed less frequently: *Principles of Punishment, Limit setting* (28%); *Principles of Positive Reinforcement* (21%). Moderate improvement on the Eyberg Child Behavior Inventory (ECBI) was observed, with 69% of children with ASD scoring below the clinical cutoff after 4 months, compared to 25% at baseline.
Conclusions: These findings represent the first observational data characterizing CMH care for children with ASD. Psychotherapy process and outcome was similar for children with and without ASD. Behavioral and specific skill building strategies were frequently observed with children with ASD. While therapists employed a number of strategies consistent with research-based ASD interventions targeting children, the observed frequency of behavioral parent training strategies was lower. These data, combined with supplemental qualitative data (to be presented) regarding therapists' perceptions of the challenges in treating these children, indicate that CMH services for children with ASD could be significantly enhanced by training providers in specialized ASD interventions.

81 117.8 Evaluating a two-level screening strategy for the early detecton of Autistic Spectrum Disorders using routine paediatric surveillance. C. Dietz*[1], S. Swinkels[2], E. Van Daalen[1], H. Van Engeland[1] and J. Buitelaar[2], (1)*University Medical Center Utrecht*, (2)*Karakter Child and Adolescent Psychiatry University Center*

Background: General agreement exists about the need to identify Autistic Spectrum Disorders (ASDs) early.

Objectives: Evidence supports a two-level screening strategy, with the use of primary care facilities at the first level, followed by specialist screening, and clinical evaluation at the second level. The effectiveness of this strategy in identifying ASD in children younger than 3 years was investigated.

Methods: Physicians of well-baby clinics identified children at risk of ASD during routine developmental surveillance. In total 41,445 children living in a geographically defined area (the province of Utrecht, the Netherlands) were examined. Children considered at risk were screened with the 14-item Early Screening of Autistic Traits (ESAT). Those who tested positive were then clinically evaluated at the UMC Utrecht. Diagnoses were confirmed at follow-up, when the children were about 42 months.

Results: Physicians identified 109 children as being at risk of ASD, and these children were tested with the ESAT when they were 27±6 months old (mean±SD). Of these children, 73 tested positively on the ESAT and 66 (90%) were clinically evaluated. Thirty-nine children (53%) were diagnosed with ASD. The positive predictive value of the ESAT was 59% (39 of 66 children who tested positive); 81% of the children who tested false positive with the ESAT had other developmental disorders according to DSM-IV. False negatives included three children that were diagnosed with ASD, after a positive result at follow-up screening.

Conclusions: The two-level screening strategy appears to be effective, especially in lowering the age of diagnosis; however, the rate of detection of ASD is moderate.
Recommendations include providing physicians red flags for ASD.

82 117.9 Announcing the diagnosis of autism to the parents in France: Past and Present. B. Chamak*[1], B. Bonniau[2], L. Oudaya[2], A. Danion[3], V. Pascal[3], D. Cohen[4], V. Guinchat[4] and A. Ehrenberg[1], (1)*CESAMES*, (2)*University of Paris Descartes, CESAMES*, (3)*Hôpitaux universitaires de Strasbourg*, (4)*Groupe hospitalier Pitié-Salpêtrière, APHP*

Background: French psychiatrists used to be reluctant to announce the diagnosis of autism to parents. Nowadays, the families still deplore how difficult it is to obtain the diagnosis despite the recent recommendations of the Haute Autorité de Santé (HAS) published in June 2005 in France.

Objectives: This study was performed: 1°) to analyse the difficulties encountered by the French parents in obtaining a diagnosis; 2°) to compare the practices of the professionals in the past and today; 3°) to evaluate the improvements but also the problems which persist.

Methods: A questionnaire was conceived for the parents and diffused in France by the associations, the psychiatrists, various structures and on the Internet (http://www.cesames.org/spip/IMG/Qparents8.pdf): 248 questionnaires were collected. All the questionnaires were computerized using Modalisa software and data were analysed both with a quantitative and a qualitative approach.

Results: The mean age for obtaining the diagnosis was 6 ± 5 years: 5 ± 3 for the children and teenagers and 10± 6 for the adults (≥ 18 year-old) showing a real improvement. However, 62% of the parents of autistic children and 92% of the parents of autistic adults declared being unsatisfied by the way the diagnosis was announced. They deplored the delay in obtaining a diagnosis (85% of the parents would prefer to get the diagnosis earlier), as well as the lack of information and help and sometimes the blunt way the diagnosis was given.

Conclusions: Progress remains to be made to improve the way the diagnosis is announced. Autism is not simply a disease or a handicap; it is also a social and human problem. The lack of help and services and the pessimistic prognostic expressed by psychiatrists seem to play a role in the parents' feeling of hopelessness when they get the diagnosis of autism for their children.

83 117.10 A Model for Regional Training and Service Delivery for Children with Autism. P. Doehring*, *Delaware Autism Program*

Background: Despite advances in early identification and treatment, it is difficult to estimate the extent to which we can successfully serve an entire population of persons with autism. We present examples of analyses conducted for the public schools in the state of Delaware that document meaningful progress towards this goal.

Objectives: To establish: (a) how many children with autism receive highly specialized educational services; (b) how many educators receive training and support within a more specialized program, and (c) how many children and families receive other specialized supports.

Methods: We estimate the proportion of children identified and receiving services within the public school system relative to an estimated 1/150, and as a function of the child's characteristics and type of program received. We also report the proportion of educators serving children within highly specialized programs, who have received training in essential elements of evaluation and ABA. We then present data on the delivery of respite and residential services statewide, as well as consultation and review regarding severe behavior problems.

Results: We have identified about one-half of the children likely to require relatively more intense and specialized programs, and most of these are enrolled in highly specialized programs. Though most staff members in such programs have additional training, training outside of this program is much more limited. Few children required some form of residential services, though respite was used by more than 20%. Additional oversight was required for more than 15% of students demonstrating chronic and/or severe behavior problems.

Conclusions: Together, these results illustrate how programs with a regional mandate might establish goals for identification and treatment, and track progress towards ensuring equal access to highly specialized services and supports. It remains, however, more challenging to identify and develop services for higher-functioning children.

84 117.11 FINANCIAL AND SOCIAL COSTS OF PERVASIVE DEVELOPMENTAL DISORDERS (PDD) IN SARDINIA. M. Testa*[1], L. Anchisi[1], G. Melis[1], G. S. Doneddu[2], M. Brunetti[3], P. Atzori[1] and A. Zuddas[1], (1)*University of Cagliari*, (2)*Asl N. 8 - Cagliari*, (3)*Centro per la Valutazione dell'Efficacia dell'Assistenza Sanitaria*

Background: Specific demographic and clinical variables appear to influence PDD costs. Very few studies have analyzed the economic burden of PDD: none have considered both direct and indirect costs and their relation with demographic and clinical characteristics.

Objectives: To document the total direct (public and private) and indirect health costs associated with PDD.

Methods: Information were collected by 99 PDD-parent questionnaire completed at two specialized Centres. Both public and private health costs (health services, prescription medications, complementary and alternative therapies, hospital and emergency services, home health and medically related travel, home modification) as well as the expenses for teacher's aid, personal assistant and/or specialized educator costs (school costs) were considered. Loss of work and cost of time spent by families in patient care-giving were calculated as indirect costs.

Results: 75% (n=74) of children and adolescents with PDD were males, average age was 9+6 years. 75% had autistic disorder (n=74), 11% Asperger's syndrome (n=11) and 14% PDDNOS (n=14). Preliminary analysis indicated an average cost of 30.000 euro/patient/year. Psychiatric comorbidities were associated to a significantly increase of total (€ 36,214 vs 20,586 for no comorbidity; p=0.001) and private costs (€ 3,396 vs 223, respectively; p=0.15). Total costs were higher in Autistic Disorder (€ 30,00; p=0.7) and Asperger's Disorder (€ 33,400; p=0.58), compared to PDDNOS (€ 18,870). Parent direct costs were significantly higher in low IQ subject. Age range was also related to specific costs: at age 0-4 significantly lower total (€ 11,630; p=0.008) and school (p=0.006) costs were reported; school costs were significantly higher (12,000 €; p=0.42) in age range 5-9; at age range 10-14 significantly higher total (34,200 €; p=0.11) and indirect costs (12,740 €; p=0.39), were reported.

Conclusions: To improve the allocation of economic and social resource, further studies are warranted to identify variables that influence PDD costs.

85 117.12 Service and support use of families of preschoolers with autism and other developmental disabilities: More similar than different?. V. Lopes*, T. Clifford, P. Minnes and H. Ouellette-Kuntz, *Queen's University*

Background:

Research has consistently found that parents of children with autism spectrum disorders (ASD) and other developmental disabilities (DDs) report experiencing more parenting stress than parents of children without disabilities. It has been suggested that services and supports may help parents cope with this stress. It has been noted clinically that parents of children with ASDs tend to feel more connectedness, and may be more likely to become involved in certain types of support than parents of children with DD.

Objectives:

The goal of the current study was to compare the reported service and support use of parents of children with ASD and DD, while examining other variables that may contribute to support use.

Methods:

Nineteen parents of preschoolers with ASD, 10 parents of preschoolers with other DDs, and 17 parents of children without disabilities participated in this study through telephone interviews.

Results:

Parents of children with ASD and DD reported more parenting stress, and had children with lower adaptive behaviour scores and more maladaptive behaviour than parents of children without disabilities; however, the ASD and DD groups did not differ significantly on

these variables. Parents of children with ASD and DD did not differ significantly in the number of direct services they reported using. Interestingly, more parents of children with ASD reported using parent support groups, than parents of children with DD.

Conclusions:

Further research is required to investigate the factors contributing to involvement in or development of parent support groups for families of children with disabilities.

86 117.13 Randomized Controlled Study of Collaborative Parent-Teacher Consultation in Autism. L. Ruble*[1], J. H. McGrew[2] and N. Dalrymple[1], (1)*University of Kentucky*, (2)*Indiana University - Purdue University Indianapolis*

Background:The National Research Council (2001) has called for more trained school personnel with child-specific consultation skills related to autism. However, there is little research that actually has investigated consultation as an intervention. To begin to address this problem, outcomes from a collaborative intervention planning framework developed specifically for children with autism called COMPASS (Collaborative Model for Promoting Competence and Success; Ruble & Dalrymple, 2002) were evaluated.

Objectives: To evaluate the impact of COMPASS vs. "usual" educational program development practice and to explore additional factors (school organization, teacher, parent, and child) that may account for variance in teacher, child, and family outcomes.

Methods: A randomized controlled design was used to determine the effectiveness of COMPASS consultation and teacher coaching sessions on teacher, parent, and child outcomes. During year one, twenty-four teachers, children with autism and their caregivers were randomly assigned to COMPASS and teacher coaching or a treatment as usual group (TAU; regular school program based on child's IEP). Participants completed pre- and post-evaluation assessments. Following the pre-evaluation, participants were randomly assigned to either the experimental (n=13) or the TAU condition (n=11). Thirteen teachers in the experimental condition participated in a half-day consultation that included the parent. Three skills were prioritized and targeted for the current school year and specific teaching plans were generated. Following consultation, teachers also received four 1.5 hour teacher-coaching sessions.

Results: Compared to those in the control group, children in the treatment group (*N*=13) achieved higher goal attainment scores on both social (p=.1) and communication goals (p=.2), as rated by observers blind to group assignment. Children in the experimental group also were reported by their caregivers to have better social behaviors (p=.2).

Conclusions:The presentation will conclude with preliminary results based on a larger sample of 36 participants as well as recommendations for future research in parent-teacher consultation.

87 117.14 Sleep Quality in Mothers of Children with an Autism Spectrum Disorder (ASD). A. Richdale* and J. Chu, *RMIT University*

Background:

Children with a developmental disability (DD) have behavioural and sleep difficulties, and their mothers may have poor psychological well-being. However the impact of these factors on mothers' sleep quality has not been explored.

Objectives:

To explore relationships between children's sleep and behaviour and mothers' psychological well-being and sleep quality in children with an ASD and or a DD.

Methods:

Mothers of children with an ASD or other DD returned demographic information, a children's sleep questionnaire, the Strengths and Difficulties Questionnaire, the Pittsburgh Sleep Quality Index (PSQI), the Parenting Hassles Scale (PHS), and the DASS-21 depression and anxiety scales by mail. Data were analysed

using *t*-tests, MANOVA and correlations as appropriate.

Results:

Forty-four mothers returned questionnaires. Twenty-six children had an ASD (6.9 ± 2.1 yrs) and 18 children had another DD (8.0 ± 3.0 yrs); their mothers' mean ages were 39.2 ± 6.1 yrs and 42.0 ± 6.3 years respectively. Age differences were not significant. There were no significant group differences for total scores for any parent or child measures. Both groups of mothers PSQI scores indicated poor sleep quality. Nevertheless differences between the ASD and DD groups emerged. The only ASD child variable significantly associated with the PSQI was hours of sleep per night, but both DD children's sleep and behaviour were significantly associated with the PSQI. While depression, anxiety and total stress were associated with poor sleep quality for both groups of mothers, associations with PHS subscales largely differed; child-related issues were important in the ASD group and siblings and finances featured for the comparison group.

Conclusions:

Mothers of children with developmental disabilities have poor sleep quality, but factors contributing to this are not consistent across disabilities. In particular, child-related stress appears to contribute to ASD mothers' poor sleep quality but not DD mothers' sleep quality.

88 117.15 THE SCHOOL TRAJECTORIES OF CHILDREN WITH AUTISM SPECTRUM DISORDER OVER THE COMPULSORY SCHOOLING. V. Zbinden Sapin*[1], E. Thommen[2] and S. Wiesendanger[3], (1)*University of Applied Sciences Western Switzerland of Fribourg (HEF-TS)*, (2)*University of Fribourg and University of Applied Sciences Western Switzerland of Lausanne (EESP)*, (3)*University of Applied Sciences Western Switzerland of Lausanne (EESP)*

Background: Early detection of children with high functioning autism spectrum disorder is not yet accurate in European French countries, partly due to the French classification of mental disorders. It follows that school trajectories could be chaotic.

Objectives: The aim of our research is to show the variety of the school trajectories and the consequence of this on the developmental process in term of integration.

Methods: Extensive interviews were conducted with 2 groups of families of young adults with ASD (15 with autism, 18 with high functioning autism or Asperger syndrome). The life trajectories of the children were reconstructed (diagnosis, child development, living places, schools, therapies, educational approaches). Young adults were assessed by the ADI-R. Results about the number and type of schools frequented during the compulsory schooling will be presented here.

Results: First results show that people with high functioning autism tend to go through more different places during the compulsory schools than people of the other group ($F (1, 33) = 6.14$, $p < .2$). Integration in regular education without support lead to difficulties: 61% lived at least one rupture in their compulsory schooling, like a transition from the regular education to the specialized schooling, sometimes followed by a new transition to regular education, a stopping of going to school and staying at home without education.

Conclusions: Our results show the need to better organize the school trajectories and the transitions over the compulsory schooling.

89 117.16 Developing the subject matching system for the Interactive Autism Network (IAN). P. K. Maulik*[1], A. R. Marvin[2] and P. Law[2], (1)*Johns Hopkins School of Public Health*, (2)*Kennedy Krieger Institute*

Background: Many autism research studies are delayed or fail because of difficulties with subject recruitment.

Objectives: To establish an efficient web-based matching system to facilitate efficient subject recruitment for Autism Spectrum Disorder (ASD) research projects.

Methods: A literature review of USA-based studies published in PubMed and PsycInfo between 2000 and 2005 was performed to identify inclusion/exclusion criteria and demographic characteristics that autism researchers use most. This information provided the core content for the Interactive Autism Network (IAN) database.

Results: The initial literature search generated 2,890 articles. Saturation point for generation of criteria for incorporation into the database was reached after detailed review of the initial 166 eligible articles. Study types were primarily clinical observation studies (59%) and genetic studies (14%). The most common characteristics/criteria sought by researchers were: specific ASD diagnosis, age, gender, medical history, IQ, scores on autism instruments, and medication history. 20,442 subjects have joined IAN, including 7,512 children with ASD (82.6% males), since its April 2007 launch. Data provided by families include those identified as key to subject recruitment selection. Only 15% of affected children have ever been part of an ASD research study before. Researchers wishing to recruit subjects through IAN specify their study eligibility criteria. IAN then identifies and contacts potential participants. The subject recruitment service became fully functional in August 2007. Fifty subject recruitment applications have been initiated, with half complete. Over 5,000 recruitment emails have been received by IAN participants. A broad range of studies from doctoral dissertations to multi-centre studies and drug trials are using IAN for subject recruitment. 55% of studies are non-commercially funded, 23% are commercially funded, and the remainder have no external funding.

Conclusions: A web based national registry can rapidly evolve and contribute to the efficiency of autism research.

90 117.17 HANDS in Autism: Development and Evolution of an Intensive Hands-On Professional Training Model. N. B. Swiezy*, M. L. Stuart and P. Korzekwa, *Indiana University School of Medicine*

Background: The HANDS (Helping Answer Needs by Developing Specialists) in Autism professional training model began in 2004 as a result of foundational funding from the CDC. Community professionals commented that traditional didactic conferences were not adequate for developing practical tools applicable in the natural environment. They became discouraged with the methodologies as they struggled to effectively apply them in their naturalistic settings. It was hypothesized that professionals would benefit from a more active learning process allowing them to better comprehend, apply, maintain, and generalize information. The framework of this model, incorporating practice, coaching, and feedback strategies, developed from blended ABA principles and evidence-based methodology.

Objectives: The goal was to determine the efficacy of the model as it has evolved over three years of implementation.

Methods: Participants were assessed for their gain in knowledge and use of evidence-based methodologies. *Year 1.* Participants completed ratings each day of the training. *Year 2.* Participants completed ratings immediately before and after training. *Year 3.* Participants completed ratings immediately before and after training and again 4 months later. Following each training year, methodologies and procedures for collecting data were assessed and revised.

Results: *Year 1* (n=10). There was significant improvement from the pre-test (M=34.6%) to the post-test (M=45.4%) for the overall training ($p<.001$). *Year 2* (n=27). Participants were significantly improved at the post-test (M=90.0%) compared to the pre-test (M=74.5%, $p<.5$). *Year 3* (n=39). Participants were significantly improved at the post-test (M=83%) and at the 4-month follow-up (M=82%) compared to the pre-test (M=73%; $p <.001$). Across all three years (N=76), there was an average 12% increase in participants' knowledge gained through the model.

Conclusions: Across all three years, the HANDS in Autism model, emphasizing hands-on learning through practice, coaching, and feedback, demonstrated improvements in

knowledge and use of methodologies for working with children with autism.

91 117.18 Depression as a Predictor of Marital Quality for Mothers and Fathers of Toddlers with Autism Spectrum Disorder (ASD). K. M. Dame*[1], S. A. Grossman[1], M. B. Kadlec[1] and A. Carter[2], (1)*Boston University School of Medicine*, (2)*University of Massachusetts Boston*

Background: Parents of children with ASD report higher levels of depression and lower marital quality than parents of unaffected children or those with other developmental disabilities. However, few studies have examined changes in depression and marital quality in parents of toddlers with ASD. Objectives: **To investigate how change in self and partner depression contribute to change in marital quality over 1 year in parents of toddlers with ASD.** Methods: **Parents of toddlers between 18 and 33 months with ASD were recruited into a longitudinal study. Mothers and fathers answered questions about depressive symptoms on the Center for Epidemiologic Studies Depression Inventory (CES-D) and about marital quality on the Dyadic Adjustment Scale (DAS) at two time points (Y1 and Y2) with a one-year time interval.** Results: **Participants included 83 mother-father dyads. In Y1, 29% of mothers and fathers were above the clinical cut-off for depression. Mean CES-D and DAS total scores did not change significantly from Y1 to Y2 for mothers or fathers. A regression analysis predicting to mothers' Y2 marital adjustment indicated that, after accounting for mother's Y1 marital quality ($R^2\Delta$=.54), mothers Y2 depression ($R^2\Delta$=.5) and fathers change in marital quality ($R^2\Delta$=.2) each accounted for unique variance. In a second analysis, predicting to fathers' Y2 marital quality, after accounting for father's Y1 marital quality ($R^2\Delta$=.50), fathers' Y2 depression ($R^2\Delta$=.5) and mothers' Y1 marital quality ($R^2\Delta$=.2) each accounted for unique variance in father's Y2 marital quality.** Conclusions: **Consistent with a family systems perspective, depression and martial quality are integrally linked for mothers and fathers of toddlers with ASD. Our results suggest that it is important to identify and treat both parents' depression early in their child's development, as this can have a positive impact on their marital quality over time.**

92 117.19 HANDS in Autism: A Collaborative Community Classroom. P. Korzekwa*, N. B. Swiezy and M. L. Stuart, *Indiana University School of Medicine*

Background: The framework of the HANDS in Autism model developed as an intensive, hands-on training blending ABA principles and evidence-based practices. As an extension to the model, a collaborative classroom was developed to bridge clinical, home, and educational settings, and to demonstrate the use of evidence-based methodologies. The development of a collaborative classroom includes three phases: 1) assessing the classroom's strengths and needs; 2) training the classroom staff on methodologies individualized to the classroom; and 3) fading of training staff with an assessment of the classroom staff's ability to self-sustain. The process takes approximately two academic years. The current study is in phase 2.

Objectives: The goal was to collaborate by working within an existing classroom to develop a model site utilizing evidence-based practices.

Methods: Effectiveness was assessed through improvement in student behavior, and increased classroom staff fidelity to methodologies. Students were observed for rates of behavior, functional communication, and task independence. Classroom staff were observed in their contingent response to behaviors and positive interactions with students.

Results: Three students and 5 classroom staff participated in phase 1 and 2. Overall, staff showed an improvement in contingent response to behavior (M: 14.6% in phase 1 to 9.8% in phase 2). Staff also improved in their use of appropriate positive attention (M: 0.6 attention/minute in phase 1 to 0.7 attention/minute in phase 2). The most striking improvement was in the students' use

of functional communication (M: 0.3 communications/minute in phase 1 to 0.25 communications/minute in phase 2). Data are currently being collected regarding rates of behavior and task independence. However, the general trend indicates a decrease in frequency of behaviors and an increase in percent of tasks performed independently.

Conclusions: Thus far, the HANDS in Autism collaborative classroom has demonstrated efficacy for both students and classroom staff.

74 117.20 Does Living in a Rural State Make A Difference When Raising a Child with ASD? Analysis of Data from the Interactive Autism Network (IAN). J. E. Farmer*[1] and A. R. Marvin[2], (1)*University of Missouri*, (2)*Kennedy Krieger Institute*

Background: Children with autism spectrum disorders (ASD) living in rural areas may be vulnerable due to a lack of specialized services.

Objectives: To examine diagnostic patterns and educational settings for children with ASD living in US states that vary by percentage of rural population.

Methods: Web-based, parent-reported data were analyzed for 40 states with at least 25 IAN participants. Selected variables were correlated with percentage of state rural population (based on Census Bureau 2000 data). States also were assigned to three groups based on percent rural population. The "rural" group was ≥30% rural (n=14 states, max = 59.8% rural); the "mixed" group was >16% and <30% rural (n=13); and the "urban" group was ≤16% rural (n=13). ANOVA was performed to determine group differences on IAN indicators.

Results: State rural percentage was strongly correlated with mean age at first diagnosis, $r(38)=.51$, $p<.001$. The three state groupings also differed significantly, $F(2, 37)= 5.31$, $p<.1$: the mean age of first diagnosis for children in the rural states ($M=4.15$, $SD=.396$) was higher than that of the mixed group ($M=3.97$, $SD=.248$) and the urban group ($M=3.70$, $SD=.414$). However, there was no correlation or significant difference between the groups for age at parent's first concern. The three groups differed significantly on percent enrolled in public schools, $F(2, 37)= 3.70$, $p<.5$: more children in the rural group were enrolled in public schools ($M=63.1\%$, $SD=12.6\%$) than in the mixed group ($M=55.1\%$, $SD=8.7\%$) or the urban group ($M=52.8\%$, $SD=8.7\%$). Children in public schools were more likely to have opportunities for inclusion with typically developing peers, $r(38)=.64$, $p<.0001$.

Conclusions: Living in a more rural state may delay ASD diagnosis and limit access to private schools, but encourage community inclusion. Further examination of such state and regional differences may improve service delivery and enhance child outcomes.

Poster Presentations Program

118 Comorbidity Posters

93 118.1 Psychiatric Comorbidity in Children and Adolescents with High Functioning Autism. S. Herguner[1] and N. M. Mukaddes*[2], (1)*Istanbul Faculty of Medicine, Istanbul University*, (2)*Istanbul University,Istanbul Faculty of Medicine*

Background: Few systematic and structured studies have investigated the comorbidity of psychiatric disorders with autism spectrum disorders.

Objectives: The present study aimed to assess the psychiatric comorbidity in a sample of clinically referred children and adolescents with High Functioning Autism.

Methods: Participants were 30 children and adolescents (29 male, 1 female), aged between 6–15 (10y 2m ± 2y 2m) years old, who met DSM-IV criteria for Autistic Disorder, and had a Performance IQ over 70 on WISC-R. Psychiatric comorbidity was assessed using the Schedule for Affective Disorders and Schizophrenia for School Age Children - Present and Lifetime Version (K-SADS - PL).

Results: 90% (n=27) of the children had at least one comorbid psychiatric disorder, while 76.6% (n=23) had two or more. Of all the cases, 76.6% (n=23) suffered at least from

one subtype of Anxiety Disorder, and 63% (n=19) of the children received the additional diagnosis of Disruptive Behavior Disorders. The most frequent psychiatric diagnoses were Attention Deficit Hyperactivity Disorder (ADHD) (60 %), Specific Phobia (SP) (53, 3 %), Oppositional Defiant Disorder (% 30), and Obsessive Compulsive Disorder (OCD) (20 %).

Conclusions: The results of the present study show the presence of very high rate of psychiatric disorders in this group. The detection and treatment of these disorders is critical to achieve a good outcome in this group.

94 118.2 ASD and psychoses - misdiagnoses or comorbidity? Findings in a clinical practice. L. Nylander* and M. Holmqvist, *University Hospital of Lund, Sweden*

Background: Since autism was originally described, its relationship to psychotic disorders has been debated. With the recognition of autism spectrum disorders (ASD) in adults, this debate has become even more relevant.
Objectives:

To determine the number of patients with coexisting ASD and psychotic disorder in a clinical sample of adult patients referred for assessment.

Methods:

All patients were examined by a specialized team (psychiatrist and psychologist). Medical charts were reviewed, and a developmental history was always taken. Most patients were neuropsychologically tested with the WAIS-R or WAIS-III. The DISCO (The Diagnostic Interview for Social and COmmunication disorders) was used in several cases.

Results:

68 out of 476 consecutive patients had a clinical diagnosis of psychosis prior to assessment. In 12 a new diagnosis of ASD, instead of psychosis, was assigned. In 11 cases, psychosis and ASD coexisted. In 11 cases with a "psychosis only" diagnosis the DISCO was used. 10 of these cases, according to the DISCO algorithm, met criteria for PDD-NOS, which, however, could not be clinically verified.

Conclusions: These cases show that it is possible that psychiatric services sometimes misdiagnose psychotic disorders in adults whose problems are better described in terms of autism spectrum disorders. Furthermore, schizophrenia and other psychotic disorders or psychotic symptoms may be comorbid with ASD.
The figures must be interpreted with caution, since the patient group was a clinical sample referred to a highly specialized service for diagnostic assessment, and therefore biased to cases where diagnostic difficulties had been recognized. The numbers thus do not reflect the true ratio of "misdiagnoses" in patients given diagnoses of psychotic disorders. Nor can any conclusions be drawn about the true prevalence of comorbidity. Interestingly, the symptoms of atypical ASD may be similar to symptoms of psychosis, as shown in the DISCO results.

95 118.3 Psychiatric Symptoms in School Age Children with Autism Spectrum Disorders. L. Lecavalier*[1], K. Gadow[2], C. DeVincent[3] and M. Edwards[1], (1)*Ohio State University*, (2)*State University of New York*, (3)*State University of New York,*

Background: Youngsters with ASD have high rates of behavior and emotional problems. There is a growing body of evidence indicating that behavioral syndromes in ASD are phenotypically similar to conventional DSM-IV-defined psychiatric syndromes. However, support for such taxonomy in ASD is lacking. A valid taxonomy is a necessary step in order for psychopathology research to move forward.

Objectives: To assess the validity of parent and teacher reported DSM-IV disorders in school aged children with ASD. Data were collected with the Child Symptom Inventory-4, a DSM-IV-referenced rating scale. Items from the Attention Deficit Hyperactivity Disorder, Oppositional Defiant Disorder, Conduct Disorder, Generalized Anxiety Disorder, and Major Depressive Disorder subscales were

submitted to confirmatory factor analysis (CFA). Models were assessed for fit, and compared to those obtained for a sample of outpatient school age children without ASD with similar demographic characteristics.

Methods: Children were recruited through University-based specialized diagnostic clinics. The total ASD sample consisted of 498 children (average age=8.4 years; 83.9% male). The non-ASD outpatient comparison groups consisted of 167 parent ratings and 172 teacher ratings. CFA were conducted separately for parent and teacher ratings, using diagonally weighted least squares and polychoric correlations.

Results: Parent ratings of psychiatric symptoms for the ASD sample yielded a Root Mean Square Error of Approximation (RMSEA) of 0.468 and a Standardized Root Mean Square (SRMR) of .959. Teacher ratings of psychiatric symptoms for the ASD sample yielded a RMSEA of .687 and a SRMR of .164. Fit indices compared well to those obtained for the outpatient comparison groups.

Conclusions: The data yielded good fit indices, particularly for parent ratings. This lends support to the validity of DSM-IV disorders in the ASD population. The field is in need of a concerted effort to elucidate and validate a taxonomy of behavior and emotional problems for this patient population.

96 118.4 Anxiety, Social Skills, and Loneliness in Children and Adolescents with Autism Spectrum Disorders. S. W. White*, R. Roberson-Nay and J. Schneider, *Virginia Commonwealth University*

Background: Anxiety is often seen in children and adolescents with autism and related conditions; however, little is known about how anxiety may be related to the core social deficits of the autism spectrum disorders (ASD).

Objectives: This study sought to explore relationships among anxiety, loneliness, and degree of social skill deficit in a well-characterized sample of higher functioning youth with ASD.

Methods: Parent- and self-report data were collected from a sample of children diagnosed with ASD (n = 20), age rage: 7 - 14 (mean = 12 years). All participants were verbal and had low average or higher assessed intelligence (average IQ = 92 ± 14.41), with clinical diagnoses of ASD confirmed by ADOS.

Results: There were no significant correlations among global measures of degree of social disability (Social Responsiveness Scale: SRS; Constantino & Gruber, 2005; Social Competence Inventory: SCI; Rydell et al., 1997), loneliness (Loneliness Questionnaire; Asher et al., 1984; Bauminger & Kasari, 2003), and anxiety (Multidimensional Anxiety Scale for Children: MASC; March, 1997; Child Behavior Checklist: CBCL; Achenbach, 1991). However, children who self-reported elevated levels of anxiety on the MASC also reported greater feelings of social loneliness. Those participants earning 'above average' total anxiety scores reported significantly more loneliness than those with less anxiety ($F = 6.60$, $p < .5$). A significant relationship between parent-reported anxiety symptoms on the CBCL and social initiative on the SCI ($r = -.59$, $p < .1$) also was found.

Conclusions: This correlation may indicate that children whose parents view them as more anxious or depressed have less ability to initiate and get involved with peers. These findings are explored from scientific and clinical perspectives. Recommendations for the assessment of potentially co-occurring problems with anxiety and mood and their impact on treatment planning and success for youth with ASD are offered.

97 118.5 A Case of Autistic Disorder with Merosin Deficient Congenital Muscular Dystrophy. C. K. Gürkan[1], T. Türkbay*[2] and I. Durukan[2], (1)*Ankara University*, (2)*Gülhane Military Medical Academy*

Background: Autism is a neuropsychiatric disorder that can coexist with a variety of medical conditions. It is shown in the previous studies that muscular dystrophies, such as Duchenne muscular dystrophy or myotonic dystrophy, may also be associated with autism.

Objectives: The authors report a patient with merosin deficient congenital muscular dystrophy (MDCMD) who had autistic disorder. Although coexistence of autism and some other variants of muscular dystrophies were described, this association has never been reported with MDCMD.
Methods: A 37-months-old girl who had been previously diagnosed with MDCMD and referred to a child and adolescent psychiatry department for developmental evaluation was assessed via clinical observation, a rating scale and a semi structured interview form.
Results: Developmental history was obtained from her parents. She had severe muscle weakness which renders her unable to walk. Her language was delayed and there was no meaningful speech. Developmental delays were also documented by developmental testing. Parents also reported that she had lack of social interest. In clinical setting, she was observed to be having poor eye contact, peripheral gazing, stereotypic hand and body movements and lack of gestures. She had lack of joint attention and there was no imitative play. Subsequent psychiatric assessment with a semi-structured Autism Diagnostic Interview Form proved that the child met diagnostic criteria for autistic disorder. Her total score in Childhood Autism Rating Scale was 46, as well.
Conclusions: This case indicates that autism may coexist with MDCMD. It also suggests a previously unreported association between MDCMD and autism, and underlines the importance of neurological examination in children with autism spectrum disorders.

98 118.6 Comorbidity in autism spectrum disorders. R. Canitano* and V. Scandurra, *University Hospital of Siena, Italy*

Background:

Additional disorders are common in ASD but are still poorly defined. It is an issue of growing interest because of the implications on clinical ground, etiology and classification. There is still disagreement regarding the relationships betweem associted disorders and the core symptoms of ASD.
Objectives:

to evaluate the prevalence of associated conditions in a group of children with ASD and to describe the clinical characteristics.

Methods:

56 children and adolescents with ASD, age 8.7+/-3.5, were further evaluated for the presence of associated disorders. Intellectual disability was present in the majority of patients, n=52 (96.5%). Assessment of additional symptoms was obtained using the following scales: Yale Global Tics Severity Scale (YGTSS), Children Yale-Brown obsessive compulsive scales (CY-BOCS), Yale-Paris Self-Injurious Behavior Scale. Autism Diagnostic Observation Schedule (ADOS) and Childhood Autism Rating Scale (CARS) were used for. Genetic and medical conditions were also screened. Standard electroencephalogram was performed in all participants.

Results:

9 children had epilepsy (16%), 15 (26%) children had epileptiform abnormalities without seizures. Tourette syndrome was found in 3 children (5.5%), Self Injury Behaviors in 2 children (3.5%). 3 boys (5.5%) had a known medical conditions adding to ASD as follows:1 had mild paraparesis and blindness. 1 boy had neurosensorial deafness and the last one had FRA-X syndrome.

Conclusions:

The prevalence rates of associated disorders in ASD found in this study are consistent with current reports. In this study the use of standardized scales was the first step to improve diagnostic reliability of associate diusoredrs in ASD

99 118.7 Most prevalent problems of children with PDD according to their parents. K. Greaves-Lord*, M. Dekker, F. Verhulst, F. Verheij and A. Huizink, *Erasmus MC - Sophia*

Background:

The word 'pervasive' in the term 'Pervasive Developmental Disorders' (PDD) represents the broad range of problems that individuals diagnosed with these disorders encounter. Children with PDD are typically characterized by problems in social interaction, communication, and by stereotype behaviors. However, problems in other domains often also occur (i.e. reduced motor skills, hypersensitivity, internalizing problems, externalizing problems).

Objectives:

In the current study we investigated which problems are most frequently classified as 'profound and often' by parents of children with PDD.

Methods:

At registration parents were asked to complete the Child Behavior Checklist (CBCL), which covers a wide range of social, emotional, and behavioral problems. Parents indicated whether a problem was 0) not present, 1) mild/occurred sometimes, or 2) profound/occurred oftenly. For each problem, the percentage of parents that scored 2 (profound/often) was calculated. Data were analyzed for categories of children in different developmental stages: pre-school, school, and adolescence.

Results:

At pre-school age, problems in the externalizing domain, such as 'quickly changes from one activity to the other' and 'concentration problems' were most prevalent (65.7% and 62.9% respectively). During the ages 6-12 both externalizing and internalizing problems were present. In adolescence, internalizing problems like 'nervous/tense' or 'worries' were most prevalent (71.4% and 61.5% respectively).

Conclusions:

Apparently in children with PDD accompanying problems shift from externalizing to internalizing during development. Parents of children with PDD regard these accompanying problems as profound and highly present. Therefore, accompanying internalizing and externalizing problems in children with PDD need more attention and treatment of these problems might improve family functioning. The question whether these accompanying problems stem from the same etiological mechanisms as the typical PDD symptoms needs further investigations. Future research plans on the etiology of PDD and accompanying problems will be discussed.

100 118.8 Utility of the Child Behavior Checklist in Screening for Psychopathology in Youth with Autism Spectrum Disorders. C. I. Magyar*[1] and V. Pandolfi[2], (1)*University of Rochester*, (2)*Rochester Institute of Technology*

Background: Individuals with Autism Spectrum Disorders (ASD) exhibit a wide range of co-morbid psychiatric disorders. Clinicians are challenged to distinguish co-morbid psychiatric disorders from core and associated ASD features. The Child Behavior Checklist-6 to 18 (CBCL), a norm-referenced caregiver report measure of emotional/behavior problems has not been investigated in ASD samples.
Objectives: To evaluate the utility of the CBCL-6 to 18 in screening psychopathology in youth with ASD.
Methods: The Schedule of Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS) and clinical judgment were used to diagnose psychopathology in 76 youth with confirmed ASD. Caregivers completed the CBCL and participants received comprehensive psychological assessment. Significance tests, sensitivity, specificity, and predictive value data were obtained for 6-11 (n=42) and 12-18 (n=34) year olds corresponding to CBCL normative age groups.
Results: There was a high rate of psychiatric disorders the most frequent being mood and anxiety disorders, and ADHD. In the 6-11 age group, 61.9% were positive (K-SADS+) for at least one psychiatric disorder. No significant differences in mean raw scores were obtained between K-SADS+ or K-SADS negative (-) groups across CBCL scales. In the 12-18 age group, 64.7% were K-SADS + and scored significantly higher than K-SADS- group on most CBCL scales. Within each age group no significant differences between K-SADS +/-

were observed in age, FSIQ, adaptive behavior, and ASD symptoms. Across age groups acceptable sensitivity but low specificity for mood disorders was obtained, and findings were mixed for anxiety disorders and ADHD.
Conclusions: The CBCL may help identify ASD youth at risk for mood disorders. Significant elevations could reflect broad functional impairment. Further research with larger samples and multivariate analyses are needed to identify the relative contribution of CBCL data, autism symptomatology, and developmental level to the prediction of psychopathology in ASD.

101 118.9 Assessment of Psychiatric Comorbidity in ASD: Investigation of the Recently Developed "Autism Comorbidity Interview" and Issues of Self-report. C. Mazefsky*[1], D. Oswald[2] and J. Lainhart[3], (1)*University of Pittsburgh School of Medicine*, (2)*Virginia Commonwealth University*, (3)*University of Utah*

Background: Clinicians view psychiatric comorbidity in ASD as the rule. However, comorbid disorders in ASD are poorly understood, partly due to measurement problems. Assessment measures have varied across studies, and typically involve questionnaires or measures not validated for use in ASD. Objectives: Explore a new interview for assessing psychiatric comorbidity in ASD and establish the utility of self-report.

Methods: Participants will include forty adolescents (mean age = 12; range 10-17) with ASD (verified by the ADOS and ADI) and IQs over 70. Probands and parents are interviewed with the Autism Comorbidity Interview (ACI) regarding the proband's mental health. Participants complete a variety of commonly used self-report questionnaires (e.g. Child Depression Inventory, Reynolds Child Manifest Anxiety Scale).

Results: Preliminary analyses from 20 participants indicate that 26% and 31% of the sample met criteria for DSM-IV depressive and anxiety disorders respectively based on the ACI; these rates were 52% for both when subsyndromal and subthreshold diagnoses were included. Many symptoms were inapplicable to the child with ASD via the ACI's additional queries. For example, 67% of parents reported that their child cannot recognize when others are annoyed, which makes the "purposefully annoys others" symptom of oppositional defiant disorder inapplicable. Chi-square tests indicated lack of agreement between parent-based ACI diagnoses and self-report on both the ACI and screening questionnaires.

Conclusions: Many children with ASD suffer from psychiatric comorbidity that causes additional impairment. The ACI shows promise for differentiation of psychiatric disorders in ASD. Its strengths include consideration of baseline functioning and applicability to the child with ASD. Determining applicability is necessary to avoid misdiagnoses and accurately reflect the underlying causes for problem behavior. Weaknesses of the ACI are the long administration time and extensive examiner expertise needed. Extreme caution should be used when assessing for comorbid disorders via both interview- and questionnaire-based self-report.

102 118.10 PARENT AND SELF REPORT OF SOCIAL ABILITY AND ASSOCIATED PSYCHIATRIC SYMPTOMS IN ADULTS WITH AUTISM SPECTRUM DISORDER. L. Sterling*, S. J. Webb, J. Greenson, G. Dawson and E. Aylward, *University of Washington*

Background: High rates of depression and anxiety have been reported in individuals with autism. Direct assessment of internalizing symptoms in autism is difficult due to issues such as lack of insight or verbal ability. Thus, clinicians often depend on parent-report of associated symptoms in individuals with autism.

Objectives: Investigate correspondence between parent- and self- report of psychiatric symptoms in adults with autism.

Methods: Participants were assessed as part of the STAART Center of Excellence Study at the University of Washington. A psychiatric history interview was administered to adults with an autism spectrum disorder, which included assessment of level of depressive and

anxious symptoms. A medical/psychiatric history interview, assessing presence of depression and anxiety, was administered to parents of participants with autism. Participants also completed self-report measures of social competence, including the Social Avoidance and Distress Scale (SADS) and the Social Communication Scale (CommQ). Diagnosis of an autism spectrum disorder was confirmed using the ADOS and parent interview (ADI).

Results: Data were collected on 36 adults with autism. Rates of depression were 60% (parent-report) and 46% (participant-report); rates of anxiety were 26% (parent-report) and 24% (participant-report). Rates of psychiatric symptoms did not significantly differ when assessed via parent- versus participant-report. Level of self-reported social competence and parent-reported social ability, however, did not correlate.

Conclusions: Accurate assessment of psychiatric symptoms in individuals with autism is crucial for appropriate diagnosis and treatment. Results suggest that parent- and participant- report of psychiatric symptoms yield similar rates, despite differences in perception of social ability. Individuals with autism may have more self-awareness of psychiatric symptoms than social difficulties.

103 118.11 Asperger Disorder(AD):Co-existance with Other Psychiatric Disorders. N. M. Mukaddes*, *Istanbul University,Istanbul Faculty of Medicine*

Background: Despite the presence of significant psychiatric comorbidity among individuals with AD, a limited number of researches have been done regarding this topic.

Objectives: To provide clinical data on comorbidity of psychiatric disorders in subjects with diagnosis of AD.

Methods: Thirty seven subjects (32 male and five female, age range: 6-20 years old, mean age: 10.9 years) with diagnosis of AD according to DSM-IV criteria were evaluated and followed up for 1-5 years. Fourteen (3 female, 11 male) out of 37 were postpubertal individuals. Comorbidity was assessed using the Schedule for Affective Disorders and Schizophrenia for School Age Children - Present and Lifetime Version (K-SADS - PL).

Results: Thirty five out of 37 subjects (90%) had at least one additional psychiatric disorder. The most common psychiatric disorders in this group were ADHD (45%), Obsessive compulsive diaorder (29%), Major depressive disorder (29%), Tic Disorders (18%).In addition, a wide variety of other psychiatric disorders were seen in this group.While ADHD (54%) was the most common additional diagnosis in prepubertal children, major depression (%50) and OCD(%50) were the most common disorders in adolescents. Six out of 14 adolescents displayed either severe suicide ideation, or suicide attempts. Three out of 6 subjects with suicide attempts were female.

Conclusions: The rates of psychiatric disorders in this group seem higher than previous studies. The high rates of comorbidity in this group may reflect a referral bias; individual with multiple disorders and consequently greater impairment are more likely to search treatment. Therefore, they need a more varied treatment approach.

104 118.12 Obsessive and Compulsive Symptoms in children with Asperger Syndrome. L. Ruta*[1] and L. Mazzone[2], (1)*University of Catania, Italy*, (2)*Division of Child Neurology and Psychiatry, University of Catania, Italy; IRCCS Centro Neurolesi Bonino Pulejo, Messina, Italy*

Background: Repetitive thoughts and behaviours are characteristic and disabling symptoms of Obsessive-Compulsive Disorder (OCD). Obsessive and compulsive traits are also often displayed by children with Autism Spectrum Condition (ASC), but this has not been systematically investigated in past research.

Objectives: To examine the occurrence and characteristic features of obsessive-compulsive behaviours in children and adolescents with

Asperger Syndrome (AS), with respect to a matched OCD and typically developing group (CG).

Methods: 60 consecutive subjects (20 OCD; 18 AS; 22 CG), aged 8-15 years, matched for age, gender and IQ were compared. AS and OCD patients were diagnosed according to the DSM-IV-TR criteria. The Autism Diagnostic Interview-Revised and the Autism Diagnostic Observation Schedule were used to assist in the AS diagnosis; the WISC-R was administered to assess IQ. Obsessive and compulsive symptoms were evaluated by using the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS).

Results: The AS group presented significantly higher frequencies of Hoarding (p=0.2) obsessions and Repeating (p=0.001), Ordering (p=0.001), and Hoarding (p=0.13) compulsions compared to CG. Slightly higher, but not statistically significant, frequencies of Hoarding (p=0.36) obsessions and Ordering (p=0.34) and Hoarding (p=0.22) compulsions were scored by the AS group compared to the OCD group. Finally, the OCD group reported significantly higher frequencies of Contamination (p=0.009) and Aggressive (p=0.009) obsessions and Checking (p=0.003) compulsions compared to both the AS group and CG.

Conclusions: Children with AS showed higher frequencies of obsessive and compulsive symptoms with respect to typically developing children, and these features seem to cluster around Hoarding behaviours. Additionally, a different pattern of symptoms is shown in OCD as compared to AS. Further research should be conducted to better understand the characteristics of repetitive thoughts and behaviours in ASC, and to clarify the underlying neurobiological basis of these symptoms.

105 118.13 Female-to-male transsexuals and autistic traits. R. M. Jones*[1], S. Baron-Cohen[1], S. Wheelwright[1], K. Farrell[1], E. Martin[2], R. Green[3] and D. Di Ceglie[4], (1)*Autism Research Centre*, (2)*Transsexual Support Group*, (3)*Imperial College,Claybrook Centre*, (4)*Tavistock Clinic*

Background:Females with autism spectrum conditions (ASC) are hyper-masculinized in specific aspects of their behaviour and cognition. Objectives:Here we test the prediction that those females with extreme Gender Identity Disorder (GID) who opt for gender reassignment and who can therefore be assumed to be masculinized will have elevated AQ scores. Methods:5 groups were compared: (1) female-to-male (FM) transsexuals (n = 61); (2) male-to-female (MF) transsexuals (n = 198); (3) typical males (n = 76); (4) typical females (n = 98), and (5) individuals with Asperger Syndrome (AS) (n = 125). All participants completed an online version of the AQ. Results:The FM transsexuals' mean AQ score (x = 23.3, sd = 9.1) was significantly higher than both typical females (biological sex-matched controls) (x = 15.4, sd = 5.7), typical males (gender-identity matched controls) (x = 17.8, sd = 6.8) and MF transsexuals (16.6, sd = 6.9), but significantly lower than individuals with AS (x = 36.7, sd = 8.0). Approximately 30% of the FM transsexuals had an AQ in the Medium (MAP (AQ = 29-34)) or Narrow Autism Phenotype (NAP (AQ = 35+)) range. FM transsexuals had a 14-fold increase in the rate of NAP relative to typical males. Conclusions:These results confirm that those females with GID who opt for gender reassignment have a higher number of autistic traits. We speculate that these biological females, being masculinized in their autistic traits, may have had difficulties socializing with a female peer group and therefore found it easier to identify with a male peer group. This research illustrates how carefully selected groups in the population (e.g., congenital adrenal hyperplasia) can inform the extreme male brain (EMB) theory of autism.

106 118.14 Psychiatric Differential Diagnosis and Comorbidity In Children And Youth Referred For Assessment Of Possible ASD. V. Dua*[1], K. Kalynchuk[2] and S. Wellington[1], (1)*University of British Columbia*, (2)*Sunny Hill Health Centre for Children*

Background: Children and youth (C&Y) with ASD have a higher risk for comorbid psychiatric disorders. Research has also found substantial symptom overlap between ASD

and psychiatric disorders. Previous reports have utilized standardized diagnostic procedures for either ASD or psychiatric disorders, but rarely both.

Objectives: To investigate the patterns of differential diagnosis and psychiatric co-morbidity in C&Y referred for assessment of possible ASD utilizing standardized ASD and psychiatric diagnostic measures.

Methods: C&Y referred to the British Columbia Autism Assessment Network (BCAAN) between 2002-2007 were included (n=580; age range=1-18; mean age=7.65). Subjects were assessed for both ASD and psychiatric disorder by an experienced child psychiatrist (utilizing ADI-R, ADOS, and DSM-IV psychiatric diagnostic assessment). Pediatric, psychological and communication assessments were available for most subjects. DSM-IV/TR multi-axial diagnoses were arrived at for each subject.

Results: 2/3 of C&Y referred were between 4 - 11 years old (33.1% <6 years; 66.9% >6 years). ASD was diagnosed in 196 (33.8%), and ASD was excluded in 384 (66.2%) subjects. As a group, the most frequent comorbid syndromes were ADHD (59.1%), Anxiety Disorders (ANX) (45.4%), Mental Retardation (MR) (25.3%), and Tic Disorders (19.3%). Between groups, children with ASD <6 years were more likely to have to have MR (43.8%), whereas non-ASD children < 6 years had a higher frequency of Communication Disorders (91.1%), ADHD (50.9%), and ANX (44.8%). Amongst C&Y > 6 years, non-ASD subjects had a higher frequency of ADHD (73.5%) and learning disorder (39.7%).

Conclusions:C&Y referred for possible ASD have a high baseline rate and complex pattern of comorbidity that is relevant to both differential diagnosis and comprehensive functional formulation. In general, all younger children have less psychiatric comorbidity. In school-age subjects, non-ASD subjects appear to have a more complex comorbidity burden. Implications for assessment, service development, and research will be described.

107 118.15 ADHD item profiles in children and adolescents with autism spectrum disorder. J. Sinzig*, *University of Cologne*

Background: Although attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorders (ASD) represent different nosological entities they share symptoms such as hyperactivity, impulsivity, and inattention. Psychopathological, genetic and neuropsychological findings indicate an association between both disorders.

Objectives: The aims of this systematic prospective study were to evaluate ADHD like symptoms in ASD children based on single item-analysis and their association with ASD diagnosis, age, gender and IQ as well as the comparison of a non-ADHD (ASD-) and an ADHD (ASD+) sample.

Methods: Participants were 83 children and adolescents with ASD. Dimensional and categorical aspects of ADHD were evaluated using a diagnostic symptom checklist and a parent ADHD symptom questionnaire according to DSM-IV. Furthermore PDD and ODD/CD symptoms were assessed.

Results: 53% of the sample fulfilled DSM-IV criteria for ADHD. The comparison of the ASD+ and the ASD- sample revealed differences in age and IQ. The severity of ADHD symptoms in the ASD+ sample was associated with the type of ASD diagnosis. Correlations of ADHD and PDD showed significant results for symptoms of hyperactivity with impairment in communication and for inattention with stereotyped behaviour. Item profiles of ADHD symptoms in the ASD+ sample were similar to those in a pure ADHD sample.

Conclusions: Results of our study revealed a high phenotypical overlap between ASD and ADHD. Two subtypes, one being "inattentive-stereotyped" and the other "hyperactive-communication impaired" can be identified. This fact reflects the DSM-classification for ADHD and may theoretically be a sign of two different neurochemical pathways, a dopmaninergic and a serotonergic.

A very detailed examination and exploration can help to understand within the presented child with ASD whether the reported ADHD like symptoms support the notion of an ADHD behavioural syndrome or an increased rate of single behaviours in order to provide the adequate treatment.

108 118.16 Mental Health Problems In Autism Spectrum Disorders. K. Xenitidis[1], E. Paliokosta*[1], S. Maltezos[1] and V. Pappas[2], (1)*Adult ADHD Service, The Maudsley Hospital*, (2)*Ioannina General Hospital*

Background:

Children and adults, diagnosed with Autism Spectrum Disorders (ASD) can suffer from other mental health problems. However, the exact extent of overlapping between autism and mental health problems is not very clear. There is lack of information about the exact prevalence of psychiatric comorbidity in children and adults with autism.

Objectives:

To identify and describe comorbidity of mental health problems in the ASD population.

Methods:

Literature review will be conducted, taking into account that the majority of the evidence comes from case reports and small studies with large epidemiological studies still lacking.

Results:

People with autistic disorders are more likely to have additional conditions emerging in the developmental period (such as ADHD and personality disorders) as well as mental health problems acquired later in life (such as depression, anxiety or psychotic illness). Anxiety and depression are probably the most common lifetime diagnosis, reaching rates up to 44% and 25% respectively.

Conclusions:

Accurate and reliable diagnosis of mental health problems in people with autism is of major importance as comorbid disorders may cause significant impairment and additional burden of illness both on them and their families. Furthermore these difficulties can jeopardize the placement of the child or adult in educational or community settings respectively. While treatment of comorbid mental disorders does not cure underlying autistic symptoms, it often results in a substantial degree of improvement in the level of functioning and the quality of life of the affected person. The assessment of mental health problems in people with autism is particularly important as there is no evidence that individuals with autism spectrum disorders respond less well to treatments for these comorbid problems than do those without a diagnosis in the autism spectrum.

109 118.17 POTENTIAL AUTISM RESEARCH GAPS SUGGESTED BY ANALYSIS OF LITERATURE AND COMORBIDITIES. M. A. Corrales*[1], A. P. Ringer[2] and M. Herbert[2], (1)*US Environmental Protection Agency*, (2)*Mass Gen Hosp/Harvard Med School*

Background: Although the autism research literature has grown dramatically in recent years, research on related disorders may suggest topics not yet pursued in pervasive developmental disorder (PDD) research.
Objectives: We sought an objective, quantitative, comprehensive method to compare the topics studied in PDD, related disorders, and biomedicine overall.
Methods: We developed software to analyze >250,000 PubMed records encompassing PDD and disorders with elevated prevalence in PDD (Rzhetsky 2007): ADHD, epilepsy, bipolar disorder, depression, schizophrenia, and others.
We calculated the share of publications indexed by each of >15,000 Medical Subject Heading (MeSH) terms and substance names. We grouped terms using a hierarchy, from molecular to behavioral levels, and by "types" of terms from the Universal Medical Language System (UMLS) ontology. We quantitated occurrences of the terms as the subjects of literature on PDD vs. each disorder. We also compared PDD literature to all of PubMed.
Results: The PDD literature has been far more focused on behavioral/cognitive levels (three

times as often), and less on molecular or cellular levels, than biomedical literature overall (56% vs. 38% of publications were indexed with chemical substances in PubMed vs. PDD literature, 2000-2006).
At the molecular level, while almost 2,000 substances were identified in PDD literature, about half appear only once. A handful dominate the literature (MECP2, serotonin, MMR vaccine, risperidone, secretin, thimerosal). Under-studied substances relative to PubMed include TNF-alpha, IL-6, estrogen receptors, insulin, and calcium channels.
We also summarize key symptoms, systems, brain regions, cell types, pathways, and substances studied in comorbid disorders relative to PDD.
Conclusions: Objective and quantitative summaries of topics studied in PDD can inform research prioritization. Our analysis suggests several research topics that have not yet received significant attention in PDD research.

110 118.18 Investigating the nature of the association between autistic traits and anxiety-related behaviours within the general population: A quantitative genetic approach. V. J. Hallett*[1], A. Ronald[2] and F. Happé[1], (1)*Institute of Psychiatry, KCL*, (2)*Birkbeck College*

Background: Recent research has suggested that children with autistic spectrum disorders (ASD) often experience comorbid symptoms of anxiety or depression, which can be both distressing and debilitating. Despite the prevalence of anxiety in this group, no research to date has addressed the association between characteristics of ASD and anxiety with regard to their genetic and environmental influences.

Objectives: This study aimed to investigate the aetiological overlap between autistic traits and anxiety-related behaviours within the general population using quantitative genetic techniques. In addition, it aimed to establish whether anxiety-related behaviours were most strongly associated with the social, non-social or communicative traits characteristic of ASD.

Methods: We investigated the phenotypic and genetic overlap between measures of autistic traits and anxiety-related behaviours in a population-based sample of 3827 twin pairs at age 9, using both parent and teacher ratings.

Results: Our results showed that there was a modest correlation between characteristics of ASD and anxiety within the general population (0.31 for parent data, 0.33 for teacher data). For the parent data, a modest but significant proportion of genetic influences overlapped across autistic traits and anxiety-related behaviours in the general population, but there was also evidence for genetic influences that were specific to each. With regard to particular autistic traits, communicative difficulties showed the strongest phenotypic and genetic overlap with anxiety-related behaviours. Model-fitting using the teacher data produced similar results.

Conclusions:There appears to be a moderate overlap between ASD characteristics and anxiety-related traits, mirroring findings from clinical studies. This overlap appears to be caused in part by shared genetic influences between autistic traits and anxiety-related behaviours, particularly autistic communication difficulties. This has implications for understanding the causes of the overlap between anxiety and autistic behaviours.

Keynote Address Program

119 Synaptic and clock genes in autism spectrum disorders

Speaker: T. Bourgeron*Institut Pasteur*

Autism spectrum disorders (ASD) are characterized by impairments in communication skills and social interaction, as well as restricted, repetitive and stereotyped patterns of behavior. Our genetic studies point to one synaptic pathway, including cell adhesion molecules (neuroligins NLGN3, NLGN4 and neurexins NRXN1) and scaffolding proteins (SHANK3) associated with the disorder. This pathway is crucial for synapse formation/maintenance as well as correct balance between GABAergic and glutamatergic synaptic currents. Interestingly, mice with neuroligin mutations show reduced social interactions and ultrasonic vocalizations.

Beside this synaptic pathway, we recently reported genetic mutations altering melatonin synthesis in ASD. Melatonin plays a key role in the regulation of circadian rhythms such as sleep-wake cycles and was shown to modulate GABAergic currents, as well as neurite and memory formation in different animals such as fish, birds, and mammals. Based on these results, we propose that, in some cases, ASD could be the consequence of an excess of GABAergic currents in specific regions of the brain. This excess of inhibitory current could be the consequence of an alteration of synaptic genes revealed or amplified by an alteration of the circadian rhythms. Hence, a better characterization of the interplay between synaptic and clock genes may shed light on several atypical features that are frequently observed in individuals with ASD such as sleep alterations and memory storage/formation.

119.1 Introductory Remarks: Autism Speaks - Geraldine Dawson.

119.2 Keynote Speaker.

Invited Educational Symposia Program

120 Pathology and Neruoananatomy of Human Brain Tissue in Autism

Organizer: E. London*NYS Institute for Basic Research in Developmental Disabilities*

Speakers: C. Schmitz[1]J. Wegiel[2]M. F. Casanova[3]J. LaSalle[4](1)*Dept. Psychiatry & Neuropsychology, Div. Cellular Neuroscience*, (2)*New York State Institute for Basic Research in Developmental Disabilities*, (3)*University of Louisville*, (4)*University of California, Davis*

Autism is a heterogeneous developmental disorder which is clinically defined. Although the clinical diagnosis is reliable, taking the next steps and determining etiology, pathophysiology and treatment targets will require a greater understanding of the neurobiology of the brain. One of the methods used to understand the brain in autism includes the use of animal models. Using knockout animals among other strategies, we are able to create neuronal systems which have commonalities with autism. Unfortunately, these are just models and serve a purpose but ultimately must be shown to be relevant to the clinical syndrome seen in humans. The neuroanatomic findings in human tissue provide a baseline by which animal models can be generated. Surprisingly little is known about the neuroanatomy of autism, especially on a microscopic level. This is also true about neurodevelopment, and much of the physiology and chemistry of the brain in autism. Until fairly recently it was very difficult to study the brains of autistic individuals. With the advent of scanning techniques a wide range of information has become available. Nevertheless there are severe limitations to scanning, most obviously the fact that the resolution of scanning technology limits it' use to investigating fairly large neuronal systems. Human brain tissue supplies a "missing link" which compliments and in some cases replaces other methods of study or the brain . Although very difficult to collect, especially with the caveat that the tissue quality must be in excellent condition for at least certain studies, we will attempt to illustrate the value of this type of research. We will present the work of four scientists who have been using human brain tissue to study autism for anatomical, developmental, environmental and genetic studies. We will also advance some of the hypotheses currently being generated by their work.

120.1 Introductory Remarks.

120.2 Structural correlates of functional deficits in Autism Spectrum Disorder. J. Wegiel*, T. Wisniewski, I. Cohen, E. London, M. Flory, H. Imaki, I. Kuchna, J. Wegiel, S. Y. Ma, K. Nowicki, K. C. Wang and W. T. Brown, *New York State Institute for Basic Research in Developmental Disabilities*

Background: Etiological diversity with genetic, pre-, peri-, and postnatal pathological factors and concurrent diseases contribute to interindividual clinical and neuropathological differences. While genetic and clinical studies of autism are based on examination of thousands of patients and siblings, the search for morphological and molecular equivalents of genetic and clinical abnormalities is limited to about forty brains.

Objectives: Designing of postmortem studies to detect markers of developmental abnormalities corresponding to (a) impairments in reciprocal social interactions, (b) impairments in verbal and nonverbal communication, (c) restricted repetitive and stereotyped patterns of behavior and (c) mental retardation, (d) causes and effects of epilepsy, (e) sudden and unexpected death.

Methods: Future application of same protocols of postmortem MRI, neuropathological studies, unbiased stereological methods, immunocytochemistry and biochemistry will identify differences between patterns of developmental and aging-associated changes in (a) low and (b) high functioning subjects with autism and people diagnosed with (c) Asperger's syndrome and (d) chromosome 15 duplication.

Conclusions: Current studies revealed pivotal role of (a) expanded protocol of neuropathological screening to improve inclusion/exclusion criteria, (b) postmortem quantitative MRI and 3-D reconstruction to monitor changes in size of the brain and brain subdivisions, (c) stereological methods to detect brain structure specific dynamics of developmental changes of size of neuron and neuronal nucleus and patterns of aging associated pathology, (d) immunocytochemistry to characterize metabolic shift resulting in enhanced activity of lysosomal pathways and intracellular deposition of amino-terminally truncated Aβ, and (e) electron microscopy to identify ultrastructural equivalents of pathological changes.

120.3 Convergence of behavioural dysfunction, abnormalities in functional imaging and neuropathology in the fusiform gyrus in autism. C. Schmitz*[1], S. Palmen[2], H. Heinsen[3], H. Van Engeland[4], P. R. Hof[5], H. W. M. Steinbusch[1] and I. Van Kooten[1], (1)*School for Mental Health and Neurosciences, Div. Cellular Neuroscience*, (2)*University Medical Center Utrecht*, (3)*University of Wuerzburg*, (4)*University Medical Center-Utrecht*, (5)*Mount Sinai School for Medicine*

Abnormalities in face perception are a core feature of social disabilities in autism. Recent functional magnetic resonance imaging studies showed that patients with autism can perform face perception tasks. However, the fusiform gyrus and other cortical regions supporting face processing in controls are hypoactive in patients with autism. The neurobiological basis of this phenomenon is unknown. Here, we tested the hypothesis that the fusiform gyrus shows neuropathological alterations in autism, namely alterations in neuron density, total neuron number and mean perikaryal volume. We investigated the fusiform gyrus (analyzing separately layers II, III, IV, V, and VI), in 7 postmortem brains from patients with autism and 10 controls for volume, neuron density, total neuron number and mean perikaryal volume with high-precision design-based stereology. To determine whether these results were specific for the fusiform gyrus the same analyses were also performed in the primary visual cortex and in the cortical gray matter as a whole. Compared to controls, patients with autism showed significant reductions in neuron densities in layer III, total neuron numbers in layers III, V, and VI, and mean perikaryal volumes of neurons in layers V and VI in the fusiform gyrus. None of these alterations were found in the primary visual cortex or in the whole cerebral cortex. Although based on a relatively small sample of postmortem brains from patients with autism and controls, the results of the present study may provide important insight about the cellular basis of abnormalities in face perception in autism.

120.4 Autism as a Minicolumnopathy. M. F. Casanova*, *University of Louisville*

Autism is a brain disorder characterized by abnormalities in how a person relates to others. Both postmortem and neuroimaging studies indicate the presence of increased brain volume and, in some cases, an altered

gray/white matter ratio. Research findings suggest widespread cortical abnormalities explainable within the context of a minicolumnopathy. Characterization of these minicolumnar abnormalities suggests a deficit of surround inhibition and/or the possibility of ephaptic interactions. Due to the orientation of inhibitory fibers in the peripheral neuropil of minicolumns some of these deficits may be amenable to therapy with transcranial magnetic stimulation (TMS). Minicolumnar abnormalities also account for a diminution of the gyral window. The resulting space constrain biases the ratio of short and long corticocortical connections in the brain. A significant portion of these retractive events occur postnatally. This bias in corticocortical connectivity characterizes elements of a cognitve style and some of the regressive events observed in autistic patients.

120.5 Epigenetic Clues in Autistic Brain. J. M. LaSalle*, *University of California, Davis*

Epigenetics refers to heritable and reversible modifications to DNA or chromosomes that control gene expression and phenotype without altering the genetic code. Examples of epigenetic mechanisms include X chromosome inactivation in females in which one of the two X chromosomes is epigenetically inactivated, and parental imprinting in which maternal or paternal genes are epigenetically silenced. An emerging area in the field of epigenetics is the impact of diet and environmental pollutants on epigenetic marks important for neural development. Epigenetic mechanisms are at the interface of genes and environment and are therefore attractive marks for finding clues to complex multiple etiologies of autism spectrum disorders. While genetic analyses can be performed on blood or transformed cells lines, epigenetic marks are often tissue-specific and dynamic in cell culture. Therefore, postmortem brain samples are imperative for investigating epigenetic alterations in autism. Current evidence for epigenetic alterations in autism frontal cortex includes decreased expression of two known neurodevelopmentally important genes, MECP2 and UBE3A, correlate with detectable changes in DNA methylation. Furthermore, the GABA-A receptor GABRB3 is epigenetically dysregulated in autism brain through altered parental imprinting. As the field of epigenetics of autism is still in its infancy, future studies using higher throughput epigenomic approaches are expected to reveal further epigenetic clues in autistic brain that could be useful for targeted therapies or molecular diagnoses.

Oral Presentations Program

121 Language and Communication

121.1 Comprehension of Nouns and Verbs in Toddlers with Autism: An Eye-Tracking Study. L. R. Edelson*, A. Fine and H. Tager-Flusberg, *Boston University*

Background: Language delay is one of the core symptoms of autism, but traditional linguistic tests may be too difficult for low-functioning children. With eye-tracking, we can test language comprehension using simpler, more passive tasks.

Objectives: Study 1 explores whether eye-tracking can be used to test children's comprehension of nouns. Study 2 investigates the comprehension of verbs and the ability to use verbs to anticipate a direct object.

Methods: Children (ages 2;11-6;0) with and without autism participated in these experiments; within the autism group, there was a wide range of language abilities on the PPVT. Each child completed the PPVT, while the parent filled out a shortened version of the MCDI. The children then sat in front of the TOBii eye-tracker, which recorded their eye-movements as they looked at two pictures while listening to prerecorded sentences. In Study 1, the sentence said "Look at the [target word]!", while in Study 2, the verb varied, sometimes biasing toward the target noun ("*Drink* the coffee!") and sometimes remaining ambiguous ("*Touch* the milk!"). Analyses were conducted to examine looking-time and latency to look at the target picture.

Results: Both Study 1 and Study 2 showed that children look longer at the target picture than at the foil, but only for words that parents reported as known (MCDI). Study 2 also demonstrated that typically-developing children were able to use the semantics of verbs to predict the direct object, resulting in a shorter latency to target noun, while the

children with autism did not show this pattern, regardless of PPVT score.

Conclusions: Eye-tracking may be a promising way to test language comprehension in children with autism. Further, it may elucidate ways in which children with autism may have impaired processing, such as their lack of anticipatory looking in response to verbs.

121.2 Do People with Autism Process Words in Context? Evidence from Language-Mediated Eye-Movements. J. Brock*[1], C. Norbury[2], S. Einav[3] and K. Nation[3], (1)*Macquarie University*, (2)*Royal Holloway, University of London*, (3)*University of Oxford*

Background: According to the 'weak central coherence' (WCC) account, individuals with autism process information out of context. Supporting evidence comes from studies of language comprehension where, for example, individuals with autism fail to use sentence context to derive the correct meaning of ambiguous words. However, it is unclear whether such findings reflect specific difficulties in using contextual information or confounding linguistic demands.

Objectives: We used eyetracking methodology to investigate ongoing sentence comprehension and determine the effect of sentence context on spoken word identification as a function of (a) participants' autism diagnosis and (b) their language ability.

Methods: We tested 24 adolescents meeting ADOS criteria for autism spectrum disorder and 24 non-autistic adolescents closely matched on language ability. Eye-movements were recorded as participants listened to sentences, responding when they heard a word that matched one of four objects on a computer display.
Results: Eye-movements were affected by the phonological overlap between the spoken words and the names of objects in the display. For example, on hearing the word "hamster", participants looked more at a picture of a hammer than at other unrelated objects. However, this effect was significantly reduced if the sentence context made the 'competitor' (hammer) an unlikely referent, as in the sentence "Joe stroked the hamster". Contrary to predictions, the effect of context on eye-movements was comparable across groups. Instead, regardless of diagnosis, individuals with poorer language skills showed reduced influence of context on eye-movements.

Conclusions: Our results contradict previous findings supporting the WCC account, suggesting that context-processing difficulties are related to language impairment rather than being autism specific. Together, these findings point towards a more refined version of WCC. This in turn has implications for theories regarding the neural basis of autism.

121.3 Atypical Cry Characteristics in Infants at Risk for Autism. S. J. Sheinkopf*[1], J. Iverson[2] and B. M. Lester[1], (1)*The Warren Alpert Medical School of Brown University*, (2)*University of Pittsburgh*

Background: Autism is associated with atypicalities in pitch, prosody, and other features of vocalizations. Infant cry can also be described along similar dimensions. Thus, infant cry characteristics may provide an early indicator of neurobehavioral status in ASD.

Objectives: To conduct preliminary tests of whether early infant cry acoustics differentiate infants at high and low risk for autism.

Methods: Vocal samples were recorded at home in 6-month-old infants at risk for autism (younger siblings of children with ASD; n= 21) and low risk infants (n= 18). Standard definitions were used to identify cries and fusses. Samples with adequate recording quality were selected for analysis. Samples were excerpted to audio tape and processed by cry analysis software. Samples were filtered (5 kHz), digitized (10 kHz), and separated by utterance. The log magnitude spectrum for each 25-ms utterance block was computed (using a Fast Fourier Transform).

Results: Vocalizations of high risk infants showed less variability in energy and greater variability in fundamental frequency (pitch). Two children had confirmed autism diagnoses at age 3; one had vocalizations that could be analyzed. Z-scores were calculated to compare this child's scores to the control group. This child's cry had low energy (Z= -3.0), high fundamental frequency/pitch (Z= +1.4), and high dysphonation (Z= +2.4). This pattern

was not fully observed in other infants. One low risk infant had low energy and high dysphonation, but differences were smaller and there were no differences in pitch. One high risk infant had a similar pattern of low energy and high dysphonation, but did not differ in pitch.

Conclusions: Infant cry may be one early indicator of disrupted vocal development in autism. These findings raise the hypothesis that autism may be associated with disruptions in the coordination of vocal production during infancy.

121.4 EARLY RISK FOR AUTISM: THE CONTRIBUTION OF MEASURES OF MOTHER-INFANT INTERACTION, NONVERBAL COMMUNICATION, AND LANGAUGE. A. Rozga*[1], M. Sigman[2], S. Ozonoff[3], G. S. Young[3] and S. J. Rogers[3], (1)*Georgia State University*, (2)*UCLA*, (3)*University of California, Davis MIND Institute*

Background: Evidence of language delays, joint attention deficits, and difficulties in the use of social gaze and affect among preschool-age children with autism suggests these domains may tap early manifestations of autism in infancy.

Objectives: To examine whether social-interactive skills at 6 months, nonverbal communication at 12 months, and language development from 12 to 36 months may be disrupted in siblings of children with autism who go on to show signs of the disorder.

Methods: Data was drawn from a larger sample of siblings who met clinical cutoffs on the ADOS at least once at 18/24/36 months (ever-affected), siblings who never met ADOS cutoffs (never-affected), and typically-developing infants (control). Frequencies and durations of infants' socially-directed gaze, smiles, and vocalizations during a free-play interaction with the caregiver were coded at 6 months (n: ever=10, never=40, control=40). The ESCS was administered at 12 months to examine rates of joint attention and requesting behaviors (n: ever=21, never=77, control=56). Overall language abilities were measured at 12/18/24/36 months using the Mullen (n: ever=43, never=158, control=97).

Results: Infants who went on to show signs of autism did not differ from never-affected siblings and control infants in the extent to which they directed gaze, smiles, and vocalizations toward their caregivers at 6 months. By 12 months, the ever-affected infants exhibited lower rates of high-level joint attention (pointing, showing) and requesting behaviors, and language delays that averaged 1.8 months. The ever-affected infants also had lower rates of language growth between 12 and 36 months.

Conclusions: We found no behavioral markers of autism at 6 months of age among siblings who went on to show signs of the disorder. However, deficits that cut across both verbal and nonverbal communication emerged by 12 months of age, with language delays becoming more pronounced across the 12 to 36-month period.

121.5 Language and Reading Abilities of Children with Autism and SLI and Their First-Degree Relatives. K. A. Lindgren*[1], S. E. Folstein[1], J. B. Tomblin[2] and H. Tager-Flusberg[1], (1)*Boston University School of Medicine*, (2)*University of Iowa*

Background: Autism and specific language impairment (SLI) are developmental disorders that share language as a deficit. Past research suggests that there is an increased incidence of language difficulties in families of children with autism and SLI. Few studies have directly compared autism to SLI, and the exact relationship between the two disorders remains unclear.

Objectives: To examine the language and reading abilities of children with autism, children with SLI, and their first-degree relatives.

Methods: Participants were 51 autistic children, 34 children with SLI, their siblings, and their parents. The autism group was divided into two groups: those with and without language impairment (ALI, N=31; ALN, N=20). Participants were tested and compared on a battery of IQ, language, and reading assessments, including the WISC/WAIS, CELF-III, CTOPP, PPVT, WJ-R, and non-word repetition. Relationships to

severity of autistic symptoms were also examined.

Results: ALI and SLI probands performed similarly on most measures while ALN probands scored higher. CELF-III and non-word repetition scores in the autism group were not correlated with symptom severity on any of the algorithm domains of the ADI-R or ADOS. SLI family members performed poorly on most measures, and over half scored in the LI range on CELF-III or non-word repetition. Similarly, the percentage of ALI relatives scoring in the LI range on these measures was significantly higher than in ALN relatives, especially in mothers, despite a lack of significance on group comparisons.

Conclusions: These findings suggest considerable overlap in ALI and SLI beyond basic language abilities and that language difficulties in the autism group are not related to autism severity. Also, although as a group relatives of autistic children performed better than those of SLI children, a significant proportion did perform poorly on clinically relevant language assessments.

121.6 Eliciting Sentence Production In Nonverbal Children With Autism. M. McGonigle*, *University of Edinburgh*

Background: This research is an extension of computer touchscreen assessments of executive control in children with autism (Chalmers-McGonigle et al, 2007; McGonigle and Chalmers, 2002), and is based on the finding that elementary sequential skills could be elicited in minimally verbal and nonverbal children with such techniques, indicating a possible latent capability for 'sentence' production. Objectives: The hypothesis tested in the current study was that the sequential skills of nonverbal children with autism could be elicited in the form of elementary sentence production provided a) that the context was not socially demanding, and b) that a strong learning incentive is provided. Methods: An entertaining touchscreen game, the 'Eventaurs' was developed, in which nonverbal, severely echolalic and minimally verbal children aged between 7 and 14 years are encouraged to make grammatically appropriate sentences by touching pictographs displayed randomly on the screen. These are divided into actors (e.g. pirate, dinosaur, robot), actions (e.g. jump, fly, spin) and prepositions (with and on). When touched in the correct order, the touch icons are followed by an animated version of the events they describe (e.g. monkey kisses pirate). Only syntactically correct sequences produce events, incorrect sequences or long delays between touches have no animated consequences. Results: All children (n=7) exceeded their production length, within six sessions, as measured against their expressive language as well as the Picture Exchange System used in school. Some entirely nonverbal children proceeded to three-word strings such as 'monkey kisses pirate' and one to four word strings such as 'dinosaur dances with wizard'. Conclusions: Focussing on non-social routes to syntactic development in children with autism could provide an important platform for building on their communicative development by allowing them to discover for themselves the power of language production in order to 'make things happen'.

121.7 ACOUSTIC AND PERCEPTUAL MEASUREMENTS OF PROSODY PRODUCTION ERRORS ON THE PEPS-C BY CHILDREN WITH AUTISM. J. J. Diehl* and R. Paul, *Yale University*

Background: Since the first identification of the autistic syndrome, prosody has been reported to be impaired in individuals who speak (Kanner, 1943). Research has begun to identify profiles of deficits in this population across domains of prosodic function (Paul et al., 2005; Peppé et al, 2007). These studies have relied on perceptual judgments. Objective measurement of production patterns in autism is needed.

Objectives: Our objective is to examine the profile of prosodic deficits in children with autism, and to describe the acoustic differences that characterize them.Methods: Twenty-five youth (ages 8-16) with autism spectrum disorders (ASDs) and average general language functioning and 34 typical controls (ages 8-17) matched on chronological age and gender participated. Participants were given the Profiling Elements of Prosodic Systems in Children (PEPS-C), a norm-

referenced measure of prosody perception and production for children 4-16. This measure provides data in the domains of affect, sentence stress, phrase structure, and discourse structure. Utterances produced by participants were scored perceptually according to PEPS-C scoring rules. They were also acoustically analyzed using PRAAT, a program for speech analysis and synthesis.

Results: Participants with ASD performed significantly worse than controls in using prosody productively for sentence stress, $F(1,57)=6.19$, $p<.2$, $d=.67$, and marginally worse for discourse structure, $F(1,57)=3.17$, $p=.8$, $d=.48$, and affect, $F(1,57)=2.92$, $p=.9$, $d=.46$. They also performed worse than controls on all measures of receptive prosody ($p<.5$), with effect sizes ranging from $d=.5$ to $d=.9$ Analysis of fundamental frequency patterns used to convey linguistic and affective cues also suggests differences between diagnostic groups. Conclusions: This study found pervasive deficits in prosody production and comprehension in ASDs that are present for both linguistic and affective domains of function. Moreover, differences between children with autism and typical controls can be measured objectively through acoustic analyses.

121.8 Semantic activation and suppression in single word and sentence context in children with high functioning autism. L. M. Henderson*, P. Clarke and M. J. Snowling, *University of York*

Background: Children with autism frequently show impairments in language comprehension. These impairments are often attributed to weak central coherence (i.e. failure to integrate context), but could also be due to poor executive control (e.g. inefficient suppression of irrelevant information).

Objectives: These hypotheses were tested by investigating the time course of activation and selection of homonym meanings in single-word and sentence context using cross-modal priming. Children with high functioning autism (HFA; n=23), and chronological (CA; n=23) and verbal age (VA; n=23) matched controls participated.

Methods: In Experiment 1 children heard homonym primes (BANK) and unrelated primes (CAKE) and named dominant (MONEY) or subordinate (RIVER) picture targets. Experiment 2 investigated sensitivity to biasing context in facilitating appropriate meanings; children heard neutral (Helen walked towards the bank) or biased (Harry fished from the bank) sentences and named appropriate picture targets (RIVER). To measure inappropriate activation, children heard inappropriately related (Helen fished from the bank) or unrelated control sentences (Harry fished from the stream) and named inappropriate targets (MONEY).

Results: Experiment 1 revealed priming effects for dominant targets at 250ms and 1000ms ISI but subordinate priming only at 250ms ISI. There were no Group interactions. In Experiment 2 the control groups showed appropriate facilitation at both ISIs; the HFA group only demonstrated appropriate facilitation at 250ms ISI. VA controls and the HFA group showed inappropriate facilitation at 250ms; only the HFA group showed inappropriate facilitation at 1000ms.

Conclusions: Children with HFA showed similar single-word semantic processing to controls. They showed sensitivity to context to activate appropriate meanings but this diminished over time, suggesting a difficulty with maintaining appropriate activation. Only the HFA group showed inappropriate meaning activation after 1000ms, suggestive of inefficient suppression. The extent to which these results can be attributed to weak central coherence and/or an inefficient suppression mechanism will be discussed.

Oral Presentations Program

122 Sensory Processing

122.1 A controlled study of a qigong massage treatment for sensory impairment in autism. L. M. Silva*[1], M. Schalock[1], R. Ayres[1], C. Bunse[1] and S. Budden[2], (1)*Western Oregon University*, (2)*Legacy Emmanuel Children's Hospital*

Background: Autism is commonly associated with disturbances of the sensory nervous system, digestion and sleep.

Objectives: to evaluate a treatment for autism based on a model that proposes autism is a global condition in which the primary impairment is sensory, and the developmental delay and abnormal behavior are secondary. Treatment is directed at sensory impairment, digestion and sleep, and allows the child to be more comfortable, more aware, and better able to pay attention and learn. The result of treatment is movement towards normal on the autism spectrum. Hypothesis: A five-month qigong massage intervention aimed at improving the function of multiple physiological systems will significantly improve the severity of autism as measured by standardized tests of behavior and language/social abilities.

Methods: A randomized, controlled trial design was employed with 46 children assigned to intervention or wait-list control conditions. Pre/post testing was done by blinded pre-school teachers and parents. The intervention is two-pronged with parents and trained staff giving children a parent or trainer version of the protocol directed at selected acupuncture channels and points. Setting/Participants: Home and Educational Service District-based training program. A volunteer sample of children & parents completed the program. Selection criteria were: 1) age under six 2) educational diagnosis of autism 3) no additional medical diagnoses. Standardized tests were used: Vineland, Pervasive Developmental Disorder Behavioral Inventory and Autism Behavior Checklist. Changes in sensory impairment, digestion and sleep were evaluated by parent questionnaire.

Results: Blinded teacher evaluations showed treated children had significant improvement of language/social skills ($p<.4$) and reduction in autistic behavior ($p<.3$) compared to controls. Parent data confirmed the findings ($p<.1$) and showed stability of results at ten months.

Conclusions: This research indicates that children receiving the five-month qigong massage intervention had significant improvement of measures of autism. Regression analysis gave support to the autism model proposed.

122.2 Eagle-eye visual acuity in autism. E. Ashwin*, C. Ashwin, D. Rhydderch, J. Howells and S. Baron-Cohen, *University of Cambridge*

Background: Autism spectrum conditions (ASC) are neurodevelopmental conditions diagnosed on the basis of difficulties with social interaction and communication, alongside overly narrow interests and repetitive behaviour. The first reports of autism and Asperger's Syndrome noted that people with these conditions commonly show atypical perceptual processing, including greater perception of details. Cognitive theories of ASC have focused on high-level processes such as impaired empathy, but it has also become evident that there is superior sensory discrimination in the modalities of vision, audition, and touch. These differences may underlie their excellent attention to local detail and a strong drive to systemise. However, no studies to date have used fundamental measures of visual acuity in ASC.

Objectives: To test the possibility that cognitive differences in visual discrimination and attention to detail may actually involve atypical low-level visual thresholds.

Methods: 15 adult males diagnosed with High-Functioning autism (HFA) & Asperger Syndrome (AS) and 15 control adult males took part in the study. Participants were administered the Freiberg Visual Acuity and Contrast test (FrACT), a standardised optometric test.

Results: The ASC group scored a mean visual acuity measure (20:7) that was significantly better than the control group (20:13) by a factor of two. To put this in perspective, birds of prey have visual acuity approximately two and a half times better than humans.

Conclusions: The results provide a possible explanation for enhanced perceptual functioning and attention to detail seen in ASC; indicating that remarkable visual acuity may be an underlying factor. The results of this study also suggest that inclusion of measures of sensory hypersensitivity as diagnostic criteria is justified and that basic

standardised tests of sensory thresholds may inform causal theories of ASC. Since ASC are genetic in origin, this points to genes involved in sensory neurophysiology playing a key role.

122.3 Visual Sensitivity to Human Movement and the Magnitude of Autistic Traits. M. D. Kaiser*, Z. Fermano and M. Shiffrar, *Rutgers University*

Background: Studies in our lab indicate that individuals with Autism Spectrum Disorder (ASD) show equivalent visual sensitivity to human and object movement, while typical controls demonstrate heightened visual sensitivity to human movement. These findings suggest that perceptual processes may contribute to social deficits in ASD. Notably, autistic traits are not limited to clinical populations. The Autism-Spectrum Quotient (AQ) measures autistic traits in adults with normal IQ.
Objectives: Our goal is to understand how individuals with ASD perceive their social worlds. We begin by identifying the relationship between the magnitude of autistic traits and visual sensitivity to social (i.e., human) and non-social (i.e., object) movement.
Methods: Participants completed the AQ and a classic psychophysical motion detection task. Point-light displays of a walking person and moving tractor were constructed from motion capture data. In a blocked design, the points depicting the person or tractor were presented coherently or scrambled. Displays were embedded in point-light masks that limited the utility of local motion processes. Participants reported whether or not they detected the presence of the person or tractor.
Results: Observers with low AQ score (i.e., less autistic traits) showed greater visual sensitivity to human movement than object movement. Observers with high AQ scores (i.e., more autistic traits) showed equivalent visual sensitivity to human and object motion. This group had patterns of perceptual performance that resembled that of observers with ASD in our previous studies.
Conclusions: These results indicate that typical individuals with more autistic traits may perceive human and object motion similarly to individuals with a diagnosis of ASD. Assessing neurotypical participants' AQ scores is a useful way of studying the broader autism phenotype while avoiding the difficulties, such as co-morbid diagnoses, associated with testing clinical populations.

122.4 Gaze Fixation of Children with and without Autism Spectrum Disorder (ASD) on Human Face Photos. F. Ishikawa*[1], S. Sakaguchi[2], N. Inada[1] and Y. Kamio[1], (1)*National Center of Neurology and Psychiatry, Japan, National Institute of Mental Health*, (2)*University of Kyushu*

Background: Recent advances in eye-tracking technology have facilitated studies of visual scanning in ASD (Boraston et al, 2007). Male adolescents and young adults with ASD exhibit an atypical visual scanning pattern focusing on areas other than the eyes (Klin et al, 2002). However, the development of differences in visual scanning patterns between young children with and without ASD is not yet well understood.

Objectives: Our study aimed to identify whether there was a difference between ASD and typically developing (TD) children in the duration and frequency of gaze fixation on face features.

Methods: 23 children with ASD (3 girls, 8 boys) and without ASD (4 girls, 8 boys) aged 24-64 months (mean age: 37 months) were presented with 20 picture stimuli composed of 12 human headshot photos, 4 puppet headshot photos and 4 object photos. For eye tracking purposes, the human headshot photos were divided into facial and non-facial regions. The facial regions were then further subdivided into right eye, left eye, nose, mouth and other regions.

Results: Eye tracking analyses suggested that there was no significant difference between the two groups in both duration and frequency of gaze fixation on the right eye, left eye, and nose. However, the TD children tended to look at the mouth area significantly more frequently, but not longer, than the ASD ones. No difference was found in either duration or frequency of gaze fixation on familiar and unfamiliar human headshot photos between the two populations of TD and ASD.

Conclusions: TD children fixated at the mouth area more frequently than those with

ASD. In fact, six-month-old babies who look at their mothers' mouths were found to have stronger language abilities by 3 years of age (Young et al, in press). One interpretation may be a difference in IQ; children with TD have better language abilities.

122.5 Oculomotor Correlates of Enhanced Visual Search in Autism Spectrum Disorder: A Study of Binocular Coordination. S. Sanchez*[1], B. Keehn[2], L. Brenner[3], S. P. Marshall[1], A. Lincoln[4] and R. A. Müller[1], (1)*San Diego State University*, (2)*San Diego State University/UC San Diego*, (3)*University of California, Los Angeles*, (4)*Center for Autism Research Evaluation & Service*

Background: Previous studies have shown atypical eye-movements in autism spectrum disorder (ASD), mostly in response to social stimuli. Studies of binocular coordination during reading suggest that ocular disparity is related to task difficulty. Binocular coordination may thus provide added insight into the mechanisms contributing to superior search abilities in individuals with ASD.
Objectives: To investigate the degree of binocular coordination in a visual search task and to relate frequency of aligned and disparate fixations to task performance in children with ASD.
Methods: Seventeen ASD and 11 age- and IQ-matched typically developing (TD) children participated, but three ASD and one TD participant had to be excluded for noncompliance. Binocular coordination was measured as the proportion of aligned and disparate (crossed or uncrossed) fixations. Search difficulty in the visual search task was manipulated by varying set size (6, 12, 24), distractor composition (heterogeneous, homogeneous) and target presence (present, absent)
Results: We found significant main effects of target presence, $F(1,20)=7.67$, $p<.5$, and set size, $F(1,20)=4.29$, $p<.5$, indicating that the proportion of aligned fixations decreased in conditions with greater task difficulty. In addition, there was a significant group by target presence interaction, $F(1, 20)=4.84$, $p<.5$, as the proportion of aligned fixations remained equivalent in target absent and present conditions for the ASD group, but increased in target present compared to absent for the TD group.
Conclusions: Consistent with findings by Juhasz et al. (Quart J Exp Psy, 2006), the proportion of disparate fixations increased with added demands on the visual system. Previous research has demonstrated that accelerated response time in target absent conditions drives the superior performance of individuals with ASD in visual search tasks. Our data suggest that target absence does not increase the task difficulty for individuals with ASD as it does for typically developing individuals.

122.6 Mechanisms underlying poor speech-in-noise perception in ASD individuals. J. I. Alcántara*, C. Füllgrabe and E. J. Weisblatt, *University of Cambridge*

Background: In addition to the triad of symptoms required for a diagnosis of autism spectrum disorder (ASD), individuals with ASD also commonly display abnormal sensory sensitivity (e.g. hypersensitivity to acoustic stimuli), although the underlying mechanisms responsible for this phenomenon remain unclear at present. In particular, parental and self-report data suggest that individuals with ASD experience a greater-than-normal difficulty in the perception of speech in the presence of interfering background sounds, be they noise or competing speech. Objectives: To conduct a series of studies designed to investigate the mechanisms underlying speech-in-noise perception in ASD individuals. Methods: Adaptive psychophysical procedures were employed to assess: (1) the detection of sinusoidally amplitude-modulated noise carriers for a range of modulation frequencies (2-512 Hz); and (2) speech-in-noise perception (i.e. speech reception thresholds (SRT), defined as the signal-to-noise ratio required for 50% speech intelligibility), using a range of background speech-shaped sounds, including a steady-state noise, a single competing talker, a temporally modulated noise, a spectrally modulated noise, and a spectro-temporally modulated noise. Three age- and IQ-matched normal-hearing groups were used: high-functioning individuals with autism (HFA); individuals with Asperger's syndrome (AS); and typically-developing control participants. Results: Individuals with HFA and AS had higher (i.e. poorer) modulation detection thresholds than control participants at all modulation frequencies

tested. In addition, both groups displayed poorer SRTs than the controls, but only for background sounds that contained temporal modulations in amplitude. Conclusions: Individuals with ASD appear to be less capable of extracting target speech signals present in regions where the background contains energy minima, than the control participants. This does not seem to be due to a deficit in temporal resolution (i.e. fast temporal processing deficit), but rather as a result of poorer-than-normal temporal processing efficiency. No significant differences in performance were found for the HFA and AS groups.

122.7 Early middle ear disease in children with Autistic Spectrum Disorder. A. J. Hall[1], C. D. Steer[1], A. M. Emond[1], D. Pothier[2], R. Maw[1] and J. Golding*[1], (1)*University of Bristol*, (2)*University of Bath*

Background: The aetiology of the autistic spectrum disorders (ASD) is largely unknown.

Objectives: To assess whether signs and symptoms related to common health problems in childhood are associated with ASD.

Methods: The Avon Longitudinal Study of Parents and Children (ALSPAC; n=14000) started in early pregnancy. Data collected on the child during the first years of life included signs and symptoms of the infant/child. A 10% subsample underwent tympanometry which identifies middle ear disease (9 occasions) and word recognition tests (2 occasions) from 8-61 months.

Results: Only two of the 9 signs and symptoms in the first 42 months were consistently reported more often by mothers of ASD children. Associations of 'ear discharge comprising pus not wax' with ASD were observed after 6 months ($P<0.5$). Mothers also reported failure of their ASD children to react to noise from 18 months ($P<0.001$). By age 38 months, 80% of ASD children had been suspected of having a hearing deficit. The frequency of normal tympanograms up to 61 months was inversely associated with ASD (OR zero occurrences=25 [95% CI 2.58, 242]; OR for one or two occurrences=4.14 [0.34,50.46]; *P* trend=0.003). Hearing tests involving speech showed significant impairment at 43 and 61 months ($P<0.1$). By 7 years of age however ASD children had normal tympanometry and normal audiograms.

Conclusions: We have shown that the only common sign or symptom associated with ASD related to middle ear disease. Objective tympanograms confirmed the association. Affected children showed signs of hearing loss during these early years and were shown to be less able to distinguish speech. This suggests that affected children are less able to hear speech distinctly in early life, and raises the hypothesis that inability to hear during a key period of development may result in the development of traits associated with ASD in susceptible children.

122.8 Barking Frogs and Chirping Frogs: A behavioral and brain EEG study of multisensory matching among persons with Autism Spectrum Disorders. N. Russo*[1], J. A. Burack[2], A. Hosein[3] and B. Jemel[4], (1)*City College of New York*, (2)*McGill University*, (3)*Riviere Des Prairies Hospital*, (4)*Hopital Riviere des Prairies/University of Montreal*

Background:The N400 is an electrophysiological response to a stimulus that is incongruent with expectations derived from its context. The N400 effect, an index of differences between the way the brain processes congruity and incongruity, is commonly seen in both the auditory and visual modalities among typically developing persons. However, individuals with autism do not show an N400 in either modality. This finding may be consistent with the notion that individuals with autism may rely on more perceptually based processes in solving cognitive tasks.

Objectives:To test the notion of enhanced perceptual functioning within a multisensory context using a semantic matching task that was designed for use with Event-Related Potentials (ERP's).

Methods:Fourteen participants with ASD and 14 typically developing participants matched on IQ, gender and handedness, decided whether an auditory (dog bark) and a visual stimulus (a picture of a dog or a cat) matched or did not match. The stimuli could either be presented simultaneously or sequentially with

an SOA of 650msecs. The measures of interest were RTs as well as the onset of a divergence between the processing of congruent and incongruent stimuli as measured by ERP.

Results:The TD persons displayed the expected N400 effect for all conditions, whereas for the persons with ASD the difference between the processing of congruence and incongruence occured much earlier in the simultaneous condition between 120-300msecs. In the delay condition, a typical N400 effect was noted for persons with ASD.

Conclusions: The results suggest that individuals with ASD do show a congruence effect, but that the timing of the distinction between congruence and incongruence occurs earlier in ASD, in time frames consistent with exogenous rather than endogenous processing. These findings are discussed in terms of enhanced perceptual functioning among persons with autism spectrum disorders.

Poster Presentations Program

123 Developmental Stages Posters

1 123.1 Autism Spectrum Disorders: Reasons for Treatment Referrals Across the Developmental Life Span. G. Mathai*[1], H. Patrick[2] and R. A. Lisa[3], (1)*University of Louisville*, (2)*University of louisville*, (3)*University of Kentucky*

Background: Autism Spectrum Disorder (ASD)) affects 1 in 166 children (Fombonne, 2005). Treatment requirements for children with ASD vary with regard to severity of autistic symptoms, cognitive functioning and verbal language abilities.

Objectives: The purpose of this study was to examine reasons for referral for treatment of 113 randomly selected children with ASD at different ages and explore relationships between these concerns and IQ and verbal ability.

Methods: Approximately 30 children were randomly selected from 801 medical records of children who represent 4 different developmental stages: (a) preschool (2-6 years), (b) elementary (7-11 years), (c) middle (12-14 years) and (d) High school (15-21years). The Top three primary referral concerns by physician or caregiver were then classified under different categories based on the need for service such as: (a) social skills, (b) speech, (c) behavior, (d) sensory/motor issues, (e) academic concerns, (f) anxiety, (g) depression, (h) adaptive functioning, or (i) other.

Results: The top three referral reasons for the 113 cases reviewed were first: social skills issues (72.6%), second, behavior issues (52.2%), and third, speech concerns (49.6%). Social skills and behavior concerns were evenly distributed within all four developmental stages. Speech concerns were significantly higher in the preschool stage than in any other stage ($p<.001$). An IQ below 70 was significantly related to speech concerns ($p < .001$) and an IQ above 70 was significantly related to social skills concerns ($p < .001$). As expected, speech concerns were significantly higher in individuals who were non verbal.

Conclusions: These findings provide new information for treatment providers and public-funded agencies who are responsible for the provision of services for individuals with ASD, especially in planning and implementing services commonly sought by caregivers at various stages and understanding the influences of treatment concerns.

2 123.2 Pre-Language Predictors of Development Over 4-5 Years In Children with Autism. K. D. Bopp* and P. Mirenda, *University of British Columbia*

Background: Little is known about the prelinguistic predictors of language development in children with autism over time periods longer than two years. Such information can be helpful in designing early intervention programs that are maximally effective.

Objectives: To examine prelinguistic predictors of development using the MacArthur-Bates Communicative Development Inventory (MCDI, Words and Gestures) in a cohort of young children with autism who were followed over 4-5 years.

Methods: Longitudinal data were collected for 69 children with ASD prior to intervention (T1) and 6, 12, 24, 32, and 53 months later, using the Peabody Picture Vocabulary Test, Expressive One-Word Picture Vocabulary Test, Preschool Language Scale, and Vineland Adaptive Behavior Scale. Prelinguistic predictor variables were constructed using items from the MCDI. After controlling for chronological age, nonverbal IQ at T1, and autism severity, predictors of developmental trajectories for each outcome measure were examined with SAS Proc mixed analyses.

Results: Children's scores on the Games and Routines section of the MCDI at T1 predicted development on all language measures and Vineland subscales over 4-5 years, and accounted for between 14%-53% of the variance. Rates of change for children with high Games and Routines scores ranged from .40-.97 per month, while rates of change for children with low scores ranged from .12-.56 per month.

Conclusions: Games and Routines, which consists of five items (plays peek-a-boo, plays patty cake, plays 'so big,' sings, and dances) encompasses many of the individual skills that are known to be critical for social and language development. These include joint attention (both initiation and responding), immediate imitation, a desire for social interaction, and turn taking skills. Children who enter early intervention with these skills in their repertoires are likely to make more progress, even over a period of as long as 4-5 years.

3 123.3 Early signs of autism spectrum disorder in infancy and early childhood in a community sample of Australian children. M. R. Prior*[1], C. Veness[2], E. L. Bavin[2], E. Patricia[2], C. Eileen[2] and R. Sheena[2], (1)*University of Melbourne*, (2)*Royal Children's Hospital*

Background: From within a large, longitudinal community study of the natural history of language development - the *Early Language in Victoria Study (ELVS)* (N = 1911), a group of 18 children diagnosed with Autism Spectrum Disorder (ASD) by 4 years of age was identified. The developmental histories of these children could be compared with groups within the sample with Developmental Disorder, Specific Language Disorder, and typical development. Objectives: To investigate early and specific developmental 'red flags' in social and communication domains from 8 to 48 months which are predictive of ASD. Methods: The Communication and Symbolic Behavior Scales (Wetherby & Prizant 2002) and the MacArthur Communicative Development Inventory (Fenson et al., 1993) covering early communicative behaviours, gesture production, speech sound and vocabulary development, and functional and symbolic play behaviours, were used at 8, 12, and 24 months of age. Results: Group comparisons were made across early social, symbolic, and language domains to identify differences from normally developing children and to establish whether any of these were specific to ASD at any age. Using those measures which differentiated between groups, predictive analyses to four year old diagnostic status was used to assess the capacity to reliably identify children at risk the three age points Conclusions: Data analyses are ongoing at this stage; results will be discussed in light of current research and practice in the early identification of ASD and the limits of specificity and predictive power of early markers of the disorder. Fenson, L., Dale, P. et al. (1993). The MacArthur Communicative Development Inventories: Users guide and technical manual. Baltimore, MD: Paul H. Brookes Publishing Co Wetherby, A., & Prizant, B. (2002). CSBS DP Manual: Communication and Symbolic Behavior Scales Developmental Profile, First Normed Edition. Baltimore, MD: Paul H. Brookes Publishing Co.
Objectives:

Methods:

Results:

Conclusions:

4 123.4 Diagnostic Indicators for ASD in 14-month-olds. R. Landa[1], A. O'Neill*[1] and E. Stuart[2], (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins School of Public Health*

Background: Diagnostic criteria for Autism Spectrum Disorders presented in the DSM-IV and ICD-10 have limited applicability for children under 3 years of age. However, red flags for ASD have been identified in children as young as 14 months (Landa et al., 2007). Thus, there is a need for diagnostic criteria for ASD in children younger than age 3 to improve early detection and access to early intervention.

Objectives: We propose preliminary diagnostic criteria for communication and social impairment in 14-month-olds, that also indicate high risk for an ASD diagnosis at 36 months of age.

Methods: 114 participants (95 younger siblings of children with autism and 19 low risk controls) were given the Mullen Scales of Early Learning, Communication and Symbolic Behavior Scales Developmental Profile, and Autism Diagnostic Observation Schedule at 14 months of age. Outcome diagnoses were determined at 30 or 36 months of age by a blind expert coder. Classification and Regression Trees (CART) were used to identify the variables and associated cutpoints at 14 months that best differentiated children with and without ASD diagnoses at outcome. These predictors were then applied to the 14 month data to determine sensitivity and specificity.

Results: The identified variables and cutpoints included: CSBS Initiation of Joint Attention (<2) and Consonant Inventory (<4); ADOS Stereotyped Behaviors and Restricted Interests algorithm total (>0) and Response to Joint Attention (>1); and Mullen Receptive Language T Score (<33). 38 children met 3 or more of the criteria; 23 of these had ASD outcomes and 13 had outcomes of other impairments at 36 months of age. All but one child had impairment at 14 months, usually language or social impairment, or ASD.

Conclusions: We identified five indicators that, at 14 months of age, predict 36-month diagnoses of ASD or other related impairment.

5 123.5 OUTCOMES IN YOUNG CHILDREN WITH AUTISM AND DEVELOPMENTAL DELAY. K. M. Gray*[1], B. J. Tonge[1], D. J. Sweeney[1] and S. L. Einfeld[2], (1)*Monash University*, (2)*University of Sydney*

Background:

Reports suggest that in young children with developmental problems and children with autism, parents are often primarily concerned about language and cognitive development and behaviour problems.

Objectives:

To determine if early markers of cognitive, social, communication, play ability, and behavioural adjustment in young children with autism and developmental delay predict subsequent developmental and behavioural outcome.

Methods:

One-hundred and sixty-nine children with developmental delay were followed-up 2 years after their initial assessment and diagnosis. At initial assessment the children were aged 18-48 months, and approximately two-thirds received a diagnosis of a Pervasive Developmental Disorder. Information on symptomatology, behaviour problems, developmental level, expressive and receptive language ability, adaptive behaviour, parent mental health, stress and family functioning was collected at both time points.

Results:

Data will be presented on the stability of diagnosis in young children with developmental delay and on their cognitive and language development at follow-up. Associations between early developmental level, diagnosis, symptomatology and behaviour problems over time, and outcome will be explored along with associations with early gesture, play, and imitation skills.

Conclusions:

Identification of skills potentially associated with better developmental outcomes for preschool children, may result in the development of targeted intervention programmes for infants.

6 123.6 Children Diagnosed with Autism Spectrum Disorders before and after the Age of 6 Years: A Comparison Study. S. L. Jónsdóttir*[1], E. Saemundsen[1], I. S. Antonsdóttir[2], S. Sigurdardóttir[1] and D. Olafsson[3], (1)*State Diagnostic and Counseling Center*, (2)*The Service Center in Arbaer and Grafarholt*, (3)*University of Iceland*

Background: The symptoms of autism spectrum disorders (ASD) become manifest in infancy or early childhood. However, many children are not diagnosed until well into elementary school age and therefore do not benefit from specialized early intervention.

Objectives: To describe and to compare the characteristics of children diagnosed with ASD before and after the age of 6 years.

Methods: Participants were 99 Icelandic children born 1992-1995 who had been diagnosed with ASD, based on ICD-10 criteria. The children were divided into two groups based on their age at initial ASD diagnosis: 58 children were diagnosed before age 6 (group 1) and 41 after age 6 (group 2). Comparisons between the groups addressed autistic behaviors, cognitive- and adaptive measures, language status and other variables. In addition, a questionnaire was administered to parents regarding early concerns of their child's development.

Results: Children diagnosed with childhood autism were more likely to receive their diagnosis before 6 years of age compared with children with other ASDs who were more likely to be recognized later ($p < 0.001$). Comparing groups 1 and 2 did not reveal differences on ADI-R ($p = 0.255$) or adaptive behavior ($p = 0.944$), but group 1 had lower mean IQ scores ($p < 0.001$) and lower verbal status ($p < 0.001$) than group 2. Group 1 was less likely to have received other diagnoses prior to the ASD diagnosis than group 2 ($p < 0.001$). The majority of parents (76.2%) had developmental concerns prior to their child's third birthday. Upon hindsight, 83.3% of the parents thought that their children had shown autistic behaviors at or before 2 years of age.

Conclusions: ASD was recognized later in children with higher IQ scores and with higher verbal status, although the groups did not differ on measures of autistic or adaptive behaviors.

7 123.7 Screening for autism spectrum disorder in pediatric primary care: What is the best strategy?. J. Pinto-Martin*[1], L. M. Young[1], D. S. Mandell[2], L. Poghosyan[1], E. Giarelli[1] and S. Levy[3], (1)*University of Pennsylvania*, (2)*University of Pennsylvania School of Medicine*, (3)*Children's Hospital of Philadelphia*

Background: Two strategies have been proposed for early identification of children with autism spectrum disorders (ASD): 1) using a general screening tool followed by an ASD-specific screening tool for those who screen positive on the former; or 2) using an ASD-specific tool for all children. The relative yield of these two strategies has not been examined.

Objectives: This study compared the number of children identified at risk for ASD at their well child visits between the ages of 18 and 30 months using a general developmental screen tool and an autism specific screening tool.
Methods: The Parents' Evaluation of Developmental Status (PEDS) was used as the general developmental screening tool and the Modified Checklist for Autism in Toddlers (M-CHAT) was used as the autism-specific tool. These tools were administered concurrently to 152 children.

Results: Cross tabulations and chi square tests were used to determine the utility of the PEDS as the first step of a two-part screen for ASD. Of those who screened positive for developmental concerns on the PEDS (n = 38), 16% screened positive for ASD on the M-CHAT; of those who did not screen positive for developmental concerns on the PEDS (n = 114), 14% screened positive for ASD on the M-CHAT ($p=0.79$).

Conclusions:The PEDS missed the majority of children who screened positive for ASD on the M-CHAT, suggesting that these two tools tap into very different domains of developmental concerns. The findings support the use of an

ASD-specific tool for all children in conjunction with regular standardized developmental screening.

8 123.8 Prospective Identification of Autism Spectrum Disorder in Infancy and Toddlerhood in an Australian Community-Based Sample: The Social Attention and Communication Study (SACS). J. Barbaro* and C. Dissanayake, *La Trobe University*

Background: In Australia, children with an Autism Spectrum Disorder (ASD) typically do not receive a diagnosis until 3-years of age, despite many parents suspecting a problem within the first year of life. Although early markers of ASD have been found as early as 6-months, there is little research to date on the prospective identification of these children prior to 18-months.

Objectives: The overall objective in this longitudinal study was to determine whether routine monitoring within the Victorian Maternal and Child Health (MCH) service of a set of social attention and communication behaviours can facilitate the prospective identification of infants who will receive a diagnosis of Autistic Disorder (AD)/ASD, in a community based sample.

Methods: Two-hundred and forty one MCH nurses from 17 Local Government Areas in metropolitan Melbourne were trained on developmental markers of ASDs in infancy. Approximately 22,000 children were then monitored at regular intervals on key items during four routine check-ups (at 8-, 12-, 18-, and 24-months) at their local MCH centre. All children deemed to be 'at risk' of an ASD by showing a 'pattern' of failure on the key items were referred to the SACS. A thorough developmental and behavioural assessment was undertaken at referral, and all referred children were followed up at 6-monthly intervals until 24-months when the ADOS and ADI-R were administered.

Results: Data on the referred sample to date (100 children so far) will be presented, including ascertainment rates for AD/ASD (currently 80%), and the developmental profiles of the three groups of children (developmental and/or language delay; AD; ASD) at 12-, 18- and 24-months.

Conclusions: The results from this unique data set are very promising, and indicate that it is possible to prospectively identify children with an AD/ASD as early as 12-months via routine monitoring by community service providers in a community based sample of infants.

9 123.9 BEHAVIORAL AND INTERACTIVE ABNORMALITIES IN EARLY AUTISM ON HOME-MOVIES. F. Apicella*[1], C. Grassi[1], R. Marcone[2], P. Muratori[1], C. Pecini[1], A. Petrozzi[1], S. Maestro[1] and F. Muratori[1], (1)*Scientific Institute "Stella Maris"*, (2)*Seconda Università degli Studi di Napoli*

Background:

In the last 30 years, a growing number of studies on home-movies of the first two years of life of children later diagnosed with Autism, report evidences of several abnormalities in the early social development.

Objectives:

The objective is to describe influences of early signs of autism on social development and to figure-out specific features of interactions in the first 18 months of life.

Methods:

A scale for the detection of infant/caregiver social behaviors has been applied to HM of three groups (Autism (A) (n=15), Mental-Retardation (MR) (n=12) and Typical-Development (TD) (n=15)) in the first three semesters (t1-t2-t3).

Results:

No differences in t1 with the exception of higher durations of "Syntonic-responses" in TD. Differences between TD and A become significant in t2 and in t3. Infants with autism display increasing difficulties in "Maintaining-social-engagement" and "Syntonic-responses" and lower frequencies of "Pointing", "Accepting-invitation" and "Responding-to-name". Results of MR and A are similars until t3, when children with MR display significantly

better performances in behaviors such as "Smiling", "Enjoying-with-others" and "Vocalizing". Moreover A receive less solicitations than others to "Regulate-down" their behavior.
Sequential analysis shows several significant differences in infant's responses to caregiver stimulations. "Looking-at-people", "Responding-to-name", "Maintaining-social-engagement" and "Syntonic-responses" are differently connected with caregiver's regulation/stimulation behaviors. Cycles-of-interaction patterns between MR and their caregivers result more similar to TD profile than to Autism.

Conclusions:

In t1 A do not display specific impairments in basic behaviors (look, orient-himself and smile). Intersubjective impairments become evident later, when they seem not able to organize abilities to be socially engaged for enough time. To "Maintain-social-engagement" and to "Accept-invitation", children need to attune responses to solicitation, showing attention and interest into intention. "Syntonic-responses" can be considered an early indicator of emotional congruence to other's affect and behavior. This behavioral categories may represent empirical markers of typical development.

10 123.10 Comparative Analysis of Three Screening Instruments for Autism Spectrum Disorder in Toddlers at High Risk. I. J. Oosterling*[1], S. Swinkels[1], R. J. Van der Gaag[1], J. C. Visser[1], C. Dietz[2] and J. K. Buitelaar[1], (1)*Karakter Child and Adolescent Psychiatry University Center*, (2)*University Medical Center Utrecht*

Background: Several instruments have been developed to screen for autism spectrum disorders (ASD) in high-risk populations. However, little research has been completed on comparing the properties of different screening instruments at an early age in one and the same sample.

Objectives: To compare the properties of several screens and the value of their individual items in two age groups of high-risk children (8-24 months and 25-44 months). Instruments examined are: the *Early Screening of Autistic Traits Questionnaire* (ESAT; Dietz et al., 2006; Swinkels et al., 2006), the *Social Communication Questionnaire* (SCQ; Berument et al., 1999), the *Communication and Symbolic Behavior Scales-Developmental Profile, Infant-Toddler Checklist* (CSBS-DP; Wetherby & Prizant, 2002) and key items of the *Checklist for Autism in Toddlers* (CHAT; Baron-Cohen et al., 1992).

Methods: Data were gathered in 238 children (mean age=29.6 months, *SD*=6.4) at risk for ASD, because of either screen positive results on the ESAT 14-items (*n*=208) or, when screen negative, because of sufficient clinical concern (*n*=30). The SCQ and CSBS-DP were completed on average 2.6 months later (*SD*=1.7). Three questions that represent the main concepts of the CHAT were derived from the SCQ and CSBS-DP. Clinical diagnoses were made using golden standard diagnostic procedures. To compare discriminative power of instruments different test properties were calculated (Sensitivity, Specificity, PPV, NPV and ROC Area-Under-the-Curve analyses). To compare the usefulness of different screening items odds ratios per item were calculated.

Results: No instrument performs clearly better over another or meets standards for satisfactory prediction of ASD diagnosis, since the AUC's are fair at the most. However, each instrument demonstrates specific strengths and many single items on joint attention and language and communication show high odds ratios.

Conclusions: Pros and cons of instruments will be discussed and directions for future research proposed.

11 123.11 Autism onset: a study with the Early Development Questionnaire. E. Santocchi*, F. Apicella, F. Fulceri, R. Igliozzi, B. Parrini, R. Tancredi and F. Muratori, *IRCCS Fondazione Stella Maris*

Background:

Onset of autism is usually described by two patterns: an early onset when a child shows

typical symptoms within the first year of life and a regressive one when a child has a period of apparently tipical development, followed by a lost of communicative and social skills during the second year of life. Recent studies describe a third pattern of onset in which the children demonstrate mild delays during the first year of life followed by later regression.

Objectives:

To describe early development, clinical characteristics of regression and later severity of autistic symptoms in children with different type of onset.

Methods:

A retrospective measure, the Early Development Questionnaire (EDQ), has been used to collect parent-reported information about social development in the first 18 months of life and regression of skills, in 50 under-six children with a diagnosis of autism or PDD-NOS. Different instrument (ADOS-G, CARS and CBCL) were used to assess symptoms severity.

Results:

Based on their EDQ scores the children were divided into three groups: 1) early onset group (*n*=11); 2) definite regression group (*n*=15); 3) and a more heterogeneous and less clear regression group (*n*=24). Early development in children with definite regression results more typical in comparison with the other two groups, with significant differences in many social and communicative skills. Neverthless, 90,9 % of children with certain regression fail in showing two or more expected communicative or social behaviours. No significant differences in the severity of autistic symptoms were found among the three groups.

Conclusions:

In a large part of the children with regression, the early development, before the skills'lost, only apparently turns out as typical; these children fail in showing waited social behaviours.

12 123.12 Use of structured home video diaries to track the development of infants at risk for Autism Spectrum Disorders (ASD). A. M. Seery*[1], L. M. Casner[2], N. B. Leezenbaum[2], A. Zuluaga[2], A. Carter[3] and H. Tager-Flusberg[2], (1)*Boston University*, (2)*Boston University School of Medicine*, (3)*University of Massachusetts Boston*

Background: Studies of development of infants later diagnosed with ASD have relied on data from personal home videos, which typically lack standardized procedures, or laboratory-based visits, which families can find time-intensive. As an alternative, standardized home video diaries may allow for dense data collection during critical early stages of development when symptoms emerge or developmental trajectories change significantly, as in regression.

Objectives: To examine the use of semi-structured home video diaries as a novel approach for studying the development of infants at risk for ASD.

Methods: In an ongoing study, parents (with infants at risk for ASD, specific language impairment (SLI), or typical controls) were supplied with video equipment and trained on collecting semi-structured data in the home bi-weekly, beginning when their infant was 6 months old. Parents (currently n=30) also completed web-based weekly diaries and brought their infant to the laboratory for standardized assessments at 6, 9, 12 and 18 months.

Results: Families have completed .98 diaries per month on average (SD=.88; range=0-4.3). ASD-risk families (n=17) submitted .83 per month (SD=.61), SLI-risk families (n=3) submitted .93 per month (SD=.50), and control families (n=9) submitted 1.28 per month (SD=1.34). Preliminary analysis of videos suggest that infants who later exhibit ASD risk signs (on the AOSI and/or ADOS) are more likely to be unresponsive to name and fail to babble before 12 months. Ongoing work will focus on the predictive diagnostic value of video diaries and the relation between behaviors in the diaries and in laboratory-based assessments.

Conclusions: Our findings indicate that families are capable of completing one semi-structured video per month. Thus, video diaries provide a realizable, cost-effective method of collecting data more frequently than lab-based testing. Home-based diaries are accessible to families for whom laboratory participation is impossible and may help identify very early risk signs for ASD.

13 123.13 The early temperament of children with the Autistic Spectrum Disorder (ASD). J. Golding*, C. D. Steer and A. M. Emond, *University of Bristol*

Background: Early temperament has been linked to language development and it is suggested that these traits may help to explain variation between children with ASD and between ASD and non-ASD children.

Objectives: To assess whether measures of temperament predict ASD status.

Methods: Using the ALSPAC cohort of 14,062 livebirths born to pregnant women enrolled during 1991-2, mothers prospectively reported aspects of child temperament at 1 month using 14 questions, and at 6 and 24 months using over 80 questions from the Carey Temperament scales for infants and toddlers. Children who had been given a diagnosis of ASD by 11 years of age were compared with their non-ASD peers.

Results: No differences were observed between ASD children and controls at 1 and 6 months. But at 24 months, ASD children scored higher on adaptability and persistence ($P<0.0001$) and on mood ($P<0.1$) but scored lower on distractibility and threshold ($P<0.0001$). Children were 40% to 80% more likely (or less likely) to have an ASD diagnosis for a one SD increase in score.

Conclusions: Differences between diagnostic groups on temperament measures up to age 24 months were small, and the likelihood of the measures being of use in predicting children at high risk of ASD is minimal.

14 123.14 The bowel habits of young children with Autistic Spectrum Disorders (ASD). C. D. Steer*, B. Sandhu, A. M. Emond and J. Golding, *University of Bristol*

Background: There is evidence that a number of children with autism have chronic bowel disorders. It is unclear, however, how often children with ASD have such disorders or at what age they develop.

Objectives: To use the information collected by the Avon Longitudinal Study of Parents and Children (ALSPAC) to determine in what way the early bowel habits of the children diagnosed with ASD differed from the rest of the population.

Methods: Detailed information was collected from the ALSPAC mothers at 1, 6, 18, 30 and 42 months on the frequency with which they passed a motion, stool consistency (hard, soft, liquid, curdy) and colour (black, brown, green, yellow). Data were also available for bowel symptoms of colitis (diarrhoea, blood in stools and stomach pain).

Results: The 78 children with ASD were compared with the remainder of the cohort ($N = 12,993$). The only significant differences occurred at 30 and 42m. Children passing 2 stools per day were 50% more likely to have ASD compared to those passing stools once per day ($P<0.001$). Children who usually passed yellow stools were 70% more likely to have ASD than children who only sometimes had this colour ($P<0.5$). There were no strong differences earlier in the child's life or with stool consistency, other stool colours or bowel symptoms.

Conclusions: There is some indication that children with ASD have more frequent bowel movements at 30 and 42 months of age. These differences are more likely to be associated with a restrictive or unusual diet than a precursor of ASD.

15 123.15 Finger length of boys with ASD differs from those with disruptive behavior, anxiety. E. I. De Bruin, K. Greaves-Lord*, P. F. A. De Nijs and F. Verheij, *Erasmus MC-Sophia Children's Hospital*

Background: Over 125 years ago it was already shown that males had longer ring

fingers relative to their index fingers, and women showed the reverse pattern. Since then, a large amount of studies have associated the length of the index finger relative to the length of the ring finger, the 2D:4D ratio, with a variety of variables (i.e., assertiveness, breast cancer, attractiveness, fertility, female waist-hip ratio, homosexuality). Finger length is determined by hormonal influences (testosterone) in the first 3 months of pregnancy and remains stable over life. Specific patterns of the 2D:4D ratio have been associated with autism before but the milder form of ASD, PDD-NOS, has not yet been studied and also it is unknown whether certain 2D:4D patterns are specific for ASDs.

Objectives: The aim of this study was to compare finger length in boys with different psychiatric disorders.

Methods: Vernier calipers were used to measure finger length in boys with anxiety disorders (n = 20), ADHD/ODD/CD (n = 60), autism/Asperger syndrome (n = 15), PDD-NOS (n = 60), and were compared to normal controls (n = 90). Only boys were included to rule out the effect of male-female differences in finger length, and the effect of a difference male-female prevalence for the disorders.

Results: Groups differed on 2D:4D ratio for the right hand only. Boys with autism/Asperger syndrome showed the most male-like 2D:4D pattern. They had a lower ratio than boys with PDD-NOS, anxiety disorders, and normal controls. Further, boys with externalizing disorders also showed a more male-oriented finger pattern, with a lower 2D:4D ratio than boys with anxiety disorders and normal control boys. The anxious boys showed the most female-like finger pattern compared to the other groups.

Conclusions:Finger length differs in child psychiatric groups which indicates that different underlying endocrinological factors might play a role.

17 123.16 Identification of infants with autism at their first birthday through retrospective use of FYI. F. Muratori*, F. Apicella, F. Fulceri, A. Narzisi and R. Tancredi, *Scientific Institute "Stella Maris"*

Background:

Recent research (Watson et al., 2007) indicate the First Year Inventory (Reznick, Baranek et al., 2006) as a tool to identify one-year-olds at risk for autism and to describe children diagnosed with autism at their first birthday.

Objectives:

To examine the construct validity of the FYI-Retrospective form in a population of Italian preschoolers with autism.

Methods:

FYI was administered to parents of 50 preschoolers with ASD referred to the IRCCS Stella Maris for a comprehensive evaluation. Children's diagnoses were confirmed with Autism Diagnostic Observation Schedule (ADOS-G). Standard scores from MacArthur Communication Development Inventory and Leiter International Performance Scale-Revised (Leiter-R) were used to investigate language and cognitive levels. Parents (mother when possible) also completed the Early Development Questionnaire (EDQ; Ozonoff, 2005) to evaluate the presence of regression.

Results:

Preliminary analyses show: 1) higher risk scores in Social-communication domain (particularly in Social orienting and receptive communication; Imitation and Expressive communication) compared to the scores in Sensory-regulatory domain; 2) children with reported regression after 12 months of age have lower scores at the FYI; 3) a proportion of children obtained total risk scores under threshold of the cutoff; 4) some correlation of the FYI with cognitive and language impairments were found.

Conclusions:

FYI is as a useful tool to investigate early autism in its different form of onset and to better understand regressive form of autism.

18 123.17 Development of Screening Tool for Autism in Two-Year-Olds- Taiwan Version. C. H. Chiang*[1], C. C. Wu[1], Y. M. Hou[2] and J. H. Liu[2], (1)*National Chung Cheng University*, (2)*Chiayi Christian Hospital*

Background: The STAT is a twelve-item interactive screening measure for autism, which has been investigated and demonstrated strong psychometric properties and shows promising utility as a Level 2 screening measures for autism in the Western society. A modified T-STAT developed from the original STAT was used in the study. Objectives: The purpose of current study was to examine whether the T-STAT is a useful screening tool for the young children with autism in Taiwan. Methods: The participants were thirty-seven 29-month-olds (range = 24-36 months) children with autism, CA-matched eleven children with PDDNOS and twenty-four children with non-ASD. All of participants were recruited from a local hospital in southern Taiwan and assessed and diagnosed by senior psychiatrists. ADOS was administered independently by the first author. For developing new T-STAT, three items were substituted and held the nine items from the original STAT. Results: Using the same algorithm and cutoff of original STAT, yields T-STAT's sensitivity and specificity. 1. Based on the autism and non-ASDs diagnosis from ADOS, the sensitivity and specificity are .92 and .83, respectively. Based on the autism and non-ASDs diagnosis from clinical judgment, the sensitivity and specificity are .87 and .70, respectively. 2. Based on the ASDs and non-ASDs diagnosis from ADOS, the sensitivity and specificity are .83 and .83, respectively. Based on the ASDs and non-ASDs diagnosis from clinical judgment, the sensitivity and specificity are .87 and .70, respectively. Comparing the three areas of T-STAT between autism/ASDs and non-ASDs groups by ADOS classification, there were significant differences in areas of play, requesting and directing attention, but not in the area of imitation. Conclusions: Results of this study demonstrated that the T-STAT is quite good tool to differentiate the groups between autism/ASDs and non-ASDs.

20 123.18 Characterization of Autistic Symptoms in Children Diagnosed with Autism Spectrum Disorder Before Age 2. L. H. Shulman*[1], B. M. Burrows[1], M. Valicenti-McDermott[1], R. M. Seijo[1], D. J. Meringolo[1] and S. J. Goodman[2], (1)*Albert Einstein College of Medicine*, (2)*Fordham University*

Background: By definition, the onset of Autism Spectrum Disorders (ASD) is before age 3. Despite increasing evidence that children can be diagnosed by age 2, few studies have focused on symptoms in very young children.

Objectives: To compare the clinical presentation of children diagnosed with ASD before age 2 to children diagnosed after 2 Methods: Retrospective chart review of 145 children, ages 1 to 4 presenting to a University Affiliated Program for initial multidisciplinary evaluation from 2003 to 2007, who received a diagnosis of ASD. Information reviewed included demographics, maternal age, medical, developmental and family histories, DSM-IV-TR symptom checklist, Childhood Autism Rating Scale (CARS), and the Bayley Scales. Statistical analysis included Chi-Square, T test, Mann Whitney and logistic regression.
Results: Of the 145, 41 were under 24 months (age range 18-48 months). Children diagnosed under 2 were more likely to have been born to younger mothers (29 +/- 5 vs 31.2 +/- 5 p=0.3). On the DSM-IV, children under 2 were more likely to show a lack of shared enjoyment (75% vs 48% p=0.009) and a preoccupation with parts of objects (61% vs 38% p=0.2), and less likely to present with stereotyped language (18% vs 48% p=0.002) and impairments in initiating and sustaining conversation (5% vs 30% p=0.1). These differences persisted after adjusting for level of maternal education, socioeconomic status, and cognitive level. There were no significant differences in autistic symptom severity (total CARS score) or in cognitive functioning (Bayley Scales).
Conclusions:Children diagnosed with ASD under 2 may not be more severe in terms of level of social impairment or cognitive impariment. They seem to present with a different pattern of autistic symptomatology.

They are more likely to show a lack of shared enjoyment and demonstrate preoccupation with parts, and less likely to display stereotyped language and impairment in conversation than children diagnosed over 2.

21 123.19 Regression of Language and Non Language Skills in Pervasive Developmental Disorder. A. A. S. Meilleur*[1] and E. Fombonne[2], (1)*McGill University*, (2)*Montreal Children's Hospital*

Background: As part of the Autism Spectrum Disorder (ASD), a subgroup of individuals display a different pattern of onset consisting of an apparently normal early development followed by a loss of verbal and/or non-verbal skills prior to age 2.
Objectives: This study aims at comparing the symptomatology of children who displayed a regression through investigation of 2 types of loss namely language and other skill regression.
Methods: This study examined the occurrence of regression in 135 children with ASD, mean age 6.3 years. The sample was composed of 80 (59.4%) children diagnosed with autism, 44 (32.6%) with PDD-NOS and 11 (8%) with Asperger syndrome. The Autism Diagnostic Interview Revised (ADI-R) was used to evaluate the type of loss and to characterize associated factors.
Results: A total of 30 (22%) subjects regressed: 9 (30%) underwent language regression only, 17 (57%) loss a skill other than language, and 4 (13%) lost both language and another skill. Significantly higher levels of regression were found in autism (30%) compared to PDD-NOS (14%) and Asperger syndrome (0%). Children who regressed in language skills talked at a significantly earlier age (mean=12 months) than those who did not regress in this domain (mean=26 months). Parents and interviewers consistently reported developmental abnormalities prior to the loss. ADI-R domain mean scores indicated a more severe autistic symptomatology profile in children who regressed compared to those who did not, especially in the repetitive behaviour domain.
Conclusions: A loss of skill, present in 1 out of 5 children with ASD, is associated with a more severe symptomatology as measured by the ADI-R, particularly in the repetitive behaviours domain. Furthermore, although abnormalities are first noticed at the time of regression, the ADI-R reveals that other atypical behaviours are in fact present prior to the onset of regression.

22 123.20 EVALUATION OF FAMILIAL CLUSTERING OF AUTOIMMUNE DISORDERS IN CHILDREN WITH AUTISM SPECTRUM DISORDERS. A. E. Porter*[1], R. P. Goin-Kochel[1], S. U. Peters[1], D. E. Treadwell-Deering[2] and S. Wiley[3], (1)*Baylor College of Medicine*, (2)*Texas Children's Hosptial, Baylor College of Medicine*, (3)*Virginia Commonwealth University*

Background: Several research groups have suggested immunological involvement and/or a family history of autoimmune disorders (AI) as placing children at risk for the development of ASD. Additionally, limited evidence suggests that the nature of ASD onset (i.e., congenital vs. regressive) may be associated with family history of AI.

Objectives: To determine whether a positive family history of AI is related to type of ASD onset and/or a history of developmental regression in affected children.

Methods: Participants were 68 families from an eligible study population of 101 families affiliated with the Virginia Commonwealth University Autism Center Registry. Parents were mailed a questionnaire that asked about their child's development of ASD and his/her family history of AI. Analyses included χ^2 tests to determine differences among select groups and logistic regressions to determine odds ratios.

Results: To date, 68 participants with a reported diagnosis of strict autism (76%), Asperger's syndrome (7%) or PDD-NOS (16%) have been included in analyses. Average ages at the time of the questionnaire and ASD diagnosis were 10.3 years and 36 months, respectively; most focal children were male (69%). Those with a diagnosis of strict autism were 4.4 times more likely to have a history of regression than children with a diagnosis of

Asperger's syndrome or PDD-NOS. Children with autism and no second-degree relatives with AI were more likely (OR=5.9) to report a history of developmental regression than children who had any second-degree relatives with a history of AI. The presence of one or more cases of AI in any relation was not significantly associated with onset of ASD or history of regression.

Conclusions: Findings do not currently indicate an association between family history of AI and symptom onset in children with ASD, although this could result from small sample size. Data collection is ongoing at Texas Children's Hospital.

23 123.21 Diagnostic Stability Over Two Years Among Younger Siblings of Children with Autism Spectrum Disorders. K. Carr*, E. Troyb, S. Hodgson, M. Barton, J. Green and D. Fein, *University of Connecticut*

Background: Previous studies indicate that ASD diagnoses are highly stable over time, with Autistic Disorder being more stable than PDD-NOS. Diagnostic stability among younger siblings of children with ASD has received little attention. Some researchers contend that ASDs manifest themselves differently in multiplex families than in simplex families, suggesting that differences in diagnostic stability between multiplex and simplex families are possible. Objectives: To investigate diagnostic stability among younger siblings of children with ASD from age two to age four. Methods: Thirty-two younger siblings of children with ASD ("siblings") and 136 children from simplex families ("singletons") were evaluated twice as part of an early detection of ASD study. Time 1 mean age was 23 months for siblings, 27 months for singletons; Time 2 mean age was 49 months for siblings, 55 months for singletons. Both evaluations included a battery of diagnostic, cognitive, and adaptive tests. Diagnoses were assigned based on the DSM-IV symptom checklist, completed using information from testing and clinical judgment. All children received a diagnosis of Autistic Disorder, PDD-NOS, or non-ASD. Results: Chi-square analysis indicated that diagnostic stability was significant in both the sibling and singleton groups. The Positive Predictive Power (PPP) of an ASD diagnosis at time 1 for an ASD diagnosis at time 2 was .800 in siblings and .798 in singletons, indicating that approximately 80% of children from simplex and multiplex families retained an ASD diagnosis from age two to four. Consistent with other studies, a diagnosis of PDD-NOS was less stable in both groups than a diagnosis of Autistic Disorder. Conclusions: Preliminary results from our small cohort of siblings indicate that ASD diagnoses are similarly stable in siblings as in singletons over two years, and that PDD-NOS is a less stable diagnosis than Autistic Disorder.

24 123.22 Early Symptoms of Autism Spectrum Disorder in Children Identified Through Screening at a Very Young Age. E. Daalen*[1], C. Kemner[1], C. Dietz[1], S. Swinkels[2], H. Engeland, van[1] and J. K. Buitelaar[3], (1)*University Medical Centre Utrecht*, (2)*Karakter Child and Adolescent Psychiatry University Center*, (3)*Radboud University Nijmegen Medical Centre*

Background: although parents often report concerns about the development of their child as early as the second and sometimes the first year of life (De Giacomo & Fombonne, 1998; Gray & Tonge, 2001; Howlin & Asgharian, 1999), many children receive a diagnosis much later (Cox et al., 1999; Howlin & Asgharian, 1999; Charman & Baird, 2002; Lord et al., 2006). This might be partly due to the lack of clear diagnostic criteria for children at a young age. Objectives: we have developed a screening procedure, the Early Screening for Autistic Traits (ESAT) (Dietz et al., 2006; Swinkels et al., 2006). This screening procedure was applied to a population cohort of 31.724 children at 14-months of age at well-baby clinics. The aim of this part of the study is to describe early signs and symptoms of ASD, when children are ascertained at a very young age from a population-based sample which included children with developmental delay. Methods: in a prospective design preschoolers were recruited from a screening study for ASD. Diagnoses were ascertained at 26 and 42 months of age. Diagnostic instruments and symptom clusters at age 26 months were evaluated on their predictive abilities of

developmental disorders and especially ASD at age 42 months.

Results: the evaluation is still in progress. Results will be presented.

Conclusions: the conclusion will be presented.

25 123.23 Varying Pathways to Asperger's Syndrome at Age 5: A Prospective Case Series.
K. Drummond*[1], W. Roberts[2], J. Brian[3], S. Bryson[4], C. Roncadin[5], I. M. Smith[4], P. Szatmari[6] and L. Zwaigenbaum[7], (1)*The Hospital for Sick Children and University of Toronto*, (2)*University of Toronto*, (3)*Hospital for Sick Children, and Bloorview Kids Rehab*, (4)*Dalhousie University/IWK Health Centre*, (5)*Peel Children's Centre and McMaster Univeristy*, (6)*Offord Centre for Child Studies, McMaster University*, (7)*University of Alberta*

Background: There are many studies of high-functioning individuals with autism and Asperger's syndrome (AS). However, little is known about the early behavioural profiles and developmental trajectories of young children who later receive an AS diagnosis.
Objectives: The present case series describes the cognitive, language, social-communication, and behaviour patterns in high-risk infants who were followed prospectively from 6 months of age and met criteria for AS or Autistic Spectrum Disorder (ASD) between 3 and 5 years; all were high-functioning. The cases elucidate emerging signs of social-communication difficulties and/or narrow interests and repetitive behaviour that may not meet criteria for ASD at 2 years of age.
Methods: Prospective data were collected from a study of high-risk infants with a sibling with ASD (Zwaigenbaum et al., 2005). Developmental profiles included information from standardized observations (e.g., Autism Observation Scale for Infants, Autism Diagnostic Observation Schedule) and interviews (e.g., Autism Diagnostic Interview – Revised), as well as measures of cognition, language, and motor development.
Results: We described three broadly defined subgroups: (1) no identified delays or ASD signs by 2 years of age (i.e., typical cognitive and communication development; n = 3); (2) those initially identified as 'at-risk' due to communication or language delays by 2 years; n = 3); and (3) those who received a diagnosis of ASD before age 2 (n = 2). Despite different developmental pathways across groups, all children had a profile of abilities consistent with AS by 5 years of age. In most children, early repetitive behaviours and interests coexisted with atypical sensory behaviours.
Conclusions: Discussion focuses on the issues raised by the pattern of findings that may contribute to our understanding of the developmental trajectory of AS, and thereby to its early detection and treatment.

26 123.24 Early correlates of presence of comorbidity and type of pervasive developmental disorders.
M. Y. Yazgan*[1], S. Unal[2] and S. Yazgan[2], (1)*Marmara Universitesi Tip Fakultesi*, (2)*Guzel gunler saglik hizmetleri*

Background:
Older parents, being first born, greater frequencies of threatened abortion and birth complications, e.g., fetal distress were more frequently reported for **c**hildren with pervasive developmental disorders (PDD), in contrast to healthy controls.
Objectives:
We aimed to investigate perinatal and developmental characteristics of children with PDD in a sample from a clinical specialty setting to see whether these factors were associated with the presence of a comorbidity and the type of PDD.
Methods:
A detailed form inquiring information about the developmental and perinatal history of the child was filled by the parents together with a child and adolescent psychiatrist or a pediatrician, before a diagnosis was established according to the DSM-IV-TR criteria. The sample consisted of 230 children (39 F 191 M) who received diagnoses of autistic disorder (N=144, 25 F 119M), and PDD NOS (N=86, 14 F 72 M).
Results:
A series of logistic regression analysis of the factors perinatal health, and developmental milestones indicated higher significant associations of being in the autistic disorder

group (v. PDD-NOS group) with previous miscarriages (Wald score χ^2=7.9 p<.1), mother's age older at birth (χ^2=4.6 p<.5), the (later) ages of sitting without support (χ^2=4.6 p<.5) and crawling (χ^2=5.9 p<.5). Psychosocial adversities or neuropsychiatric findings (e.g. hypotonia) were not associated with the diagnostic status.
63 of these children also had at least one comorbid disorder, 38 % of the group with comorbidity had a diagnosis of PDD NOS (N=24), and 62 % had definite autistic disorder
Conclusions:
Delays in early motor development, a threat of miscarriage during pregnancy, and older age of mother were associated with being at the more severe end of the autistic spectrum diagnoses. This status was also associated with carrying at least one comorbid diagnosis.

27 123.25 White Matter Integrity in Patients with Autism Spectrum Disorders. D. K. Shukla*[1], B. M. Keehn[1], E. L. Grenesko[1], M. Shen[1], A. J. Lincoln[2] and R. A. Mueller[1], (1)*San Diego State University*, (2)*Alliant International University*

Background:

Autism Spectrum Disorders (ASD) are pervasive neurodevelopmental conditions that are characterized by atypical behavioral profiles including deficits in social reciprocity and communication. Recent MRI studies have shown that white matter tissue is affected in patients with ASD. This may impair the brain tissue connectivity resulting in neurofunctional defects.

Objectives:

The aim of this study was to assess the integrity of whole brain white matter tissue in patients with ASD.

Methods:

Diffusion tensor imaging (DTI) data of 6 children with ASD and 7 typically developing (TD) children was 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. DTI data were analyzed for fractional anisotropy (FA), mean diffusivity (MD), axial and radial diffusion of the whole brain with 80 percent probability for white matter tissue classification. Between group comparisons were performed using Wilcoxon Signed Ranks tests.

Results:

A significant difference between ASD and TD groups was observed for FA, MD and radial diffusion. In the ASD group, FA was significantly lower (0.23 ± 0.5 for ASD versus 0.37 ±0.4 for TD (p=0.3)); mean diffusivity was significantly higher (0.69 ±0.5 versus 0.61 ±0.5 *10^{-3} mm^2/s (p=0.3)), as was radial diffusion (0.60 ± 0.6 versus 0.48 ±0.5 *10^{-3} mm^2/s (p=0.3)). Decreased axial diffusion in the ASD group was non-significant (0.85 ± 0.3 versus 0.88 ± 0.4 *10^{-3} mm^2/s (p=0.17)).

Conclusions:

These results suggest widespread abnormalities in white matter tissue microstructure in patients with ASD. Significantly higher radial diffusion in ASD group may reflect disruption of myelin sheaths responsible for maintaining axonal integrity. Increasing sample sizes in the ongoing study will permit the examination of links between white matter integrity and cognitive performance.

28 123.26 Follow-up at age 11 of children referred with a suspicion af Autism Spectrum Disorders at age 3. M. E. Eriksen*[1], A. Trillingsgaard[2], M. Jørgensen[2], S. S. Pedersen[2], A. Nielsen[3] and E. U. Sørensen[2], (1)*Aarhus University*, (2)*Århus University Hospital, Regional Psychiatric Center for Children and Adolescents, Risskov*, (3)*Taleinstituttet, Århus*

Background:

Early referral and diagnosis of Autism Spectrum Disorder present the clinical practice with the need for more knowledge of developmental course, outcome and early predictors of outcome.

Objectives:

This follow-up study investigate outcome in the form of cognitive abilities, symptom severity and adaptive functioning at age 11 years of children, who under the age of 4 were consecutively referred to at child and adolescent psychiatric clinic with a suspicion of Autism Spectrum Disorders. Early predictors of these outcome measures are also investigated.

Methods:

23 of 30 children were followed up at age 11 years. Following ICD-10 criteria 14 had been diagnosed within the autism spectrum (ASD), while 9 had been diagnosed with another developmental disorder (DD).

Baseline measures were observation in a semi-structured play interaction modelled after the PL-ADOS, the Mullen Scales of Early Developmet and clinical diagnosis.

Follow-up measures were the ADI-R, the Vineland Adaptive Behavior Scale – II, ADOS-G, either a short form of WISC-III, a short form of WPPSI-R or Mullen Scales of Early Development and clinical diagnosis.

Results:

Both groups show a significant increase in cognitive abilities during the follow-up period. The ASD group shows lower cognitive scores, higher degree of autistic symptoms in social interactions and communication, and a comparable level of adaptive functioning. Cross-time correlations are found for cognitive measures and measures of symptom severity. General adaptive level is best predicted by early scores of verbal IQ.

Conclusions:

The follow-up of children referred with a suspicion of ASD shows a positive development in cognitive abilities but continuing difficulties with social interaction, communication and adaptive behaviour. The individual differences in outcome are associated with differences in early measures of cognitive abilities and symptom severity.

29 123.27 PREDICTORS IN OUTCOME OF CHILDREN WITH ASD. A. MiraCoelho*, *Hospital S.João*

Background: It is important to understand what may predict different developmental trajectories of children with ASD in order to improve intervention strategies and prognosis.We examined clinical features of 30 children with ASD,at age 3 ,who were re-evaluated at age 6.

Objectives: Compare outcome for children diagnosed with ASD at age 3 and at age 6,trying to understand predictors for different trajectories,comparing the optimal outcome group and the worse outcome group.

Methods: 30 children diagnosed with ASD at age 3 were re-evaluated 3 years later.They were assessed using the Childhood Autism Rating Scale as a measure of symptom severity and using the Psychoeducational Profile Revised (PEP-R) as a measure of developmental and behavioral profile.

Results:Findings suggest that mainly differences between children who had optimal outcome and children with worse outcome,were noticed in some PEP-R subscales,such as:Imitation;Cognitive Performance;Relating and Affect ;Play and interest in materials

Conclusions:Is difficult to find predictors in ASD but those results may suggest that is possible.Further research is necessary to confirm our findings since they may be important to predict outcome in ASD and to plan intervention priorities.

30 123.28 Regression Histories and Current Cognitive and Adaptive Status in Young Children in the Autism Phenome Project. S. Shumway*[1], A. Thurm[1], F. Van Der Fluit[1], S. Swedo[1], S. Ozonoff[2], C. Zierhut[2], C. McCormick[2] and S. Rogers[2], (1)*National Institutes of Health - National Institute of Mental Health*, (2)*UC Davis M.I.N.D. Institute*

Background: Little is known about the early developmental history and current functioning

in children with autism with a history of regression.

Objectives: This study examined regression in young children enrolled in the Autism Phenome Project, including developmental histories and current cognitive and adaptive status.

Methods: Children with ASD (N=69) and typical development (TD; N=37) from 2-6 years of age were recruited from two sites. The Autism Diagnostic Interview-Revised and Early Development Questionnaire provided early developmental histories. Cognitive measures (Mullen or DAS) and adaptive behavior (VABS) assessed current functioning.

Results: In the ASD group, 35 children had no reported regression (AUT-NR), while 34 children had reported developmental regression (AUT-R): 9 with loss of social communication skills (mean age of loss 18.1 months), and 25 with loss of social communication plus at least 3 spontaneous words (mean age of loss 18.9 months). Findings indicated no difference in age of first concern between AUT-NR and AUR-R groups (approximately 16 months for both groups). Preliminary data on a subset of children suggest that prior to regression, AUT-R showed significantly higher social and communication skills compared to AUT-NR, but lower skills compared to TD. In language, AUT-NR used first words significantly later (22 months) than AUT-R and TD groups (13 and 11 months, respectively). AUT-R and AUT-NR groups used phrases significantly later than TD. Levels of current functioning for ASD groups at a mean age of approximately 4 years revealed no significant differences in cognitive or adaptive functioning. However, differences in language were reported, with 23.5% of the ASD-R group currently using phrase speech daily, compared to 45.7% of the ASD-NR group.

Conclusions: This study contributes to understanding the ontogeny of social and communication skills in children with ASD with and without regression, and how early development and loss may affect later development of language.

31 123.29 Early Identification of Children at Risk for Autism from a Community Sample. D. Childress*[1], J. S. Reznick[1], L. Turner-Brown[1], G. Baranek[2], L. Watson[1] and E. Crais[1], (1)*University of North Carolina at Chapel Hill*, (2)*University of North Carolina*

Background: Substantial gains have been made in understanding the earliest manifestations of autism. Nonetheless, the lack of measures designed to identify infants at risk for developing autism from community based samples presents a challenge for clinicians and researchers.

Objectives: This study was designed to investigate whether infants identified as having elevated scores on the First Year Inventory (FYI), an instrument designed to identify infants at risk for developing autism, continued to show elevated scores at 3-years-old on the Social Responsiveness Scale-Toddler Version (SRS-T). Parental report information regarding developmental concerns and diagnosis information was used as an additional index of child symptoms.

Methods: A community based sample of 1360 families that had completed the FYI when their child was 12-months were mailed the SRS-T and the Developmental Concerns Questionnaire (DCQ) following their child's third birthday. 836 questionnaires were returned. SRS-T summary scores were computed according to the instrument developer's directions. Diagnostic information and parental concerns were recorded from the DCQs. Results: There was a significant relationship between the FYI (12m) and SRS-T (36m) scores ($r=.36$, $p < .0001$), but this relationship is greatly influenced by a substantial number of children with low scores at both time points. 18 children had scores ≥98% on the FYI and 10 children had scores ≥99% on the SRS-T. These numbers include four children that met cut-offs on both instruments: two had parental reports/diagnosis information consistent with autism, one had a diagnosis of sensory processing disorder and one child has issues with language development. Six children met the SRS-T cut-off and not FYI cut-off; of these

four had parental reports/diagnosis information consistent with autism.

Conclusions: An elevated score on the FYI provides a good, though not perfect, index for early screening efforts. Further efforts to refine the scoring criterion may provide better sensitivity and specificity.

32 123.30 The influence of ethnicity and SES on age at diagnosis of autism. E. Troyb*, A. Maltempo, H. Boorstein, T. Dumont-Mathieu, S. Hodgson, M. Barton and D. Fein, *University of Connecticut*

Background: Recently, several studies of Autism Spectrum Disorders (ASD) have proposed that the age at diagnosis of ASD seems to be influenced by socioeconomic status (SES) as well as ethnicity. Moreover, differences have been reported in prevalence rates of ASD across ethnicities.

Objectives: This study examined whether the age of screening, follow-up and diagnosis, as well as prevalence of ASD, vary by ethnicity or SES.

Methods: Children were diagnosed after screening positive on the Modified Checklist for Autistic Toddlers (M-CHAT), a developmental screener designed to identify children at risk for ASD between the age of 16 and 30 months, and screening positive on a follow-up phone interview. Age at screening, follow-up and diagnosis were compared for 33 non-Caucasian children and 125 Caucasian children diagnosed with an ASD. These variables were also compared between high and low SES, as defined by family's yearly household income and parental education level. Prevalence rates of ASD were compared between Caucasian and non-Caucasian children and SES of the families.

Results: An Independent Samples T-Test revealed a significant difference between Caucasian and non-Caucasian children in their age at screening ($Mean_{Cauc}$=714 days, $Mean_{nonCauc}$=763 days, t(156)=1.976, p<.5), age at follow-up ($Mean_{Cauc}$=750 days, $Mean_{nonCauc}$=812 days, t(156)=2.465, p<.5) and age at diagnosis ($Mean_{Cauc}$=800 days, $Mean_{nonCauc}$=895 days , t(156)=3.477, p<.1). No significant differences were found in age at screening, follow-up or diagnosis based on the family's yearly household income or parental education level. No significant differences were found in prevalence rates of ASD based on ethnicity or SES.

Conclusions: Disparities exist between Caucasian and non-Caucasian children in the child's age when screened for ASD, at follow-up and at diagnosis. These differences are not influenced by the SES of the families, but may be the result of cultural dissimilarities in their outlooks on symptoms of first concern or attitudes toward help-seeking.

Poster Presentations Program

124 Human Genetics Posters 2

33 124.1 Visual Attention and Attention Shifting Paradigms: Implications for Social Behavior in Autism and Fragile X Syndrome. R. J. Musci*[1], A. M. Mastergeorge[2], P. Sorenson[3] and C. Day[3], (1)*University of California*, (2)*UC Davis, M.I.N.D. Institute*, (3)*M.I.N.D. Institute*

Background: Autism spectrum disorder (ASD) and fragile X syndrome (FXS) are two related disorders that impact both cognitive development and social development. The current study examined differences and similarities between these two groups that have implications for social communication. Utilizing eye tracking paradigms, visual attention and attention shifting in young children with ASD and FXS were examined. Objectives: The purpose of this study is to examine continuities and discontinuities in the way young children with ASD and FXS attend to social stimuli. Understanding trajectories in gaze shifts and attention shifting can further inform our understanding of these disorders. Methods: Twenty six subjects (13=ASD; 13=FXS) were matched for chronological age as well as mental age on the Mullen Scales of Early Learning. They participated in watching a social interaction excerpt from a live action children's movie. The excerpt depicted social interactions among the characters. Eye tracking excerpts were coded and analyzed for location of gaze and shifting patterns. Results: A series of independent t-test analyses

demonstrated that overall, young children with ASD do not differ in gaze patterns from those individuals with FXS. There were, however, significant differences in the percentage of time spent viewing the face regions of the characters, with children with FXS spending a more significant percentage of time looking at faces in social contexts. Conclusions: The results from this study suggest that key differences between ASD and FXS may be in face processing outcomes. Further investigations should examine similarities and differences in the ways individuals with ASD and FXS process social stimuli. Implications for understanding how visual attention is related to social processes may impact both diagnosis and treatment of these young children.

34 124.2 A Large Scale Study of 7,450 Parents of Children with Autism Spectrum Disorder. C. Foster*, C. Anderson, K. Law and P. Law, *Kennedy Krieger Institute*

Background: A number of studies have focused on family members of children diagnosed with an Autism Spectrum Disorder (ASD). Family studies provide an opportunity for researchers to explore the genetic aspects of ASD, as well as the social/psychological impact of the disorder on family members. Parents serve an important role in ASD-research both as potential research participants and as a source of reliable information.

Objectives: To present preliminary analysis of data from 7,450 parents enrolled in a national online ASD registry and research database.

Methods: In less than 10 months, 7,450 parents consented to participate in the Interactive Autism Network (IAN) registry and research database. Through a series of online questionnaires, parents provided basic data on demographics, educational background, and medical history.

Results: Of the 7,450 parents enrolled in the study, the vast majority (87.3%) are mothers. Mothers also report a higher rate of previous participation in ASD-related research projects (20% versus 12% for fathers). This preliminary report focuses on parental history of language/learning problems and mental health disorders. Key findings include: 25% of fathers and 17% of mothers report a speech/language delay, a learning disability, or having received speech therapy/special education services. 46% of mothers and 22% of fathers report having been diagnosed with or treated for depression. In addition, 26% of mothers and 13% of fathers have been diagnosed with or treated for an anxiety disorder.

Conclusions: Mothers of children with ASD are significantly more likely to enroll in ASD-related research studies, or to report a history of depression or anxiety, when compared to fathers. In contrast, fathers are more likely to report a history of speech or learning issues. Additional research on parents of children diagnosed with ASD may provide further insight into biological and sociological factors related to autism.

35 124.3 Genes Analysed for Association with Autism and DBH Level. L. E. Cochrane*, J. Conroy, K. Tansey, M. Gill, R. Anney and L. Gallagher, *Trinity College Dublin*

Background: Previous studies have shown decreased DBH activity in individuals with autism compared with age-matched controls. This finding was replicated in the Irish Autism sample. Markers in the DBH gene, including rs1611115, were found not to be responsible for the decrease in activity.

Objectives: This study aimed to identify alternative genes within the Dopamine (DA) pathway and those known to interact with DBH, which may exert an influence over DBH expression or activity.

Methods: Tagging SNPs in transcription factors, DA pathway enzymes and two copper transporters known to interact with DBH/ DA pathway were genotyped. Markers were analysed for association with autism using PLINK. QTL analysis was also undertaken to identify markers associated with DBH activity in the proband and unaffected parent samples.

Results: Markers in AKR1A1 (rs2088102, p=0.33), MAO A/B (rs6651806 p=0.46; rs5905512 p=0.47) and ATP7A (rs1062472 p=0.0086, rs17218310 p=0.35, rs17139614

p=0.35) showed association with autism at the single marker level. Haplotypes in AKR1A1, COMT, ATP7A and ATP7B also showed association with autism. In the proband sample, association with DBH activity was seen in COMT (rs740601 p=0.34, rs4680 p=0.12, rs174696 p=0.14), ATP7A (rs17303393 p=0.34) and MAO A/B (rs12843533 p=0.46). In the parent sample, association was seen with markers in ATP7B (rs9526810 p=0.35, rs3825526 p=0.4, rs9568682 p=0.34).

Conclusions: These results further support the role of DA system in autism. Moreover, differences in the regulation of DBH activity and possibly the regulation of the DA pathway as a whole between the affected proband sample and the unaffected parent sample were noted.

36 124.4 IMMUNO PROFILE IN FRAGILE X AND AUTISM. F. Tassone*, P. Ashwood, R. Hagerman and D. Nguyen, *UC DAVIS*

Background: Fragile X syndrome (FXS) is a single-gene disorder with a broad spectrum of involvement and a strong association with autism. Approximately 2 to 6% of children with autism have FXS, and approximately 30% of children with FXS have autism. Altered immune responses have been described in autism and there is potential that in children with FXS and autism, an abnormal immune response may play a role. Indeed, an increased frequency of infections was reported in a subgroup of boys with FXS, especially in early childhood, which may underlie an aberrant or dysfunctional immune response.

Objectives: To delineate specific patterns of cytokine/chemokine profiles in individuals with FXS with and without autism and to compare them with individuals with autism without FXS, and with typical developing controls.

Methods: Age matched male subjects were recruited through the M.I.N.D. Institute and included: 20 subjects with autism, 19 typically developing controls, 64 subjects with FXS without autism and 40 subjects with FXS and autism. Autism diagnosis was confirmed with ADOS, ADI-R and DSM IV criteria. Plasma was isolated and cytokine and chemokine production was assessed by Luminex multiplex analysis.

Results: Preliminary observations indicate significant differences in plasma protein levels of a number of cytokines, including IL-1alpha, and several chemokines, including Eotaxin, RANTES and MIP1alpha, between the FXS group and the typical developing controls ($p<0.5$). In addition, significant differences were observed between the FXS group with autism and the FXS without autism for IL-6, Eotaxin, MCP-1 ($p<0.4$). There were also notable differences between FXS (with and without autism) and autism subjects.

Conclusions:The characterization of an immunological profile in FXS with and without autism may help to elucidate if an abnormal immune response may play a role and help to identify mechanisms important in the etiology of autism both with and without FXS.

37 124.5 A new candidate gene for autism suggested by the co-occurrence of a deletion and a mutation in a child with autism. J. A. S. Vorstman[1], E. Daalen*[1], G. R. Jalali[2], W. G. Staal[1], B. van der Zwaag[1], P. Burbach[1], R. Ophoff[1], R. S. Kahn[1], B. S. Emanuel[2] and H. Engeland[1], (1)*University Medical Centre Utrecht*, (2)*Children's Hospital of Philadelphia, Upenn, Abramson Research Center*

Background: despite the fact that the heritability of autism is thought to be high, replication of genetic linkage and association findings across different studies has been difficult. An alternative to linkage type studies is the analysis of (cyto)genetic abnormalities that co-occur with the autism phenotype, under the assumption of a causal relationship between the genetic abnormality and the autistic phenotype. In some cases, a deletion may "reveal" a recessive variation on the non-deleted allele.

Objectives: we identified an autistic proband with a maternally inherited deletion. Additional studies revealed a non-synonymous polymorphism in one of the genes in the corresponding paternally inherited non-deleted region. Additional murine studies on its expression profile and literature search

support the notion that the gene in question may be relevant to the autism phenotype. Methods: *Phenotyping:* Clinical interview of the proband, his parents and sibs, (DSM-IV interview, the ADI-R and ADOS, and WISC-III). *Genotyping*: Fluorescent-In-Situ-Hybridization and Comparative Genomic Hybridization (550K Illumina-platform), sequencing of genes in the deleted region. Function and expression: Literature search on (putative) function and interaction. RNA In Situ Hybridization during mouse embryogenesis.

Results:

1) The co-occurrence of a deletion involving DIAPH3 and a non-synonymous mutation in the same gene at the non-deleted allele in an autistic proband. While the deletion or mutation are present in his unaffected family members, they never co-occur in the same person.

2) Absence of the DIAPH3 mutation in a screen amongst 128 normal controls.

3) Highly specific expression of DIAPH3 in the developing cortex of the mouse during embryogenesis.

4) Available literature suggests that DIAPH3 is a central gene in the actin polymerization pathway, which is an essential mechanism for neuronal migration.

Conclusions: DIAPH3 is a relevant candidate gene for autism.

38 124.6 Consanguinity of parents of children with PDD: comparison between patients with and without associated medical conditions. N. Gaddour*, S. Gorchen and L. Gaha, *University of Monastir*

Background:

Estimates of consanguineous marriages are relatively high in Tunisia (30 to 34%), leading to a high rate of genetic disorders. Therefore, study of consanguinity may be relevant for the understanding of the genetic transmission of PDD.

Objectives:

To estimate the prevalence of consanguinity among parents of children with Pervasive Developmental Disorders, and to compare it in two groups: children with and without proved comorbid neurological or genetic pathology.

Methods:

Genealogic evaluation have been conducted for families of all consecutive patients of the child psychiatry clinic at the University Hospital F. Bourguiba, Monastir (Tunisia), over years 2003 to 2007, who received a diagnosis of PDD according to DSM IV criteria and to the scales CARS-T and/or PDD-MRS, and for whom a standard neurological and genetic assessment has been obtained (audiometry, EEG, brain imagery, chromosomal formula, screening for innate metabolic disorders and research for fragile X mutations when indicated) (N=186)

Results:

Overall consanguinity rate was 32,8%. It was respectively 44,6% and 28,7% for patients with and without established comorbid medical conditions. No major differences were found in familial histories of mental or language delays between the two groups.

Conclusions:

Parental consanguinity may lead to a higher heritability of pathological traits in neurodevelopmental disorders, and hence to more severe clinical pictures.

39 124.7 ASSOCIATION OF COPY NUMBER VARIANTS IN THE ASMT GENE WITH AUTISM. G. Cai[1], A. Nakamine[1], J. G. Reichert[1], J. M. Silverman[1], C. Betancur[2] and J. D. Buxbaum*[1], (1)*Mount Sinai School of Medicine*, (2)*INSERM U513, Créteil*

Background:Sleep disorders and abnormal melatonin secretion have been reported in autism subjects. Melatonin was also reported effective to treat insomnia in children with autism. The ASMT gene, located in pseudo-autosomal region 1 (PAR1) of the sex chromosomes, is involved in melatonin biosynthesis, and was recently proposed as a susceptibility gene for autism.

Objectives:The goal of this study was to investigate whether copy number variants (CNVs) at the ASMT locus might contribute to autism susceptibility.

Methods:Three hundred unrelated subjects with autism spectrum disorders (ASD) and 248 controls were screened using an MLPA probe directed to the ASMT gene. Fine-mapping of CNVs was performed by quantitative polymerase chain reaction (Q-PCR) probes directed to ASMT exons.

Results:Eighteen unrelated ASD subjects showed microduplications with probes within ASMT. The microduplications were significantly more frequent (p=0.009) in individuals with ASD compared to controls (4 subjects). Three subjects showed four copies of the microduplication. A single microdeletion was observed in an ASD subject, but not in controls. Q-PCR revealed that the CNV includes a ~18 Kb fragment spanning exon 2 to exon 8 of the gene. Typically the microduplication was transmitted (either from the mother or father), but in certain cases did not appear to segregate with affected phenotype amongst siblings. In those individuals for which sleep disorder symptoms were recorded, 75% reported sleep disorder symptoms, compared to about 50% of cases without the duplication.

Conclusions:CNVs in the ASMT gene at PAR1 were found to be associated with ASDs in this study. Further studies on the ASMT gene, the effects of the CNV on gene expression, and the relationship of this CNV to both ASDs and sleep disorders are warranted.

40 124.8 Developmental regression and GABA receptor genes in multiple racial-ethnic groups. M. L. Cuccaro*[1], D. Ma[1], E. R. Martin[1], J. R. Gilbert[1], J. Jaworski[1], R. K. Abramson[2], H. H. Wright[2] and M. A. Pericak-Vance[1], (1)*University of Miami School of Medicine*, (2)*University of South Carolina School of Medicine*

Background: Developmental regression (DR), which occurs in 20-49% of individuals with AUT and may co-exist with seizures, is a potential subsetting variable. The relationship between DR and seizures implicates the GABAergic system, as GABA transmission influences seizure susceptibility. SNPs in GABA receptor genes on chromosome 4 (GABRA4) are associated to AUT in Caucasians (CA) and African Americans (AA). However, the associated SNPs differed in the two racial groups. Objectives: Examine the effect of DR on association to AUT in GABA receptor genes and its significance for understanding observed differences in associated SNPs in AA and CA families. Methods: Using the ADI-R we identified a DR subset (N = 263; 35%) from our overall sample of 606 AUT families (54 AA, 552 CA). DR families were those with positive ADI-R regression scores in an affected individual. Using the pedigree disequilibrium test (PDT) we tested for association in the DR and non-DR subsets in 36 SNPs in GABRA4 and GABRB1. Data were analyzed by race and contrasted with overall findings. Results: In the AA-DR subset (N=17), allelic association (p<.5) was detected for the two SNPs in GABRA4 (rs2280073, rs16859786) previously identified in the overall AA group as well as for two additional SNPs in GABRA4 (rs13151769, rs2351299). In contrast, no SNPs identified in the overall CA group showed association in the CA-DR subset (N=246) although three SNPs (rs17599165, rs1912960, rs17599416) in the overall set remained significant in the CA non-DR complement. Conclusions: Subsetting on DR had an effect on association and may explain the different patterns of associated SNPs in the two racial groups. This is the first study of DR, GABA genes, and AUT. Our results suggest that DR should be explored in other candidate gene studies of AUT and extended to other racial groups.

41 124.9 A submicroscopic 5q11.2 deletion in a child with autism, mild mental retardation and mild facial dysmorphism. H. Peeters*[1], A. C. Crepel[1], K. Devriendt[1], P. De Cock[2], J. R. Vermeesch[1] and J. P. Fryns[1], (1)*Center for Human Genetics, University of Leuven*, (2)*Center for Developmental Disorders*

Background: Array-CGH is nowadays considered to be an essential aspect of the genetic analysis of patients with syndromic autism spectrum disorders (ASD) since in comparison to screening by cytogenetic methods, it allows to detect chromosomal

imbalances at a higher resolution. These chromosomal imbalances (deletions or duplications) appear to be present in about 25% of patients with syndromic ASD.

Objectives: The detection of novel chromosomal imbalances may allow the delineation of new contiguous gene syndromes associated with ASD and may allow for the identification of new ASD genes.

Methods: 1-Mb array CGH was used as a screening method. The deletion was confirmed by fluorescence *in situ* hybridisation, the duplication by means of qPCR.

Results: We report on a female patient with autism, mild mental retardation, mild facial dysmorphism and a submicroscopic 5q11.2 deletion. This deletion of approximately 8 Mb in size is flanked by the clones CTD-2276024 and RP11-210O14. In addition, a 2Mb duplication on Xp22.31 (RP11-483M24->RP11-323F16) was detected. Interestingly, a similar but possibly slightly smaller deletion on 5q11.2 has previously been described in a boy with profound speech delay, obsessional play and echolalia (K Prescott et al. 2005). In contrast to the patient we describe, this boy presented additional malformations like a cardiac defect (tetralogy of Fallot), a bifid uvula, velopharyngeal insufficiency and short stature.

Conclusions: Since autistic behaviour is the only consistent finding in 2 patients with a similar deletion 5q11.2, the location of this deletion may identify a gene that is implicated in autism spectrum disorders.

Prescott K, Woodfine K, Stubbs P, Super M, Kerr B, Palmer R, Carter NP, Scambler P. A novel 5q11.2 deletion detected by microarray comparative genomic hybridisation in a child referred as a case of suspected 22q11 deletion syndrome. Hum Genet. 2005 Jan;116(1-2):83-90.

42 124.10 Autism sibling pair discordant for 22q11 microdeletion. S. Guter*, J. Salt and E. H. Cook, *Institute for Juvenile Research*

Background:

Autism is a complex genetic disorder. The precise relationship between autism and 22q11 deletions (VCFS) is still under investigation.

Objectives:

We report the case of a sib-pair diagnosed with autistic disorder that were discordant for a 22q11 microdeletion upon genetic analysis.

Methods:

The siblings (one male, one female) met ADI-R and ADOS criteria for autism classification. They received a DSM IV best estimate diagnosis of Autistic Disorder using the ADI-R, ADOS, Vineland Scales and cognitive testing. The affected female presented with facial dysmorphic features characteristic of VCFS. This led to FISH testing using a probe corresponding to the VCFS region on chromosome 22.

Results:

These studies revealed the loss of the VCFS critical region in this patient consistent with 46,XX.ish del(22)(q11.2q11.2)(TUPLE1-). Array comparative genomic hybridization using a 19k human BAC microarray was performed on the proband, brother, and her parents and confirmed a deletion of 22q11.2 only in the female proband.

Conclusions:

Microdeletion discordance in this sib-pair is consistent with other recent reports of microdeletion in autism. As the 22q11 mutation was not inherited from a parent, but is de novo in the child, we would not expect to see concordance for the deletion, unless there was parental post-zygotic mosaicism. If females have a higher dosage threshold for the development of autism then it's feasible that the 22q11 del in our female patient is a variant that contributes to her phenotype being as severe as her brother, assuming that they shared other risk variants. Alternatively, the siblings could have independent risk variants of major effect. It is likely that the heterogeneity of autism will include common variants of weak effect and rare variants ranging from weak to strong effects. It is also

likely that many individuals and families will have combinations of such variants.

43 124.11 MicroRNA expression profiling in autism: noncoding RNAs and autism susceptibility gene identification. Z. Talebizadeh*, M. F. Theodoro and M. G. Butler, *Children's Mercy Hospital and University of Missouri-Kansas City*

Background: An estimated 98% of the transcriptional output in humans and other mammals are consisted of noncoding RNAs (ncRNAs) that do not code for protein but have other functions in cells. Two main groups of ncRNAs are microRNAs and snoRNAs. MicroRNAs are small RNA molecules containing approximately 22 nucleotides that regulate the expression of genes by binding to the 3'-untranslated regions of specific mRNA directing translational repression or transcript degradation. Despite growing evidence for regulatory influence of ncRNAs in gene expression, particularly in brain function, this group of regulatory factors has not been evaluated in autism spectrum disorders.

Objectives: To understand the role of microRNAs in the etiology of autism.

Methods: We evaluated global expression profiling of 470 mature human microRNAs in lymphoblastoid cell lines from 6 subjects with autism compared with 6 matched controls using microarray technology and quantitative RT-PCR. Samples were ascertained from the Autism Genetics Resource Exchange (AGRE).

Results: Differential expression (either higher or lower) for 9 of the 470 microRNAs (i.e., miR-132, miR-23a, miR-23b, miR-146a, miR-146b, miR-663, miR-363, miR-92, and miR-320) was observed in our autism samples compared with controls. Potential target genes for these microRNAs were identified using publically available programs: PicTar, TargetScan, and miRanda. There were several genes of neurological interest, particularly for autism, among the predicted targets for these 9 microRNAs. Our results suggest that autism candidate genes are overrepresented as targets amongst the differentially expressed microRNAs compared to a randomly selected set of microRNAs.

Conclusions: Overall, our study suggests that evaluation of microRNA expression may have potential in identifying pathways implicated in autism. To detect the impact of specific microRNA misregulation on the expression level of their target genes, a more detailed experimental design is needed to correlate microRNAs and mRNAs expression levels in an expanded number of subjects.

44 124.12 Serotonin Related Genes in Autism. J. Haines*[1], B. M. Anderson[1], N. Schnetz-Boutaud[1], M. L. Summar[1], J. Bartlett[1], M. L. Cuccaro[2], J. Gilbert[3] and M. Pericak-Vance[3], (1)*Center for Human Genetics Research*, (2)*University of Miami School of Medicine*, (3)*Miami institute of human genomics*

Background: Autism is a severe neurodevelopmental disorder with a strong genetic component. Despite numerous genome screens and individual candidate gene studies, the underlying genetic etiology remains largely unknown. Increasing evidence suggests that autism is more genetically complex than previously thought, and that single gene approaches toward dissecting autism genetics may not be informative. We are taking the alternative approach of testing for interactive effects of multiple genes within the serotonin pathway.

Objectives: To test serotonin related genes for association with autism.

Methods: We tested 75 SNPs within 13 different genes related to serotonin including TPH1, TPH2, HTR1A, HTR2A, HTR3A, SLC6A4, SLC7A5, YWHAZ, and DDC. SNPs were chosen to represent the linkage disequilibrium patterns across each gene, and included when possible common coding variants. The dataset consists of 151 multiplex families and 252 parent-child trios collected at two centers in the southeast United States. Initial analyses included single locus family-based association tests, considering both parental and proband gender. Subsequent analyses examined explicitly for gene-gene interactions using multifactor dimensionality reduction (MDR). Results: Single locus analyses generated marginally significant results for YWHAZ and HTR3A, however, only the HTR3A result

survives correction for multiple comparisons. Preliminary two-way interaction analysis with MDR did not identify any significant interactive effects; higher-order interaction analyses are ongoing.

Conclusions:

The HTR3A result is interesting and suggests at least a modest effect of this gene on autism. The lack of a strong two-locus interactive effect suggests that either interactions among these genes do not exert a strong effect on autism, or the effect requires a higher order interaction.

45 124.13 Rare Mutation Burden of the Contactin Pathway in Autism Spectrum Disorders. B. J. O'Roak*[1], B. Bakkaloglu[2], A. Louvi[1], C. Mason[1], A. R. Gupta[1], N. R. Davis[1], T. M. Morgan[3], M. T. Murtha[1], A. G. Ercan-Sencicek[1] and M. W. State[1], (1)*Yale University School of Medicine*, (2)*Hacettepe University*, (3)*Washington University School of Medicine*

Background: Autism spectrum disorders (ASD) have a largely unknown complex genetic etiology. We have characterized patients de novo chromosomal abnormities to identify candidate genes that confer risk for idiopathic ASD. We identified patients with de novo abnormities disrupting CNTNAP2, CNTNAP4, and Contactin 4 and ASD and/or developmental delay (Fernandez et al. 2004, Bakkaloglu et al. 2008, and unpublished results). Additionally, frame-shift mutations have been identified in CNTNAP2 in a recessive syndrome characterized by intractable seizures, mental retardation, and ASD (Strauss et al. 2006). We have also identified putatively functional variants at CNTNAP2 in ASD patients (Bakkaloglu et al. 2008). These data suggest that defects in a contactin pathway may confer risk for ASD. Objectives: I. To determine the burden of rare deleterious variants in the contactin pathway among ASD cases and controls. II. To test the functionality of identified variants. Methods: I. Using homologies and known interactions, a contactin pathway was determined (~40 genes). Next-generation sequencing and copy number analysis will be used to analyze mutation burden in a large case-control study. The rate of rare unique variants will be compared. II. CNTNAP2 variants were cloned into expression vectors. Vectors were then injected into chick spinal cords, electroporated, and examined for defects in neuron morphology. Results: Sequencing and copy number analysis are currently being performed on the contactin pathway. Variants have been cloned and are now being tested in our functional assay. Conclusions: Rare likely functional variants are present at CNTNAP2 in ASD cases. Our results indicate that this risk is likely moderate and will require large sample sizes to confirm these findings. Results on additional members of the contacin pathway are forthcoming. Analysis of the contactin pathway may provide valuable insights into the pathophysiology of ASD.

46 124.14 Genomic Imprinting of the X-Linked Gene Transketolase-like 1 in Mouse and Human. A. M. I. Nesbitt*, M. J. O'Neill and J. J. LoTurco, *University of Connecticut*

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.

47 124.15 Peripheral Blood Gene Expression Profiling of Autism Spectrum Disorders. C. D. Collins*[1], S. W. Kong[1], M. Galdzicki[1], D. Stephan[2], H. Peters[1], S. J. Brewster[1], I. A. Holm[1], R. J. Hundley[1], E. M. Hanson[1], L. A. Rappaport[1], L. M. Kunkel[1] and I. S. Kohane[1], (1)*Children's Hospital Boston*, (2)*Translational Genomics Research Institute*

Background: Preliminary work shows the ability to assess neuropsychiatric illnesses such as schizophrenia and Alzheimer's disease using blood gene expression profiles. We hypothesize that peripheral blood might serve as a surrogate marker for gene expression in the developing central nervous system of individuals with autistic spectrum disorders (ASD).

Objectives: To identify molecular signatures in gene expression profiles of peripheral blood from individuals with ASD.

Methods: Blood gene expression profiles of 256 ASD and control samples from Children's Hospital Boston (CHB) and the Translational Genomics Research Institute (TGEN) were analyzed with a machine learning method, Support Vector Machine (SVM). We used a dataset from one institution to build a predictor and tested the other set to validate the accuracy of the predictor.

Results: The comparison of differentially expressed genes from CHB and TGEN revealed a signature of 25 genes (16 up-regulated, 9 down-regulated) in common (nominal p-value < 0.001). Using these 25 genes, we were able to predict ASD with an accuracy of 67% when the predictor was built with the TGEN dataset and tested on the CHB dataset, and 78% when the predictor was from CHB and tested on the TGEN dataset. Interestingly, geneset analysis showed several perturbed pathways such as dendrite morphogenesis.

Conclusions: Blood gene expression profiling predicts ASD with relatively high accuracy, and shows possibility of surrogate biomarker to aid accurate and early diagnosis of ASD as well as providing interesting clues to disease process.

48 124.16 The STX1A, CYLN2, and GTF2i genes in autism-associated 7q11.2 microduplication syndrome as candidate genes for Autism Spectrum Disorders. P. Malenfant*[1], X. Liu[1], M. L. Hudson[1], Y. Qiao[2], J. M. Hildebrand[2], I. L. Cohen[3], A. Chudley[4], C. Forster-Gibson[1], S. M. E. Lewis[2], E. Rajcan-Separovic[2] and J. J. A. Holden[1], (1)*Queen's University*, (2)*University of British Columbia*, (3)*NYS Institute for Basic Research in Developmental Disabilities*, (4)*University of Manitoba*

Background: Microdeletions of 7q11.23 are relatively common and associated with the Williams-Beuren Syndrome (WBS), whereas duplications of this region have recently been reported in association with Autism Spectrum Disorders (ASDs) or autistic-like behaviours (Berg et al, 2007).
Objectives: To test candidate genes within 7q11.23 for association with autism using family-based and case-control approaches and to screen a large number of individuals with ASDs for 7q11.23 duplications and deletions.
Methods: Markers within three of the duplicated genes, *STX1A, CYLN2*, and *GTF2i* were genotyped using validated custom TaqMan SNP Genotyping Assays on an ABI Prism 7900HT. Both real-time quantitative PCR

(RTqPCR) and CGH-array were used to screen for microdeletions/microduplication in more than 900 subjects with ADOS/ADI-R-confirmed ASD. RTqPCR was used to refine the breakpoints in one identified case.
Results: The *STX1A, CYLN2*, and *GTF2i* genes were selected based on their function and tested for association with ASDs using 10 SNPs. Haplotype transmission disequilibrium testing revealed a modest over-transmission of one haplotype in each of the three genes tested (P = 0.16, 0.33 and 0.32, respectively) as well as of one 10-marker haplotype (P = 0.32). A single duplication of chromosome 7q11.23 was found in an individual with confirmed ASD, apraxia, intellectual disability and minor craniofacial dysmorphism. The breakpoints (72.37Mb and 73.80Mb) were localized to the flanking low-copy repeats that predispose to the genomic instability characteristic of the 7q11.23 deletion observed in the majority of WBS cases.
Conclusions: Association testing implicates one or more of the genes within the WBS critical region in the etiology of some cases of ASDs. The identification of a single case of the duplication among 913 individuals screened indicates that genomic rearrangements of 7q11.23 are not a common cause of ASDs.

49 124.17 Analysis of Copy Number Variation within GABRA4. H. N. Cukier*[1], M. Y. Rayner[1], D. Ma[1], H. H. Wright[2], R. K. Abramson[2], J. P. Hussman[3], J. L. Haines[4], M. L. Cuccaro[1], D. L. Hedges[1], J. R. Gilbert[1] and M. A. Pericak-Vance[1], (1)*University of Miami*, (2)*University of South Carolina School of Medicine*, (3)*Hussman Foundation*, (4)*Center for Human Genetics*

Background: Autism has a strong genetic component but studies over the past decade have demonstrated that the underlying genetics are complex. Previous studies suggest an important role for copy number variants (CNVs) in autism risk and indicate a strong association of *de novo* copy number mutations with autism. The *GABRA4* gene is implicated in autism risk through both cytogenetic alterations in autism patients in the GABR chromosome 4p region and through association with SNPs in the *GABRA4* gene in autistic families. These data point to *GABRA4* and potentially other GABR genes in this region as autism candidate genes.

Objectives: To examine the *GABRA4* gene for possible disease associated CNVs within or near the *GABRA4* gene.

Methods: Using DNA collected from 428 autism family probands and 190 controls, we performed quantitative real-time PCR (qPCR) with unique probes located within or near the *GABRA4* gene spanning an area of almost 100 kb to identify the presence of duplications and deletions. We used qPCR of *RNAse P* as an internal control to measure deviation from diploid copy number. Results were compared across assays to gauge the approximate CNV size.

Results: Preliminary results showed putative CNVs in *GABRA4* in 75 individuals (17.5%). 14 of these individuals (3.3%) were found to have deletions, 49 (11.4%) appear to carry duplications and 12 individuals (2.8%) have potentially complex rearrangements in the region. Evaluation of the same region in the 190 control individuals showed only 4 individuals with CNVs (2.1%), 2 with deletions and 2 carrying duplications.

Conclusions: Our preliminary results suggest that a larger number of both deletions and duplications occur within *GABRA4* in autism probands when compared to controls, suggesting a role in autism etiology. Validation studies are in progress as well as examination of segregation of the variations with disease status in multiplex families.

50 124.18 Chromosome 17q21.31 Microdeletion in a Patient with Autism. D. Moreno De Luca[1], A. Gennetier[1], F. Devillard[2], V. Ginchat[2], B. Assouline[3], C. Gillberg[4], M. Leboyer[5] and C. Betancur*[1], (1)*INSERM U513*, (2)*Grenoble University Hospital*, (3)*Saint Egrève Hospital*, (4)*Göteborg University*, (5)*Henri Mondor and Albert Chenevier Hospitals*

Background: Recent findings suggest that microdeletions/microduplications of chromosomal regions involved in mental retardation also play an important role in

autism. A new 17q21.31 microdeletion syndrome, caused by non-homologous recombination mediated by low copy repeats, was recently described in 11 individuals after screening large cohorts of patients with mental retardation. The subjects had overlapping deletions between 500 kb and 650 kb and they all had developmental delay, hypotonia and characteristic facial features.

Objectives: The purpose of this study was to ascertain the involvement of 17q21.31 microdeletions in autism by screening a large group of patients with autism spectrum disorders.

Methods: A total of 374 patients with an autism spectrum disorder belonging to 305 families recruited by the Paris Autism Research International Sibpair (PARIS) study were screened for deletions and duplications associated with mental retardation syndromes using multiplex ligation-dependent probe amplification (MLPA). Positive findings were confirmed with quantitative PCR.

Results: We identified one patient with a microdeletion at 17q21.31. Characterization of the breakpoints with qPCR showed that the deletion had an approximate size of 700 kb, and comprised six known genes, including MAPT and CRHR1. The deletion was not present in the mother; the father was deceased and no DNA was available. The girl had delayed motor and speech development, as well as mild dysmorphic features similar to the ones described previously, including long face, blepharophimosis, bulbous nasal tip, broad chin and long fingers. At 11 years of age, she fulfilled diagnostic criteria for autistic disorder and had a global IQ of 40.

Conclusions: This is the first report of a 17q21.31 microdeletion associated with autism. Although the prevalence appears to be low, this observation adds to the increasing list of genomic disorders involved in the etiology of autism.

51 124.19 Autism open biological resource of Fondation Autisme. M. Ferguson*[1], C. Stranieri[1] and S. Briault[2], (1)*Fondation Autisme*, (2)*Inserm*

Background:

The French Fondation Autisme, a community-based and advocacy French group, has created an autism and pervasive developmental disorders phenotypic and genetic repository.

We want to present this international program that is primarily a resource and not a research project per se.

Objectives:

The FAAV autism phenotypic registry and genetic repository has been established with the

aim of generating an extensive collection of simplex or multiplex families with autism, totally

compatible with A.G.R.E. resource.

The scientific goal of the phenotypic and genetic resources is to identify genes

involved in susceptibility to autism, and to understand the gene relationship to clinical outcome, in order to provide a better clinical intervention for autistic individuals.

This resource is available for the entire scientific community.

Methods:

The phenotypic evaluations are based on DSM-IV diagnosis and ADI-R interview.

These minimal evaluations allow uniform and research-reliable data. Phenotypical data are collected under anonymous status according to the French law and ethical bills to protect individuals.

DNA, cell lines and serum repository are housed by GENETHON which have a huge experience of biological repository for a variety of diseases. Validation : all the protocols and the good practice rules, including the parental agreement forms, have been validated by the French ethical council on 10th October, 2005.

Results:

We have today at the disposal of the entire scientific community pedigrees of 130 families, 550 individual samples of DNA, cell lines and

serum available(mother, father, affected child and siblings), we are in the process of finishing collecting DNA, cell lines and serum from 550 engaged families as well as phenotypes.

Conclusions:

Any researcher interested in using the French open biological resource can contact : Fondation Autisme, 25 Boulevard Pasteur, 75015 Paris, Phone : (00 33) (0) 1 47 83 20 23

www.fondation-autisme.org

contact@fondation-autisme.org

52 124.20 Craniofacial Dysmorphology in Autism: Embryologically-derived Measures. C. Deutsch*[1], A. Hunt[2] and L. Farkas[3], (1)*Shriver Center and McLean Hospital, Harvard Medical School*, (2)*Shriver Center*, (3)*Hospital for Sick Children*

Background: Several laboratories, including ours, have reported excessive craniofacial dysmorphology in autistic disorders. The presence of dysmorphology in a brain-based disorder is plausible, given the closely linked embryologic heritage of craniofacial and brain morphogenesis. Here, we adopt reliable quantitative methods to measure dysmorphology and apply embryologic principles to render these phenotypes biologically interpretable.
Objectives: We have applied these methods to the study of subjects with autism who have limited verbal abilities, comparing them to a group of typically-developing subjects.
Methods: We applied the Deutsch and Farkas dysmorphology protocol from the North American atlas *Anthropometry of the Head and Face*, measuring 11 subjects with autism and 22 matched typically-developing subjects. Individuals with known craniofacial syndromes were excluded from this analysis. Quantitative craniofacial measurements were conditioned on age, gender, and ethnicity, using the atlas' extensive normative database. Our approach is to examine combinations of anomalies chosen to reflect developmental factors. Here, we report on two embryologically derived classes: mechanism of alteration (malformations, primary errors of morphogenesis; and deformations, caused by mechanical constraint), and Anlagen derivatives (embryologic primordia forming the face and head: frontonasal, maxillary, and mandibular).
Results: Malformations were excessive in autism relative to the typically-developing group ($p < .5$); in contrast, deformations were not overrepresented (n.s.). There was also a marked excess of frontonasal anomaly scores ($p < .2$) in the autism group, but not of maxillary and mandibular anomaly scores (n.s.).

Conclusions: Using these objective, reliable measures, we determined that there was excessive dysmorphology in an autistic sample characterized by limited verbal abilities. There was a preponderance of malformations, as well as anomalies arising from frontonasal prominence derivatives. These findings may find application in studies of the pathogenesis of autism, potentially revealing more homogeneous subgroups with respect to etiology.

53 124.21 Association of the homeobox transcription factor gene ENGRAILED 2 (EN2) with autistic disorder in Chinese children. F. W. Lung[1], J. Hallmayer*[2], P. Yang[3], B. C. Shu[4] and L. C. Lee[5], (1)*Kaohsiung Armed Forces General Hospital*, (2)*Stanford University*, (3)*Kaohsiung Medical University*, (4)*National Cheng Kung University*, (5)*Johns Hopkins Univ. School of Public Health*

Background: Autism is a neurodevelopmental disorder with a strong genetic component. Previous studies have mapped the disease to chromosome 7q, where the homeobox transcription factor ENGRAILED 2 (*EN2*) gene is located. *EN2* is specifically involved in patterning the region that gives rise to the cerebellum.Objectives: In present work, we carried out a case-control study to determine whether two intronic SNPs of *EN2* is a susceptibility to autism in a Han Chinese population.

Methods: The participants included 190 cases of DSM-IV-TR diagnosed autistic disorder, and

918 controls of unrelated healthy volunteers recruited from community. Three single nucleotide polymorphisms (SNP) (rs3824067, rs1861972, rs1861973) at the *EN2* gene that have been reported to be associated with autism underwent analysis among our studied cohorts. Both UNPHASE and PHASE statistical programs were utilized for evaluating the association of *EN2* SNPs to autism base on allelic, genotypic frequencies and haplotype compositions accompanied with goodness of fit method of Chi-square test.

Results: Both allelic and genotypic distributions of three polymorphisms were concordant to Hardy-Weinberg equilibrium. Significant differences were found for case vs. community and overall controls. Three-marker haplotype A-A-C of *EN2* was identified to have a protective effect for the autism by using UNPHASE (OR=0.23) and PHASE (OR=0.36) programs, indicating the racial difference might confound for *EN2* association with autism.

Conclusions: Therefore, more *EN2* gene association studies of Han Chinese populations are warranted to confirm this finding.

54 124.22 Network oriented variant analysis of the serotonin transporter regulome. N. G. Campbell, E. Crawford, R. Game, R. D. Blakely and J. Sutcliffe*, *Vanderbilt University*

Background: Autism has a predominantly genetic etiology but one characterized by substantial heterogeneity. Heritable hyperserotonemia in ~30% of cases points to dysregulation of serotonin being an important clue to genetic liability in autism. We have described rare serotonin transporter (SERT) coding variants that confer a gain-of-function and are associated with autism and related disorders showing rigid-compulsive behaviors. Objectives: We hypothesize that loci encoding molecules regulating SERT harbor alleles conferring risk for autism. We examined loci for the A3 adenosine receptor (ADORA3), 5-HT1B receptor (HTR1B), neuronal nitiric oxide synthase (NOS1), and syntaxin 1A (STX1A) for evidence of autism related alleles. Methods: To test for allelic associations, tag SNPs representing common haplotypes (>5%) and coding polymorphisms were genotyped in a sample of 940 autism families. Preliminary resequencing analysis was performed using a panel of unrelated autism probands to identify novel variants in transcribed and potential regulatory regions. Results: Preliminary association studies suggest that common alleles at the ADORA3 and HTR1B loci are not significantly associated with autism. One marker (rs9654749) within STX1A shows nominally significant association. NOVA has identified several synonymous and nonsynonymous variants in these SERT regulome genes ADORA3 and NOS1. While control sequencing is ongoing, genotype analysis of one ADORA3 and two NOS1 novel coding variants suggests that they are not disease-related. Conclusions: Despite the absence of strong association or disease-causing variants in these initial studies, further examination of the SERT regulatory network hypothesis is warranted. Additional allelic association and resequencing studies including controls where appropriate are ongoing to address disease susceptibility within these genes.

55 124.23 HLA-DR4 as a Risk Allele for Autism, Acting in Mothers of Probands During Pregnancy. W. G. Johnson*[1], S. Buyske[2], A. E. Mars[1], M. Sreenath[1], E. S. Stenroos[1], R. Stein[3] and G. Lambert[1], (1)*UMDNJ - Robert Wood Johnson Medical School*, (2)*Rutgers University*, (3)*Harvard University*

Background: Previous studies of *HLA-DR* alleles in autism have consistently shown increased frequency of *HLA-DR4* in autism probands and mothers but not fathers. However, this has been documented only in case-control studies and not by a more robust study design to determine whether *HLA-DR4* might act in mothers to contribute to autism in their offspring.
Objectives: To determine whether *HLA-DR4*, acting a mother during pregnancy, contributes to the autism phenotype in her affected offspring.
Methods: We genotyped *HLA-DR* alleles in members of 34 families with parents and maternal grandparents whose autism proband was tested by ADOS-WPS and ADI-R. Analysis was by standard transmission/disequilibrium testing (TDT). The present study had 80%

power to detect an odds ratio of 3.6. The present families were all from New Jersey, and their number was similar to those from geographically defined areas in the earlier studies of autism and *HLA-DR4*.
Results: Significant transmission disequilibrium for *HLA-DR4* was seen (p=.0076; Odds Ratio 4.67 [OR], 95% confidence interval of OR 1.34, 16.24) for transmissions to mothers of autism probands from maternal grandparents, supporting a role for *HLA-DR4* as an autism risk factor acting in the mothers. To examine an additional explanation, that *HLA-DR4* is a risk allele in probands due to maternal imprinting and mothers are necessarily enriched for *DR4*, we did a secondary TDT test with probands and parents. Transmission disequilibrium was not seen for *HLA-DR4* transmissions from parents to probands or from mothers to probands.
Conclusions: Thus, *HLA-DR4* (or a closely linked gene) may act in mothers of probands during pregnancy to contribute to autism in their offspring. Further studies are required to confirm these findings.

Poster Presentations Program

125 Social Function Posters 1

56 125.1 VALIDATING THE STRESS SURVEY SCHEDULE FOR PERSONS WITH AUTISM AND OTHER DEVELOPMENTAL DISABILITIES. M. Goodwin*[1], J. Groden[1], W. F. Velicer[2] and A. Diller[1], (1)*The Groden Center, Inc.*, (2)*University of Rhode Island*

Background:

Despite a growing appreciation for the role stress plays in the behavior of persons with autism, little work has been done to develop tools that assess reactions to stressors in this population.

Objectives:

To validate the Stress Survey Schedule for Persons with Autism and Other Developmental Disabilities (SSS; Groden et al., 2001) in a large sample of individuals with autism, varying in gender, verbal ability, and age.

Methods:

86 staff (22 men and 64 women) ranging in age from 20 to 52 years (*M* = 27.2) rated the perceived intensity of reactions to each of the 49 items on the SSS for clients with whom they were familiar. The 180 individuals with DSM-IV diagnoses of autism being rated (142 males and 38 females) ranged in age from 3 to 41 years, with a mean age of 17.4 years. Of the 180 individuals, 128 (71%) were reported to be verbal and 52 (29%) nonverbal.

Results:

One-way MANOVAs, univariate ANOVAs, Tukey tests, and effect size estimates (h^2) were computed to evaluate whether there were group differences on mean stress scale scores for the overall sample as a function of gender, verbal ability, or age group. There were no differences in any of the eight stress scale scores for males and females. There were moderately large differences in two stress scales, *Unpleasant* and *Pleasant Events*, for verbal and nonverbal persons. There were also moderately large differences in mean stress scale scores for *Anticipation/Uncertainty*, *Sensory/Personal Contact*, and *Food Related Activity* as a function of age.

Conclusions:

The SSS was able to identify dimensions of stressors that are perceived to be the most and least stressful for subgroups of persons with autism, suggesting that the SSS is a valid tool for assessing perceived stress reactions in persons with autism.

57 125.2 Utilizing Social Stories for Behavior Change in Preschoolers with Autism. L. A. Wright* and R. McCathren, *University of Missouri*

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

intervention on the social behavior of 4 young children with autism. The following research questions were addressed:
In preschoolers with diagnoses of autism:
(1) Does the Social Story intervention increase pro-social behavior and decrease problem behavior?
(2) Do the social behavior rates approach those of age and gender-matched typically developing peers?
(3) Are the effects of intervention maintained over a one month period?
(4) Do teachers support the social validity of Social Stories?
Methods: This study used a multiple-baseline across participants design to evaluate the effects of the Social Story on the pro-social and problem behaviors of the participants in comparison to gender and age-matched peers in the inclusive preschool classroom.
Results: The results of this study indicate that the Social Story was effective in increasing pro-social behavior rates in 3 of the 4 participants. None of the participants reached the pro-social behavior rates of age and gender-matched peers, though one child's pro-social behaviors exceeded the rate of peers on three occasions. The problem behaviors of all 4 participants decreased with the intervention. Maintenance of skills over a 1-month period was demonstrated for all of the participants.
Conclusions: The present research adds to the current small though growing literature base in support of the use of Social Stories. Due to the call for scientifically based research in the classrooms, this study contributes to the support of Social Stories as an evidence-based practice for recommended use by practitioners in the field.

58 125.3 MEASUREMENT OF PEER INTERACTION IN SCHOOL AGED CHILDREN WITH HFA. C. Koning*, J. Magill-Evans and J. Volden, *University of Alberta*

Background:
Peer interaction in children with ASD may be measured using parent/teacher report and/or direct observation. Parent and teacher reports may provide a biased overview of general skills while direct observation in natural settings is challenging and often affected by a lack of interaction opportunities. The Autism Diagnostic Observation Schedule measures only social interaction with an adult. As part of a multi-method assessment of social skills, a standardized measure of peer interaction in a simulated situation was developed to measure the skills a child with ASD already uses as well as the effects of social skills intervention.
Objectives:
This poster describes the initial development of an observational measure of peer interaction for children with high-functioning autism (HFA) or Asperger Syndrome (AS). The aim is to provide a "standardized" peer interaction scenario which allows the researcher to observe the child's ability to initiate and respond appropriately to peer interaction.
Methods:
Sixteen boys with HFA or AS aged 10-12 will participate in a waiting room scenario lasting about 10 minutes. A paid child actor, playing a hand-held video game, sits in a waiting room where the child with ASD is sent to wait. The actor follows a script outlining opportunities to initiate interaction and responses to potential overtures. Interactions are videotaped and then scored from the video according to a coding protocol.
Results:
Inter-rater reliability based on coding from videotape is reported. Scores on the scenario and correlations with measures of social perception (Child and Adolescent Social Perception measure), social responsiveness (Social Responsiveness Scale), social interaction (Vineland), and pragmatic language (Children's Communication Checklist and Test of Pragmatic Language) will address preliminary validity.
Conclusions:
This measure of peer interaction provides an innovative, socially valid measure of peer interaction using a "standardized" situation intended to produce social initiations and maintenance of conversations.

59 125.4 AN INVESTIGATIVE STUDY INTO THE EFFECTS OF REGULAR EDUCATION TEACHER ATTITUDES ON THE SUCCESSFUL INCLUSION OF STUDENTS WITH ASPERGER SYNDROME PLACED IN REGULAR EDUCATION CLASSROOMS IN

NEW SOUTH WALES. C. Little*, *University of Sydney*

Background: In the past, students with autism tended to be segregated from their peers. The trend in Australia appears to be similar to that of the United States in that there now appears to have been an increasing trend towards the inclusion of children with autism in regular education settings as part of the movement towards including all students with disabilities in regular education. Currently, in NSW schools, students with an Autistic Spectrum Disorder (ASD), including Asperger Syndrome (AS), are catered for in both regular education (general) and special education settings.

Objectives: As part of a Doctoral thesis investigating the effects of mainstream teacher attitudes upon the successful placement of students identified as having AS into regular education classrooms in NSW schools, a pilot study was implemented with 30 regular education teachers. This pilot was used to test the integrity and applicability of a specifically developed questionnaire designed to identify attitudes which supported success of AS student placement in regular education classrooms in NSW schools. It sought to identify what teacher factors influence the successful inclusion of these students into regular classrooms? Are these results indicative of what research has identified in other countries? Are critical features identified which require further investigation?

Methods: Teacher attitudes were obtained through a specifically designed questionnaire composed of 20 closed-question items answered on a Likert scale response format, and 5 open-ended items which required a more detailed response to the major themes targeted within the research.
Results: Items such as involvement in student placement, teacher training, whole school support, peer support for student, teacher confidence and positive approach, previous special education experience and understandings between academic and social inclusion were all identified to varying degrees as impacting upon successful placement.
Conclusions: Following analysis of the data, results are presented both graphically and in formal discussion.

60 125.5 Contribution of executive function to participation in school activities of children diagnosed with HFA ages 6-9. C. Zingerevich*[1] and P. D. LaVesser[2], (1)*Rady Children Hospital San Diego*, (2)*Washington University*

Background: A growing number of children diagnosed with high functioning ASD are attending the regular education system, and facing difficulties to take part in school activities. This study is looking at the executive functions of elementary school aged children with high functioning ASD related to participation in the school setting.
Objectives: 1) to describe the components of executive functions in children with ASD, as measured by the Behavior Rating Inventory of Executive Function (BRIEF) and the Wisconsin Card Sorting Test (WCST). 2) to examine the relationship between executive functions, sensory processing as measured by the Sensory Profile, and participation in school activities of children with high functioning ASD, as measured by the School Function Assessment (SFA), and 3) to determine the relative contribution of executive functions to participation in school activities of children with ASD controlling for sensory processing issues.
Methods: Twenty-four children, ages 73-112 months (SD=11.4), diagnosed with high functioning ASD were assessed with the Wisconsin Card Sorting Test. Their teachers completed the Behavior Rating Inventory of Executive Function, and the School Function Assessment questionnaire. Parents completed the Sensory Profile and a demographic questionnaire.
Results: We found that executive functions contribute to participation in school activities over and above the contribution of sensory processing. In particular, the abilities to resist impulsive responses, to stop a behavior at the appropriate time, and to regulate emotional responses contributed to participation.
Conclusions: The findings of this study indicate that executive functions are fundamental for successful participation in school activities of children with high

functioning ASD, in addition to sensory processing abilities. School-based therapists need to address executive functions, along with the traditional emphasis on sensory processing. In addition, this study indicates that sensory processing issues, specifically auditory processing, contribute to participation of children diagnosed with high functioning ASD.

61 125.6 PREDICTING FRIENDSHIP QUALITY IN AUTISM SPECTRUM DISORDERS (ASD). N. Bauminger*[1], S. J. Rogers[2] and M. Solomon[2], (1)*Bar - Ilan University*, (2)*UC Davis*

Background: Friendship in typical development is considered essential for children's well-being, yet, it is viewed as a major difficulty for children with ASD. In recent years, studies have shown that subgroups within the spectrum are able to develop friendships and experience loneliness in its absence. The components that may contribute to the formation of friendship are not yet well understood.
Objectives: The current study examines the roles of attachment security and mother-child relationship qualities, Theory of Mind (ToM), age, language ability, and their interactions in predicting and explaining variation in observed and perceived friendship variables in ASD and typical development
Methods: Participants included 164 children (age 8-12) with high-functioning ASD (n=44) and with typical development (TYP) (n=38) and their 82 close friends. Groups were matched on SES, receptive language vocabulary, child age, and gender (each study group included one girl).
Multidimensional assessments included observation on child-friend dyadic interaction during construction and drawing scenarios; target child's self perceived friendship qualities; security of attachment; mother-child relationship qualities; ToM-2nd order false belief task and the PPVT.
Results: Our hypothesized predictors involving attachment security and mother-child relations and their interrelations had direct and indirect effects on friendship for both ASD and TYP, highlighting the important contributions of these factors to children's friendship performance and suggesting both compensatory and amplification mechanisms for friendship qualities.
Conclusions: Discussion focuses on role of attachment and parent-child relations in development of friendships; implications of similar friendship predictors in typical and ASD development; and practical and clinical implications.

62 125.7 Self-reported Social Behaviors of Adults with Autism Spectrum Disorder (ASD). S. L. Bishop*, M. M. Seltzer and J. S. Greenberg, *Waisman Center, University of Wisconsin-Madison*

Background: Few studies have attempted to describe the profile of social difficulties exhibited by adults with ASD. Recent retrospective and prospective investigations (e.g., Seltzer et al., 2003; Shattuck et al., 2007; Howlin et al., 2004) have reported general improvement in ASD symptoms over time, but these studies have focused primarily on parent-reported changes in childhood symptoms.
Objectives: This study investigates the social symptoms of ASD in adulthood from the adult's perspective. We combine information obtained from standardized questionnaires with semi-structured interview responses in order to describe the range of social strengths and difficulties experienced by adults with ASD.
Methods: Data were collected as part of a longitudinal study supported by the NIA (R01 AG08768). Eighty five adults, all previously diagnosed with ASD, between the ages of 18 and 53 years (*M*=25 years) who had provided data about social relationships were included in the current study. Approximately 34% of those who completed cognitive testing received a full-scale IQ score of 70 or below.
Results: Only 13% of individuals scored above the suggested ASD cut-off on the Autism Spectrum Questionnaire (Baron-Cohen et al., 2001). Participants generally reported high levels of social interest; 73% preferred to do things with others rather than alone, and 67% enjoyed social chit-chat. However, according to the social relationships interview, only 41% had contact with their closest friend more than once per month.

Conclusions:Preliminary analyses suggest a discrepancy between the amount of social contact desired by adults with ASD and the amount that they actually experience. Further analyses of the interview data will allow more detailed examination of this question. Information about the social symptom profile of adults with ASD is critical to the improvement of assessment and diagnostic techniques, as well as to the development of effective social skills interventions.

63 125.8 The Father's Role in the Development of Children with Autism. S. A. Donaldson*, E. S. Hilliard and J. H. Elder, *College of Nursing*

Background: The NINR/NIH funded intervention study "In-Home Training for Fathers of Children with Autism" uses a novel approach of training fathers of children with autism in techniques to assist their child's language and social development. This report provides additional important qualitative information and cumulative themes of fathers' commentaries about their roles and their participation in the 4-year on-going quantitative study.

Objectives: To describe how fathers of children with autism view their roles and whether the father training intervention changes how they view their role.

Methods: Video taped interviews of the fathers participating in the In-Home Training for Fathers of Children with Autism are conducted in the home setting. Questions developed for the study guide the interview and allow the father to express his thoughts and feelings about his role, child, family and other issues related to autism. The interviews are transcribed and reviewed for common themes and significant statements.

Results: Themes discovered thus far (N=12) indicate that the fathers experience many of the same feelings that fathers of normally developing children have and that the in-home training project has a positive influence on their father role which may in turn affect the family as a whole.

Conclusions: As more interviews are collected, existing themes are reinforced and some new ones are discovered. Overall fathers of children with autism appreciate the influence that the in-home training program has in bringing them back into the nucleus of the family.
Sponsor: NINR/NIH

64 125.9 Social Perception in Children with High functioning Autism and Asperger Syndrome. S. Stagg*, P. Heaton, K. Linnell and T. Valentine, *Goldsmiths College, University of London*

Background:
Impairments of social functioning are the primary diagnostic criteria for autism with children and adults displaying a lack of interest in, and attention to, social objects. However, adults on the autism spectrum form social stereotypes (White et al.,2006) and similarly affected children demonstrate a viewing preference for people over objects (Van der Geest et al., 2002).
Objectives:
The aim of this study was to determine whether children with an ASD display greater interest in sets of figures in interaction than in non-interaction, and to extend findings to a comparison of children diagnosed with High Functioning Autism (HFA) and Asperger Syndrome (AS).
Methods:
13 children with HFA, 12 children with Asperger Syndrome all of which had typical language onset and cognitive development in the first three years of life, and 12 typically developing children participated. The children were presented with two sets of figures (interaction v. non-interaction) displayed on a monitor for 10 seconds whilst eye-movements were recorded using a head mounted eye-tracker.
Results:
The ASD group spent less time looking at the head regions of the figures than the control group; however, there was no qualitative difference in looking patterns with viewing times longest for interacting figures. Whilst both HFA and AS groups displayed similar looking times to the head regions of the figures the AS group looked significantly longer at the interacting figures with the opposite pattern of viewing displayed in the HFA group.
Conclusions:

The differentiation between AS and HFA is still controversial; our results suggest that advantages in early development may lead to later gains in social skills within Asperger Syndrome.

65 125.10 PSYCHOSOCIAL DIFFICULTIES IN YOUNG ADULTS WITH AUTISTIC TRAITS. S. Kanne*[1] and S. Christ[2], (1)*Thompson Center for Autism and Neurodevelopmental Disorders*, (2)*University of Missouri*

Background: Past research has demonstrated that traits of autism are continuously distributed in the population (e.g., Constantino & Todd, 2003). It is also been found that adolescents and young adults with Autism Spectrum Disorders (ASDs) are at greater risk for experiencing other psychosocial difficulties, including depression and anxiety (e.g., Ghaziuddin, Ghaziuddin, & Greden, 2002; Seltzer et. al., 2003).

Objectives: To explore whether young adults who report a greater degree of ASD traits, but without an ASD diagnosis, also report experiencing a greater degree of other psychosocial difficulties.

Methods: A screening version of the Social Responsiveness Scale (SRS) was administered to over 2000 students and used to identify 45 individuals (ages 18-21) reporting greater social difficulties (High SRS Group). Seventy-five individuals reporting minimal difficulties were also identified (Low SRS Group). The Autism Spectrum Quotient was administered and confirmed a significant difference in the reporting of autism traits between the groups. Gender was evenly distributed evenly. A 2-way (Gender X SRS Group) ANOVA compared responses on the BASC-2 Self-Report.

Results: Individuals in the High SRS Group reported significantly more difficulties with personal adjustment, attitude towards school, interpersonal relations, self esteem, and self-reliance. They also reported significantly more atypicality, external Locus of Control, social stress, symptoms of depression, but less hyperactivity and less sensation seeking. Females in the High SRS Group reported significantly more difficulties with emotional symptoms, anxiety, and a sense of inadequacy.

Conclusions: Similar to the extant literature on individuals diagnosed with an ASD, young adults reporting a greater degree of autistic traits via a SRS screening measure also reported greater difficulties across a wide psychosocial range. The results also indicate that females reporting more autistic traits report more problems in many areas relating to internalizing symptoms compared to males reporting more autistic traits.

66 125.11 Social communication and social cognition in children with congenital visual impairment (VI). V. Tadic*[1], N. Dale[2] and L. Pring[1], (1)*Goldsmiths, University of London*, (2)*Great Ormond Street Hospital / University College London, Institute of Child Health*

Background: Previous research has shown that the pattern of socio-communicative and socio-cognitive development in children born with severely impaired vision often bears a striking resemblance to that of sighted children with autism. **Objectives:** It is now critical to provide a more detailed picture of such development and in particular to focus on children with IQ's in the normal range. **Methods:** 15 children with congenital VI and no other impairments were matched on verbal IQ, age and gender to a group of 26 typically developing children with normal vision. The behavioural ratings of every-day social communication were obtained through parental reports using the Social Communication Questionnaire (SCQ) and Children's Communication Checklist -2 (CCC2). An adaptation of Rieffe & Terwogt (2000) emotion understanding task was used to examine the children's spontaneous use of mental state language when explaining other people's emotional states.

Results: In comparison to the sighted controls, the children with visual impairment showed significantly poorer socio-communicative outcomes on the SCQ and the pragmatic and social aspects of the CCC-2. A considerable proportion of children with visual impairment exhibited socio-communicative profiles that were consistent with Autism

Spectrum Disorders (ASD) (33% on the SCQ and 64% on the CCC-2). However, the children with visual impairment were comparable to their sighted controls in their ability to predict emotional states of story characters and used mental-state language to describe emotions as frequently.
Conclusions: The findings are considered in the context of identifying a broader autism phenotype in children born with severely impaired vision and the potential for language-based interventions.

67 125.12 Sexual Well-Being of High-Functioning Adults with Autism Spectrum Disorders. S. Nichols*[1] and S. Byers[2], (1)*NSLIJ Health System*, (2)*University of New Brunswick*

Background: Healthy and safe sexuality for individuals with autism spectrum disorders (ASDs) is an important developmental goal, yet it has received little attention in the literature. What research has been done has focused primarily on negative markers and problematic sexual behavior. 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). The relationship between severity of social impairment and sexual functioning was also explored.

Methods: High-functioning male and female adults between the ages of 21-65 years with self-reported ASDs and average to above average cognitive abilities completed a comprehensive set of online questionnaires related to sexual well-being. Findings will be presented for adults who were currently in a romantic relationship or who had been in a romantic relationship of at least 3 months duration in the past. At the time of abstract completion, 40 adults had finished participation in the study. Recruitment for the study is ongoing throughout 2008.

Results: Participants' scores on measures of interest will be compared to normative samples. Canonical correlation analysis will be used to determine the relationship between demographic characteristics (e.g., age, sex, relationship status, severity of ASD symptomatology) and measures of sexual functioning.

Conclusions: We will report on the relationships between age, sex, and symptom severity profiles and sexual well-being in order to better understand the sexuality and relationships of high-functioning adults living in the community. Limitations and recommendations for future research directions in adult sexuality will be discussed.

68 125.13 Emotion Recognition in Boy and Girls with Autism Spectrum Disorder. T. McMullen*[1], A. Perry[2] and W. Roberts[3], (1)*York University and SickKids Hospital*, (2)*York University*, (3)*SickKids Hospital*

Background: Individuals with autism spectrum disorder (ASD) have demonstrated impairments in emotion recognition. Most of this research has only been done with males and gender as a variable has not been studied. Gender is an important factor in emotion recognition because research has implicated a female advantage. Objectives: To examine emotion recognition skills in children with ASD and to determine if there are differences in ability for boys with ASD compared to girls with ASD. Methods: Twenty boys and 20 girls with ASD (ages 6-12 years) were required to choose between the options of happy, scared, angry, or fearful when presented either with a picture of a child displaying an emotion or a recording of a child's voice with emotion. For group results, the performances of the 40 children with ASD were compared to the age-matched normative sample. Results: As a group, the boys and girls with ASD were more impaired on total scores of both modes of emotion recognition when compared to the normative sample. On the measure of emotion recognition of faces, the ASD group (M = 7.40) made significantly more errors than their age-matched comparison group (M = 4.39; $F(78) = 13.40$, $p < .001$). On the measure of emotion recognition in voice, the ASD group

(*M* = 8.80) also made significantly more errors than their age-matched comparison group (*M* = 6.36; F(78) = 8.1, p < .1). Boys (*M* = .22) had significantly more difficulty recognizing sadness as a facial expression than the girls (*M* = .12; F(38) = 4.37, p < .5). Conclusions: Children with ASD demonstrate impairments in recognizing affect in voice and on faces. In particular, boys with ASD demonstrate more impairment in recognizing sad faces than girls with ASD.

69 125.14 Documenting the Functional Profile of Adolescents with Autism Spectrum Disorders: Applications of the International Classification of Functioning, Disability, and Health (ICF). K. Poon*[1] and R. Simeonsson[2], (1)*Nanyang Technological University*, (2)*University of North Carolina at Chapel Hill*

Background:

Although the DSM-IV and the ICD-10 diagnostic criteria is helpful in identifying individuals with autism spectrum disorders (ASD), their utility for providing a description of the profile of functional skills is limited. The establishment of such a system of functional profiling will enable programs to more effectively plan intervention programs and to evaluate programs.

Objectives:

This study sought to examine (a) the utility of the International Classification of Functioning, Disability, and Health (ICF) in documenting the functional profile of adolescents with ASD and to (b) describe the functional skills of adolescents with ASD.

Methods: The responses from parents of 15 adolescents with ASD attending specialized educational settings in Singapore were gathered via a semi-structured interview mapped upon the ICF.

Results:

The interviews revealed a profile of functional skills for the adolescents with ASD consistent with the core deficits of ASD (i.e., social and communication areas). However, other areas of poor functioning were also identified.

Conclusions:

The ICF appears to be a useful system for the study of functional skills of adolescents with ASD. There also needs to be further focus on other aspects of functioning among adolescents with ASD for intervention planning.

70 125.15 Global affective quality and discrete synchronous behaviours in the interactions of mothers and children with Autism Spectrum Disorders. P. Venuti*[1], S. De Falco[1], G. Esposito[1], A. Bentenuto[1], P. Villotti[1] and M. H. Bornstein[2], (1)*University of Trento*, (2)*National Institute of Child Health and Human Development, National Institutes of Health, Department of Health and Human Service*

Background: Parent-child interaction is as essential to the early development of special needs children as it is for typically developing children. Although children with ASD have a specific deficit in social interaction, they can still profit from harmonious interactive exchanges to develop their potential. To date, however, mother-child interaction in ASD dyads has not been adequately explored.
Objectives: In this study we aimed to investigate the global affective quality as well as the synchrony of discrete behaviors, in mother-ASD child dyads by means of two different observation techniques.
Methods: Fifteen children with ASD aged 3 to 6 years and their mothers participated. Verbal mental age-matched Down syndrome (DS; *n* = 15) and typically developing children (TD; *n* = 15) served as comparison groups. Children and their mothers were videorecorded during free play, and their interactions were coded with the Emotional Availability Scales (EAS; Biringen, Robinson, Emde, 1998) and with an independent coding system that focused on the occurrence of mother and child initiations and responses classified in terms of dyadic synchrony.
Results: ASD children showed significantly lower EAS scores and lower occurrence of synchronous behaviuors than the other two groups of children. Mothers in the three groups showed few differences to one another. Sequential analyses revealed that child

responses are more likely to follow synchronous maternal behaviours. Global affective quality in the dyads correlated with discrete synchrony behaviuors.
Conclusions: This study pinpoints strengths and deficits in mother-ASD child interaction and helps to identify areas of potential remediation through intervention. Future research in this direction should implement intervention programs focused both on specific emotional dimensions of child development and of the mother-child relationship.

71 125.16 The Relationship Between Pragmatic Language, Peer Relations, and Socioemotional Functioning in High-Functioning Children and Adolescents with Autism Spectrum Disorders. L. Goodman* and E. Kelley, *Queen's University*

Background: High-functioning individuals with autism spectrum disorders (ASD) may have a normative verbal performance on general tests of intelligence. However, these individuals continue to experience a wide variety of difficulties pertaining to the social uses of language. Although research has investigated how deficits in pragmatic language impede relationships, there has been no research investigating the broader repercussions of poor social communication. Objectives: This research study aims to examine the relationship between pragmatic language, socioemotional adjustment, and peer-inflicted victimization. Specifically, we are investigating if poor pragmatic language and maladaptive behaviours are related to an increase in the incidence of peer-inflicted victimization for school-age individuals with high-functioning autism and Asperger syndrome. Furthermore, we are predicting that this victimization will be related to poorer socioemotional adjustment. It is our hope that this research will be used to inform social skills intervention and increase public awareness regarding peer-inflicted victimization in the ASD community. Methods: The study is examining high-functioning participants, ages 10 to18, with a diagnosed ASD. Standardized tests are being utilized to assess the variables and confirm diagnosis. The order of tests is counter balanced. A typically developing control group is matched in regards to age, sex, and IQ. Participants are completing a battery of standardized tests in two 60-90 minute sessions in the laboratory. Results: To analyze the data, we will conduct a mediated regression analysis. We hypothesize that there will be a significant relationship between deficits in pragmatic language and poor socioemotional functioning, controlling for the variance attributed to participants' adaptive behaviour. We predict that this relationship will be significantly mediated by incidence of peer-inflicted victimization. Conclusions: No published research to date has investigated peer-inflicted victimization in adolescents with ASD. We hope that this study will begin to address the predictors and consequences of victimization in individuals with ASD.

72 125.17 Understanding and Assessing Social-Emotional Learning Processing Impairments in Children with and without Autism-Spectrum Disorders. C. McKown*, L. M. Wood and M. Lipton, *Rush University Medical Center*

Background: Social disability is a core diagnostic feature of the autism-spectrum disorders (ASDs). We currently have an incomplete understanding of the social-emotional processing impairments that give rise to social disability among children with ASD's. This presentation examines the relationship between children's ability to encode, interpret, and reason about social and emotional information (SEL ability), their ability to inhibit behavioral impulses, and their social behavior and functioning.

Objectives: The objectives of this presentation are: (a) to describe and evaluate a three-domain model of children's SEL ability, (b) to demonstrate methods of assessing the three domains of SEL ability, and (c) to examine the criterion-related validity of tests of SEL ability.

Methods: Studies 1 and 2 reflect naturalistic examinations of the factor structure and criterion-related validity of tests of SEL ability. Study 1 included 60 typically-developing children ages 5 to 14 with longitudinal data. Study 2 included 126 clinic-referred children ages 5 to 17 with cross-sectional data. Both studies included multi-method, multi-informant measures of SEL ability, behavioral inhibition, and social behavior.

Results: SEL ability includes three factors: awareness of nonverbal cues, ability to interpret social information, and ability to reason about social problems. The better children perform on measures of SEL ability and behavioral inhibition, the more prosocially they behave. Prosocial behavior is in turn associated with peer regard and teacher report of academic competence. The relationship between SEL ability, behavioral inhibition, and social outcomes is strikingly similar for typically developing and clinic-referred children.

Conclusions: SEL ability includes three domains and can be reliably measured. SEL ability and behavioral inhibition are associated with social and other outcomes. Implications for children with autism-spectrum disorders are discussed.

73 125.18 Reactions to social exclusion in adolescents with ASD. C. Sebastian*[1], E. Viding[1], T. Charman[1], K. D. Williams[2] and S. J. Blakemore[1], (1)*University College London*, (2)*Purdue University*

Background: Individuals with high functioning autism or Asperger syndrome often report feelings of loneliness and isolation (Hedley and Young 2006); they seek interaction with others, but are rebuffed due to their poor social skills (Attwood, 1998). This may contribute to high levels of comorbid mood disorders in this population (Tantam, 2000). However, no previous studies have explored how people with autism spectrum disorder (ASD) respond to a single episode of experimentally induced social exclusion. Therefore, it is as yet unclear whether theories of social exclusion developed using non-autistic populations are applicable to the experience of individuals with ASD.

Objectives: Adolescence is a time of social and emotional challenge, during which peer relationships become increasingly important (Howlin, 2003). This is also a key time for intervention, when patterns of social interaction are not yet fixed. We therefore focus on adolescents with ASD in the present study.

Methods: The method was identical to that used in a previous study by our group. In this study, typically-developing adolescents and adults played an internet-based experimental social exclusion manipulation (Cyberball). Affective and cognitive reactions to being included/excluded from the Cyberball game were then measured. The current study compared 12 high-functioning adolescent males with ASD, and 12 matched controls.

Results: The previous study found that adolescents reported greater anxiety and lower mood after exclusion than adults, while non-affective appraisals and performance on a reaction time measure did not differ between groups. This suggests that typically-developing adolescents are hypersensitive to the affective consequences of social exclusion, possibly because neural structures involved in emotion regulation are still maturing (Nelson et al., 2005). We will report novel data on the same paradigm from adolescents with ASD.

Conclusions: We hope to shed light on whether social exclusion has similar affective consequences for adolescents with ASD as in typically-developing adolescents.

74 125.19 The social behaviour between a mother and her child with autism spectrum disorder. M. Meirsschaut* and H. Roeyers, *Ghent University*

Background: The interaction between a mother and her child with autism spectrum disorder (ASD) is a dynamic and bidirectional process, influenced by both the social-communicative restraints of the child and the interaction style of the mother.

Objectives: To compare the social behaviour of a child with ASD in interaction with its own versus an unfamiliar mother.

Methods: For this study a group of 16 young children with ASD (CA, M = 37 months) were compared to a group of 15 typically developing (TD) children (CA, M = 40 months). Each child was observed during free play, first in interaction with its own mother and 2 to 8 weeks later in interaction with an unfamiliar mother. Measures of language ability, general development and ADOS-G were administered

for both groups. All play interactions were recorded and mother's and child's social behaviour was coded.

Results: Preliminary results indicate that mothers of a child with ASD reacted as responsive as control mothers, but that they took more social initiatives and were more stimulating and directing in play. Children with ASD showed significantly less social attempts and responses in interaction with their mother than TD children. When comparing the social behaviour in the 'own' versus 'other' mother-child dyad, we failed to find any differences in either group. For the ASD group however, we found a negative correlation between a mother's social behaviour and the child's responsiveness, but only within the 'other' dyad. At IMFAR, final results will be presented.

Conclusions: These results suggest that the impact of an adapted interaction style by mother is rather limited on children with ASD. Furthermore, in approaching an unfamiliar child with ASD an unobtrusive interaction style seems more appropriate.

75 125.20 More than 80% of children with PDD-NOS have co-morbid psychiatric disorders. E. I. De Bruin*, P. F. A. De Nijs and F. Verheij, *Erasmus MC-Sophia Children's Hospital*

Background: Impaired social interaction and communication, as core symtpoms of ASD are often resistant to treatment and are considered to be chronic. Interventions regularly focus on associated symptoms such as hyperactivity, anxiety or aggression. Associated medical and psychiatric symptoms have often been studied in autism but have not been studied in PDD-NOS, the milder, but much more prevalent (PDD-NOS occurs at least twice as often as autism) form of ASD's.

Objectives: The aim of this study was to assess co-morbid psychiatric disorders and symptoms in school-aged children with PDD-NOS.

Methods: In this study 94 children with PDD-NOS were studied. The Diagnostic Interview Schedule for Children-Parent version (DISC-IV-P) was administered to assess co-morbid disorders and a classification of PDD-NOS was based on standardized, reliable research criteria.

Results: More than 80% of children with PDD-NOS met criteria for at least one co-morbid disorder. Most of them were assigned even more additional disorders. Co-morbid disruptive behavior disorders such as ADHD, and particularly ODD, were present in more than 60% of the cases and more than 50% of the children met criteria for one or more anxiety disorders.

Conclusions: Co-morbid psychiatric disorders occurred in more than 80% of the children with PDD-NOS. In some cases these additional symptoms respond to treatment which subsequently will lead to a better quality of life. Therefore, clinical assessment of children with PDD-NOS should always include assessment of co-morbid psychiatric disorders.

76 125.21 MCDD: a subgroup of PDD-NOS or a psychotic disorder?. E. I. De Bruin, P. F. A. De Nijs* and F. Verheij, *Erasmus MC-Sophia Children's Hospital*

Background: MCDD in childhood is possibly a forerunner of schizophrenia in adulthood. Children with MCDD suffer from thought disorders, affect regulation problems and impairments in social communication. MCDD is currently not a DSM-IV classification and these children are often classified under PDD-NOS, because of their social difficulties. Another possibility would be to classify this concept under the psychotic disorders, but this would implicate a different approach to treatment and prognosis. Previous studies have shown that MCDD differs from autism but it has not yet been studied whether MCDD differs from PDD-NOS.

Objectives: The aim of this study therefore was to assess whether MCDD can be delineated from PDD-NOS.

Methods: MCDD children (n = 25, 6-12 years of age) were compared to children with PDD-NOS (n = 86) on the dimensions of (psychotic) thought problems, co-morbid psychiatric disorders and social contact problems.

Results: MCDD was associated with psychotic thought problems, anxiety and disruptive behavior, whereas PDD-NOS was associated with impaired social contact.

Conclusions: MCDD can be delineated from PDD-NOS and it can be questioned whether the current PDD-NOS classification is the appropriate one in all children with MCDD, and whether the overlap with psychotic disorders, or even anxiety or disruptive behavior disorders should not be emphasized more.

77 125.22 The Development of a Fast and Objective Tool for Identifying Early Autism. M. D. Rutherford*, *McMaster University*

Background: There is a pressing need for early, reliable diagnostic and screening tools for autism. Currently, an autism diagnosis typically happens at the age of 3 years or 4 years, and may happen much later, but earlier diagnosis of autism is associated with an improved prognosis. **Objectives:** Here I report a longitudinal study designed to measure early social perceptual and social cognitive development in children in the first year of life, based on children's behavioral responses to faces, emotions, eye gaze, and animate motion. **Methods:** participants visit the lab four times in their first year, at 3 months, 6 months, 9 months and 12 months of age, in order to participate in the predictive measures. These predictive tasks involve social stimuli, all presented visually, while I measured whether participants' eye direction was preferentially drawn to the social stimuli. Participants then return for the outcomes measure when they reach their second birthday. Infants are either siblings of children who already have an autism diagnosis, or serve as control participants. **Results:** A group of young infants at risk for autism can be distinguished from a control group at 6 months, at 9 months and at 12 months of age, using fast and objective measures. **Conclusions:** This is the youngest age at which clear evidence of autistic development has been documented in a controlled laboratory situation. This tool is designed to be objective and free from reliance on clinical judgment. The data collection took just 10 minutes (on each of four visits) and was meant to be fast and easy for participants and administrators. By developing a fast and objective screening tool for early autism diagnosis, the goal is to create a tool that can be used widely to identify children who will later have an autism diagnosis.

78 125.23 Video Gaming in the Autism Spectrum Population: Factors Influencing Gaming Choice in ASD and Normal Populations. G. Stobbe*[1], T. T. Olson[2], J. Davies[2] and J. Eckstrom[3], (1)*ASTAR Center*, (2)*Seattle Pacific University*, (3)*University of Washington*

Background: Video game playing has the potential for both a positive and negative impact on the social, emotional, and cognitive development of children and adolescents with autism spectrum disorder (ASD).

Objectives: To investigate children's perceptions and attitudes about video gaming choice as well as parental beliefs, attitudes and control regarding video gaming choice.

Methods: A survey of 100 children with ASD (ages 7-18) will be conducted along with a group of 100 age-matched controls. Participants will be selected from the database of a local school district. Participants will be excluded for co-morbidity with other major neurological or genetic disorders prior to inclusion. Participation and consent by the subject and parent/caregiver will be voluntary. Developmental age and cognitive ability of the ASD and control children participants will be obtained. Information regarding social development will be obtained through the Social Responsiveness Scale for all participants. Severity of autism symptoms will be measured with the Aberrant Behavior Checklist for the ASD population. Survey data will include amount of time playing video games, current game type preferences, video game-playing history including age of starting video game playing, and degree of parental control and concern.

Results: Hypotheses to be investigated: 1) The factors of developmental age/cognitive ability, severity of autism symptoms, and parental degree of concern/control influence the type of game played by the ASD population 2) Progression of age-appropriate video game

choice does not progress at the same developmental rate in the ASD population relative to age-matched controls 3) Parents of ASD children as compared to parents of control children will exhibit greater control and greater concern regarding gaming choice and play. Results from this survey will be presented.

Conclusions: Strengths and weaknesses of the methodology and implications for developing a video game that enhances social skill development will be discussed.

79 125.24 LOOKING STRATEGIES IN SCHOOL-AGED CHILDREN WITH AUTISM: INITIAL REACTIONS AFTER SCENE CUTS IN MOVIES OF COMPLEX SOCIAL INTERACTION. K. Knoch*, W. Jones and A. Klin, *Yale School of Medicine*

Background: Previous research has shown that when watching scenes of social interaction individuals with autism look less at people's eyes and more at people's mouths than their typically-developing peers. A related study found that following a movie scene cut, adolescents with autism make initial fixations in a socially random manner: they demonstrate no preference between areas with social information (character's body, mouth, or eyes) and non-social object areas. In contrast, age- and IQ- matched typically-developing adolescents show a preference for making initial fixations to the area with the most social information: the eyes of onscreen characters. The current study downward extends this research to focus on young children with autism, aged 5-13. This study explores the scanning strategies (sequence of shifting visual attention and initial, secondary and subsequent fixations) employed by individuals with autism across scene cuts in movies depicting social interaction.

Objectives: To examine the temporal dynamics of visual fixation patterns following a scene cut in children with autism and in matched, typically-developing peers.

Methods: Participants viewed scenes of dynamic social interaction. Scene cuts provided instances where new visual information required a viewer to shift attention from an old location (in the previous frame) to a new target location (in the current frame). Eye-tracking data were collected across scene cuts to measure visual scanning strategies.

Results: The initial fixations of individuals with autism occurred in a socially random manner, whereas typically-developing peers showed a strong preference for making initial fixations towards the eyes of the onscreen characters.

Conclusions: The present study suggests that initial reactions are consistent across childhood and adolescence. Furthermore, the looking strategy used by participants with autism is significantly correlated with measures of their social disability (as obtained by the ADOS).

80 125.25 Social Motivation In Autism. G. M. Fiske* and A. E. Booth, *Northwestern University*

Background:

Autism was originally described as involving a lack of *motivation for social interaction**[1]***. Social motivation has not figured prominently in subsequent theorizing regarding this disorder. Instead, theory of mind deficits have taken center stage. This is surprising because social motivation deficits appear early, and might prove to be both specific to, and universal in, autism.

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[1] Volkmar & Klin, (2005)

Objectives:

1. Do children with autism exhibit deficient social motivation in a controlled setting?
2. What is the relationship between social motivation and theory of mind competence?

Methods:

15 3-5-year-old children with autism (ASD) and 16 age-matched typically developing (TD) children participated. Measures of social motivation included: looks to experimenter, forced choice between social and nonsocial interaction a) with a toy and b) to obtain a desired food item, and score on the Dimensions of Mastery Questionnaire.

Measures of theory of mind competence assessed imitation, joint attention, and understanding of desire, intentionality and false belief. All required minimal language skills. The PPVT-IV and the Vineland Social-Emotional Early Childhood Scales were administered.

Results: The ASD children looked at, and obtained food from, an experimenter less frequently than did TD children. Parents reported that ASD children were less motivated to interact with others. ASD children were impaired on the joint attention and understanding of desire tasks, but not on imitation, or understanding of intentionality or false belief. Few relations between performance on the social motivation and theory of mind tasks were detected. However, a significant correlation did emerge between social motivation and receptive language in the ASD group.

Conclusions: The ASD group exhibited deficient social motivation. Evidence for impairments in theory of mind was less consistent, and was not tightly linked to impairments in social motivation. The current results highlight the promise of social motivation deficits in explaining symptoms of autism.

81 125.26 THE YALE SPECIAL INTERESTS SURVEY: A WEB BASED METHOD FOR ASSESSING SPECIAL INTERESTS IN ASD. J. Danovitch*[1], R. Paul[2], F. Volkmar[1] and A. Klin[1], (1)*Yale School of Medicine*, (2)*Yale University*

Background: Our preliminary work (Klin et al., 2007) demonstrated that persistent unusual and intense interests are common among children with autism spectrum disorders (ASD), yet limited empirical data exists on how these special interests develop.

Objectives: To collect data and characterize the behaviors associated with special interests in children with ASD through a user-friendly online survey.

Methods: Participants were recruited from the autism program at the Yale Child Study Center. Parents were instructed to complete an online survey about their child's special interests. The survey was responsive to user input so that parents only viewed questions pertinent to their child's age group and special interest status.

Results: Initial analyses including children ages 4 to 17 suggest that, across all age groups, children with ASD were most likely to exhibit behaviors involving memorization of facts and talking about their topics of interest. As they matured, children spent increasing amounts of time on their special interests both when alone and with other adults and peers. Parents also reported shifting attitudes toward their child's interest: parents were initially likely to encourage the child to pursue their topic of interest but, as the interest developed, they were more likely to discourage it. The majority of parents reported that they or other immediate family members share the same topic of interest with their child, suggesting that special interests may serve a social function within families that existing research has overlooked. Data collection remains ongoing and future analyses looking the relationship between special interests and measures of social functioning and language are planned.

Conclusions: Special interests are a critical symptom in high functioning individuals with ASD. Findings from the Yale Special Interests Survey elucidate important developmental issues related to learning style, and suggest that this is an area that deserves increased attention from researchers.

82 125.27 THE ROLE OF CONTEXT IN FACE PROCESSING: AN ERP STUDY OF ADOLESCENTS WITH AUTISM. S. Shultz*, W. Jones, A. Klin and J. McPartland, *Yale School of Medicine*

Background: Individuals with autism tend not to spontaneously imbue ambiguous visual stimuli with social meaning, resulting in maladaptive mental representations of the social environment. Few studies have investigated the proclivity of individuals with autism to naturally impose social meaning on what they see. Research shows enhanced face-related electrophysiological brain activity (N170) to ambiguous stimuli when typical

viewers believe a face is present. Similarly, face sensitive areas of the fusiform gyrus activate in the absence of a face when the context of a human form is presented. This suggests that typical individuals spontaneously impose social meaning on ambiguous stimuli; in this example, the N170 may index this cognitive event, vital for adaptive social behavior.

Objectives: To investigate the N170 as an electrophysiological index of imputation of social meaning in autism.

Methods: Continuous ERP data was recorded while adolescents with autism and typical controls viewed images of degraded faces in which a face is implied by context (the presence of a human body), degraded faces alone, bodies alone, clear faces alone, and clear faces on bodies.

Results: N170 analyses replicated findings of anomalous electrophysiological activity to clear faces in autism relative to typically-developing peers. Analyses are in progress to determine whether typical individuals, but not individuals with autism, exhibit enhanced N170 to ambiguous stimuli presented in social context.

Conclusions: Determining whether face-specific N170 responses can be elicited by contextual cues will provide insight into the clinical problem in autism of failing to impose social meaning on the world, a critical ability for optimizing adaptive responses to stimuli. Investigating this failure in autism has significant implications for intervention and for understanding the early unfolding of social deficits in autism.

83 125.28 COMPARING SCREENING INSTRUMENTS BASED ON CHILD CARE WORKERS' VERSUS PARENT'S EVALUATION OF SIGNS OF AUTISM SPECTRUM DISORDERS IN TODDLERS. M. Dereu*, R. Raymaekers, M. Meirsschaut, G. Pattyn, P. Warreyn, I. Schietecatte and H. Roeyers, *Ghent University*

Background: Early identification of ASD is necessary for early intervention which leads to improved developmental outcomes. To improve early detection of ASD in Flanders, we constructed a screening instrument that can be used by child care workers: the CESDD.
Objectives: To evaluate the use of child care workers as informants in the screening for ASD
Methods: As part of a larger screening project, we obtained for some children scores on the CESDD as well as on a parent questionnaire: ESAT (N = 304; mean age = 22 months; M:F = 1:1), M-CHAT (N = 680; mean age = 21 months; M:F = 1:1) or SCQ (N = 142; mean age = 26 months; M:F = 1:1). Before filling out the CESDD, the child care workers received a 3-hour training.
Results: When we compared the total scores on the CESDD with those of the parent questionnaires, all correlations were rather low but significant: Kendall's tau was .285 ($p<.001$), .82 ($p=.18$) and .201 ($p=.002$) for the correlation with respectively the ESAT, M-CHAT and SCQ. Chi-square analyses of the contingency of positive and negative screens on the different measures also revealed a significant association between the reports of both informants. When we compared the CESDD with the ESAT, M-CHAT and SCQ, we became respectively a chi-square of 21.296 ($p<.001$), 15.37 ($p<.001$) and 11.780 ($p=.001$). The signs that were most reported for the children who screened positive on the CESDD were absence of showing (63%) and pointing (53.4 %) whereas these signs were seldom reported by parents.
Conclusions: These results support the training of child care workers in recognising signs of ASD and the inclusion of their observations in the early detection of ASD.

84 125.29 MEASURES OF IMPLICIT SOCIAL ATTRIBUTION BY VISUAL SCANNING IN CHILDREN WITH AUTISM. A. M. Krasno*, C. J. Zampella, W. Jones and A. Klin, *Yale School of Medicine*

Background: In previous research, we measured whether individuals with autism attribute social meaning to ambiguous visual information (the actions of animated geometric shapes). While such attributions were common among typically-developing peers, individuals with autism were significantly impaired. In another study, we

measured visual scanning by individuals with autism while watching scenes of social interaction; their visual scanning showed evidence of altered visual salience and reduced social monitoring. In the present study, we used scenes from the classic children's film, The Red Balloon, to bring these two lines of research together. We defined a series of experiments in the film scenes when a visual fixation to a particular location at a particular time would occur only as a consequence of a viewer's attribution of intentionality to the film's main characters, a boy and his friend, the red balloon. Because the agency of the balloon is dynamic during the film—at times an ordinary balloon, at times an animate character—appropriate social monitoring is an indication of social attribution.

Objectives: To study social monitoring as a measure of implicit social attribution in individuals with autism.

Methods: School-age children with autism and matched, typically-developing peers watched scenes from The Red Balloon while eye-tracking data were collected. During scenes of interaction between the balloon and human characters, we measured social monitoring, i.e. when the viewer looks between characters to gather social information.

Results: Preliminary analyses reveal that social monitoring of individuals with autism fails to anticipate actions and reactions of the film's characters. Individuals with autism appear to be most impaired when the actions of others are dependent upon the balloon as an animate, intentional being.

Conclusions: Information gained from social monitoring is integral for successful adaptive action in everyday life. The present study offers a useful and non-verbal method of assessing this ability.

85 125.30 "CRIME AND PUNISHMENT": THE UNDERSTANDING OF VIOLATIONS OF BEHAVIORIAL NORMS IN AUTISM. C. Shulman* and A. Guberman, *The Hebrew University of Jerusalem*

Background: Proposed punishment for misbehavior has been used to assess comprehension of social conventions in typically developing children. Measures include appropriateness of the proposed judgment and degree of severity. These measures of understanding of social norms have not yet been investigated among individuals with autism.

Objectives: The present research analyzed suggested punishment for wrongdoing presented in pictures, and compared proposed punishments among students with HFA with those proposed by children with typical development.

Methods: Eighteen students with autism and 18 without autism were matched on full, verbal, and performance IQs. Autism diagnosis was ascertained by ADI and ADOS scores. Each participant was asked to assess everyday social interactions shown in 10 pictures. For behaviors judged unacceptable, the students were asked: "Should the people in the picture be punished for this behavior?"; "What is a suitable punishment?". All answers were transcribed.

Results: While no group differences emerged in the ability to judge the unacceptability of behavior, group differences emerged in the ability to match punishments to violations of socially appropriate behavior, in terms of the proposed punishment and the degree of severity. The punishments proposed by individuals with autism were more bizarre and more severe than those of typically developing children.

Conclusions: Results revealed the ability to judge acceptability of social behavior in interactions in everyday situations was similar for individuals with autism and typical development. As a group the individuals with autism suggested punishments, which were not proportional to the transgression, often containing idiosyncratic or bizarre elements, suggesting impairment in their ability to understand the effect that punishment has on antecedent behaviors.

Poster Presentations Program

126 Epidemiology Posters

86 126.1 A novel form of inflammatory bowel disease with pervasive developmental disorder: A systematic review of the state of the evidence. C. Stott*, *Thoughtful House Center for Children*

Background:,

In 1998 Wakefield et al. published details of a form of inflammatory bowel disease with regressive developmental disorder. The report concluded that '… data do not demonstrate a causal link between the disorder and MMR exposure'. Nonetheless, the paper is frequently cited as the single body of evidence supporting any association between measles containing vaccine (MCV), inflammatory bowel disease (IBD) and autism spectrum disorders (ASDs). Following publication, cases with similar presentation continued to be analysed and contributed to a working hypothesis about the putative association between autistic-like developmental regression, inflammatory bowel disease (IBD) and exposure to MCVs.
Whilst clinical evidence in support of the hypothesis has been reported, population-based studies have found no effect of MMR exposure on either onset or population frequency of the outcomes investigated. Such studies are cited as providing evidence of 'no association' between MMR, IBD and autism spectrum disorder and as refuting the Wakefield hypothesis.

Objectives:,

to examine the extent to which studies have been designed appropriately and with reference to the original Wakefield hypothesis and to examine the extent to which claims of its having been refuted or supported are valid.

Methods:

A systematic review of published and publicly available reports pertinent to the hypothesis. Further discussion and evaluation is undertaken of those studies whose design allows examination of the hypothesis. Details are provided regarding design features that mitigated against inclusion of rejected studies.

Results:

355 studies were identified. 297 were rejected and 58 underwent additional evaluation. Five were identified as meeting criteria for further evaluation.

Conclusions

Few studies claiming to test the Wakefield hypothesis have successfully addressed it. No study meeting criteria was able to unequivocally demonstrate a causal role for the MMR vaccine in ASDs, four studies provided some support in favour of specific aspects.

87 126.2 A novel form of inflammatory bowel disease with pervasive developmental disorder: Evidence for and against the existence of the clinical phenotype and its association with exposure to MMR vaccine. C. Stott*, *Thoughtful House Center for Children*

Background: In 1998 Wakefield et al. published details of a form of inflammatory bowel disease with regressive developmental disorder. The report concluded that '… data do not demonstrate a causal link between the disorder and MMR exposure'. Nonetheless, the paper is frequently cited as the single body of evidence supporting any association between measles containing vaccine (MCV), inflammatory bowel disease (IBD) and autism spectrum disorders (ASDs). Following publication, cases with similar presentation continued to be analysed and contributed to a working hypothesis about the putative association between autistic-like developmental regression, inflammatory bowel disease (IBD) and exposure to MCVs.
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Few studies claiming to test the Wakefield hypothesis have successfully addressed it. No study meeting criteria was able to unequivocally demonstrate a causal role for the MMR vaccine in ASDs, four studies provided some support in favour of specific aspects.

88 126.3 Knowledge of General Practitioners Regarding Autism Spectrum Disorders in Karachi, Pakistan. M. H. Rahbar* and K. Ibrahim, *Michigan State University*

Background: In most developing countries, including Pakistan, the level of knowledge, attitude and practices of physicians regarding Autism Spectrum Disorders (ASDs) are unknown. General Practitioners (GPs) constitute the backbone of health care system in Pakistan.

Objectives: To assess knowledge of GPs in Karachi, the largest city in Pakistan, regarding ASDs

Methods: During June-August, 2007, we conducted a survey of 347 GPs practicing in Karachi. We administered a questionnaire to collect information regarding demographics, knowledge, attitude and practices of the GPs toward ASD. Data were doubly entered into a database and analyzed. We characterize the GPs who participated in this survey. We also used multiple logistic regression models to identify factors associated with knowledge of GPs about autism.

Results: Of 347 GPs interviewed, 69% were male. These physicians had a mean of 40.5 years and treated on average 44 patients per day. About 42% reported that they had heard of the term "autism". After adjusting for year of graduation in a multivariate logistic regression model, factors that were significantly associated with knowledge about autism include: a) physician who practiced in a major Karachi hospital [AOR=2.39, 95% CI (1.21, 4.70)]; b) physicians who had completed a psychiatry rotation in medical college [AOR = 2.61, 95% CI (1.26, 5.43)]; c) physicians who had undergone a rotation in internal medicine [AOR = 1.98, 95% CI (1.14, 3.45)]; and d) physicians who had undergone a rotation in pediatrics [AOR = 2.91, 95% CI (1.68, 5.4)].

Conclusions: Our findings indicate that majority of the GPs practicing in Karachi lack knowledge about autism. Continuing medical education and further training regarding autism during medical school should be strongly encouraged. This could raise awareness among the medical community which could ultimately lead to a better identification of autistic children and perhaps meeting their special needs in Karachi, Pakistan.

89 126.4 COULD THE USE OF SCREENING INSTRUMENTS FOR AUTISM SPECTRUM DISORDER IMPROVE THE ACCURACY OF REFERRALS TO SPECIALIST PAEDIATRIC SERVICES?. S. Chandler*[1], A. Davison Jenkins[1], G. Baird[2], E. Simonoff[3], A. Pickles[4], T. O'Sullivan[5], A. Sharma[6] and T. Charman[1], (1)*UCL Institute of Child Health*, (2)*Guy's Hospital*, (3)*Institute of Psychiatry*, (4)*University of Manchester*, (5)*Lewisham Primary Care Trust*, (6)*Southwark Primary Care Trust*

Background: Research suggests that screening questionnaires for autism spectrum disorders (ASDs) have low sensitivity when used as population screens. However, they

may be more effective when used within referred samples.

Objectives: To evaluate whether the use of screening instruments would improve the accuracy of referral to specialist ASD services for pre-school children, already referred to community child health services with developmental concerns.

Methods: In the first phase of the study, the Social Communication Questionnaire (SCQ) and Modified Checklist for Autism in Toddlers (M-CHAT) were administered to 540 children referred to second-tier health services. Information regarding clinicians' concerns about possible ASD diagnoses/clinician's decision to refer to ASD services was also collected. In the second phase, a stratified sample of children was seen for diagnostic research assessments. Stratification was based on SCQ and M-CHAT scores, and whether the child was referred to specialist ASD services. 120 children were seen by the research team, who remained blind to information collected in phase one. Assessment included the Autism Diagnostic Interview (ADI-R), Autism Diagnostic Observation Schedule (ADOS-G), and psychometrics. Cases were assigned a diagnosis of autism, ASD or non-ASD on the basis of information from the ADI-R, ADOS-G and ICD-10 criteria.

Results: A statistical weighting procedure will be used to evaluate whether the screening instruments were more accurate than clinicians' decision-making in identifying ASD cases, using the recommended cut-offs on the two screens (M-CHAT, Robins et al 2001; SCQ, Berument et al, 1991). Receiver-operator-characteristic analyses will be conducted to compare the sensitivity and specificity of the M-CHAT versus the SCQ.

Conclusions: Comparison of diagnosis, scores on the screens, and clinicians' decisions will allow the sensitivity of all 3 to be evaluated. This will allow us to determine whether use of screens could improve second-tier clinicians' decisions about which children to refer to specialist ASD services.

90 126.5 ASD Services in Europe: A Pilot experience of the EAIS project. P. García-Primo*[1], M. Posada[1], C. Martín-Arribas[1], M. J. Ferrari[1], C. Rice[2], D. Schendel[2] and A. Ramirez[3], (1)*RARE DISEASES RESEARCH INSTITUTE*, (2)*Centers for Disease Control & Prevention*, (3)*Children Therapy Centre - The Hope Project*

Background: The "European Autism Information System – EAIS" is a project funded by DG SANCO for the period January-2005 to June-2008. It was approved after the European Commission stated in February 2005 that more complex monitoring systems were needed to address changes in the ASD prevalence. One of the aims of this project is to design a prevalence study duly harmonized for most of the European countries/regions. Objectives: In order to prepare the prevalence study, a questionnaire (Q-EAIS) focusing on ASD services and data accessibility was designed.

Methods: The Q-EAIS has a total of 65 different questions related to ASD diagnosis (19), public health care systems (9), educational systems (17), social services (9), parents' organizations services (6) and data accessibility (5). This survey was sent to all EAIS partners (25). Respondents were in academic institutions and were also related with ASD services.

Results: The Q-EAIS was completed by 11 partners (Portugal, France, Malta, Bulgaria, Scotland Highland Region, Poland, Czech Republic, Italy, England, Denmark and Spain). Eleven out of 21 partner countries (52%) responded to date. Seven responders referred to the whole country 4 were regional. Preliminary descriptive analysis indicate differences among countries regarding detection, diagnosis, initiation of compulsory education, services provided and data accessibility concerning ASDs.

Conclusions: The Q-EAIS provides a preliminary picture of the ASD services and data accessibility in several European countries and facilitates a more accurate understanding about the feasibility of a harmonized European prevalence study. Conducting a cross-country prevalence study

of ASDs based on existing service system data will be challenging. Pilot efforts are needed to determine if combining multiple sources of information across service providers will provide a comparable picture of the prevalence and characteristics of the ASD population in a defined time period and age across countries with diverse service systems.

91 126.6 ADOS and ADI-R Research Training in Taiwan. L. C. Lee*[1], C. Rice[2], J. Olson[3], B. C. Shu[4], P. Yang[5], Y. Y. Wu[6], C. H. Chiang[7] and F. W. Lung[8], (1)*Johns Hopkins University*, (2)*Centers for Disease Control and Prevention*, (3)*J. Olson Consulting Group*, (4)*National Cheng Kung University*, (5)*Kaohsiung Medical University*, (6)*Chang Gung Children's Hospital*, (7)*National Chung Cheng University*, (8)*Calo Psychiatric Hospital*

Background: Research reliable administrators of autism diagnostic instruments are greatly needed in Chinese-speaking regions to foster autism research in Chinese-speaking populations.

Objectives: To report on process and procedures of conducting Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview–Revised (ADI-R) research training in Chinese Mandarin.

Methods: The ADOS and ADI-R protocols and ADOS manual were translated into Chinese Mandarin. Chinese-translated materials along with English training materials were provided to trainees in advance. Trainees, who are psychiatrists and clinical psychologists, study the English and Chinese versions of ADOS and ADI-R materials in order to get acquainted with them. In February 2008, two English-speaking primary trainers and three bilingual assistant trainers will work together to train 18 trainees. Live demonstrations will be performed in Chinese Mandarin by the bilingual assistant trainers and orally translated to English-speaking trainers simultaneously. Trainees will be broken into small groups for training, each group being led by a primary trainer accompanied with an assistant trainer to facilitate communication between trainers and trainees.

Results: A workshop and four months of weekly study sessions were conducted before the training to orient trainees to training materials. Extended time for training is expected given that simultaneous oral translation is needed, both from English to Chinese as well as Chinese to English. It is more practical and feasible to have bilingual research reliable staff rate trainees' research reliability videos rather than English-speaking trainers.

Conclusions: ADOS and ADI-R research training in Chinese is a challenge for many reasons including language barriers and unknown cultural applicability of these instruments. Required research reliability can be reached; however, enormous effort and time are needed. Cultural adaption may not be a one-time task occurring during translation, as need for more adaption may be recognized and recommended after more experience is gained from ADOS and ADI-R administration.

92 126.7 Brief report: data about autism in Brazil. E. S. Arima*, D. Lima and W. C. D. Souza, *Universidade de Brasília - UnB*

Background:Considering the prevalence of autism, the early identification of autism in Brazil is important since a significant amount of children are in conditions considered at risk to development. An early identification can contribute to a different diagnosis from other development problems and support an intervention. Behavioral categories related to social skills and affection have been traditionally used for diagnosis in clinic. Those categories would be basically the ones described in ICD-10 and in DSM-IV-TR. Experienced clinicians rely mainly on social and affective criteria. Therefore, screening for autism usually takes place in the psychiatric clinic, also looking for intervention.

Objectives: The goal of this research was to collect epidemiological data about autism in child and adolescent psychiatric clinic in the Hospital of the University of Brasília - DF.

Methods: In a total of 450 appointments scheduled for 2007, there were 179 patients. Patients, whose records were not found,

without proper identification and without records from psychiatric clinic related to the year 2007, were excluded. Finally, 149 patient records were examined.

Results: There were 14 (9,40%) diagnostic hypothesis of Pervasive Development Disorder, with 8 (5,37%) specific diagnosis for childhood autism. There were 2 girls and 12 boys with 2 pairs of twins. The average age in the 1st appointment was of 8,58 years of age, the youngest being about 2,58 years old and the oldest, 13,33 years old.

Conclusions: The high prevalence of autism found may be due to special attention to autism lately and more demand as the child and adolescent psychiatric clinic is considered more specialized for those cases. One problem of this study was the loss of data due to archive research. Further studies could investigate the age of the first diagnosis, diagnostic criteria and validation, and collect data from a larger period of time.

93 126.8 Depression in mothers of children with high-functioning pervasive developmental disorders. K. Nomura*[1] and M. Tsujii[2], (1)*Nagoya University*, (2)*Hamamatsu University School of Medicine*

Background: It is not rare that mothers of children with high-functioning pervasive developmental disorders (HFPDD) fall into a depressive state, but the causes and related factors of them have not become clear.

Objectives: Objectives were 100 mothers of HFPDD children who belonged to an association of parents of HFPDD children.

Methods: The initial subjects were 100 mothers of HFPDD children who belonged to an association of parents of HFPDD children and completed a self-report inventory (Beck Depression Inventory). Seventeen subjects in the moderate depression range with scores of 19 points or more underwent a clinical interview using a structured interview (Mini-International Neuropsychiatric Interview: MINI) and DSM-IV.

Results: Thirteen women participated in the survey. A diagnosis of depression was appropriate for 10 women. The MINI and all clinical diagnoses were in agreement. The trigger for the depression was the HFPDD child for 6 women, family problems for 5 women, and human relations of the mother herself for 2. Five of the 10 women claimed a history of depression before the birth of their HFPDD child. Nine of the 10 women complained of receiving no cooperation from their husband in the home, three of whom had husbands undergoing treatment for depression. Of the 10 women, only 4 were receiving treatment, and after one year a diagnosis of depression was still appropriate in 6 of the 10 women.

Conclusions:Depression is recognized in at least 10% of mothers of HFPDD children, many of for whom it is long term. The results suggest that factors in this depression are not only the burden of child rearing, but also the inherent susceptibility to depression of the mothers themselves. Family problems including support from husbands are also thought to affect the onset of depression.

94 126.9 Does record review surveillance capture true cases of autism spectrum disorders?. R. Avchen* and O. Devine, *CDC*

Background: Most recent estimates from CDC's collaborative autism surveillance effort in the United States, the Autism and Developmental Disabilities Monitoring (ADDM) Network, indicate an average of 1 in 150 children are affected with autism spectrum disorders (ASD). Evaluating ADDM methods is necessary to ensure accurate counts and profiles of ASD are reported.

Objectives: ADDM record review methods are well operationalized and executed but have yet been validated by in-person developmental evaluations. This study is designed to measure sensitivity, specificity, and positive predictive value (PPV) of the ADDM system. This abstract will focus on PPV.

Methods: The Metropolitan Atlanta Developmental Disabilities Surveillance Program (MADDSP) is the gold standard for which ADDM methods are based. For this study, surveillance was conducted on a representative subset of the MADDSP population. A research reliable clinician

(blinded to surveillance case status) collected data on the Social Communication Questionnaire (SCQ), Autism Diagnostic Observation Schedule (ADOS), and Autism Diagnostic Interview-Revised (ADI-R) for 177, 9 year olds. Clinical case status was based on results from the ADOS and ADI-R. Surveillance case status was based on an independent review of multiple evaluation records from both educational and clinical sources. Trained clinicians (blinded to clinical case status) with expertise in ASD systematically coded the surveillance records based on the DSM-IV-TR criteria for pervasive developmental disorders to determine surveillance case status.

Results: The study yielded an 85% PPV. The 28 clinically confirmed surveillance cases were male (79%), had recorded IQ < 70 (43%), received educational services or ASD (61%), scored above the SCQ cutoff (93%), and had concordant results on the ADOS and ADI-R (79%).

Conclusions: Clinical evaluations confirmed 85% of surveillance cases were correctly classified given ASD positive ADOS/ADI-R scores. The extent that the confirmed ADDM case profile is representative of characteristics of all identified clinical cases will be examined.

95 126.10 Balancing Accuracy and Anonymity of Biological Specimens in CADDRE, SEED. G. B. Jensen*[1], P. A. Thompson[1], A. E. A. Siddiqi[1], J. E. Siebert[1], J. D. Bonner[1], S. Meyerer[2], M. F. Kuhn[1], K. L. Marable[1], S. Sharp[1], T. Holland[1], S. Chandan[2], H. Farzadegan[2], P. L. Reed[1] and M. H. Rahbar[1], (1)*Michigan State University*, (2)*Johns Hopkins University*

Background:
Protection against disclosure of personally identifiable information (PII) and maintenance of anonymity of study participants is an ethical and regulatory imperative for clinical research. The Center for Autism and Developmental Disabilities Research and Epidemiology (CADDRE) information system (CIS), developed for the national Study to Explore Early Development (SEED), anonymizes participant biological specimens and tracks them throughout the study protocol.
Objectives:
–Accurately track participant biological samples throughout the study protocol
–Minimize exposure of PII
–Blind laboratory analysts to minimize risk of associating between sample genotypes and participant phenotypes
Methods:
The study sites collect and barcode participant specimens and send them to the laboratory, identified without PII. The courier's tracking barcode is scanned into CIS, which tracks the package via link to the courier's tracking system for study sites and laboratory. At the laboratory, a receiving clerk scans the courier's barcode into CIS, records the initial condition of each sample, creates a record for each sample in the laboratory information system (LIS), links new laboratory IDs into CIS, replaces each CIS barcode with a laboratory barcode and discards the CIS barcode; thereby anonymizing the sample for all future steps. The laboratory assesses the samples and enters findings into the LIS, and CIS automatically retrieves sample assessment data using a secured Simple Object Access Protocol (SOAP) connection to the LIS. CIS imports the LIS internal specimen analysis data. Only CIS stores tracking data, PII, and associations between CIS and LIS data.
Results:
The specimen workflow design obviates the possibility of linking samples to phenotypes and adds a layer of protection against PII disclosure.
Conclusions:
The SEED study's CIS tracks and maintains information on biosamples while preventing association of PII with genotypes outside of CIS.

96 126.11 ESTIMATING AUTISM SPECTRUM PREVALENCE IN THE POPULATION: A SCHOOL BASED STUDY FROM THE UK. S. Baron-Cohen, F. Scott, C. Allison*, J. Williams, P. Bolton, F. E. Matthews and C. Brayne, *University of Cambridge*

Background: Prevalence estimates for ASC have shown a steady increase over the last 4 decades, reflecting factors such as improved recognition and detection, changes in study

methodology and widening of the diagnostic criteria.

Objectives: (1) To investigate prevalence of ASC in Cambridgeshire, UK using different methods. (2) To determine how many undiagnosed cases of ASC there are in this population.

Methods: Study 1: A population-based count of known cases, using the Special Educational Needs (SEN) Register. Study 2: A population-based count of known cases, using direct parent report, via schools. Study 3: Schools in Cambridgeshire distributed the CAST (Childhood Autism Spectrum Test) to parents from Study 2. Face-to-face diagnostic assessments were conducted, using the ADI-R and ADOS, and undiagnosed cases were counted.

Results: Study 1: 79/96 mainstream schools participated (representing a population of 8,824 children aged 5-9 years) and reported 83 known cases of ASC, representing a prevalence estimate of 94 per 10,000. Study 2: 96/175 mainstream and special schools participated. 11,700 Diagnosis Surveys were sent to parents of children aged 5-9 years old. 3,373 were returned. Parents reported 41 existing diagnoses of ASC, representing a prevalence estimate of 99 per 10,000. Study 3: 3,373/11,700 parents returned the CAST. Known cases of ASC were excluded. 52 children scored ≥15 on the CAST and were assessed. Of these, 10 were given a research diagnosis of ASC. 25 children scored 12-14 on the CAST and were assessed. 1 was given a research diagnosis of ASC. The ratio of known-to-unknown cases is approximately 5:3.

Conclusions: The prevalence estimate of known cases of ASC, using different methods of ascertainment converges around 1%. The ratio of known to unknown cases means that for every three known cases there are another two unknown cases. This has implications for planning diagnostic, social and health services.

97 126.12 Pre- and Post-natal SSRI use during Pregnancy and Breastfeeding and Risk of ASD in Children. R. A. Harrington*[1], L. C. Lee[1], C. K. Walker[2], R. L. Hansen[2] and I. Hertz-Picciotto[2], (1)*Johns Hopkins University School of Public Health*, (2)*University of California, Davis*

Background: Evidence indicates that serotonin is altered in children with ASD; however, little is known about the developmental effect of pre- or post-natal exposure to medications that act on the serotonin system. Objectives: To provide preliminary data about the developmental effects of maternal use of selective serotonin reuptake inhibitors (SSRIs), a class of antidepressants, prenatally and/or postnatally. Methods: From the Childhood Autism Risks from Genetics and the Environment (CHARGE) study, a large population-based case-control study, we examined a subset consisting of children whose mothers reported experiencing a mental health disorder pre- or post-natally. This group was composed of 32 children with autism spectrum disorder (ASD), 7 with developmental delay (DD), and 17 with typical development (TD). Children with ASD had an ADI-R and ADOS confirmed diagnosis; Vineland and Mullen scores were used to classify children as DD or TD. Exposure was defined as mothers who reported taking an SSRI at any time from 3 months prior to conception to the end of breastfeeding. Bivariate logistic regression was used to examine the association between SSRI use during the index period and developmental outcomes in children. Results: SSRIs were used by 56% of mothers who had children with ASD, 57% who had children with DD, and 65% who had children with TD. The odds of SSRI exposure was 0.70 (95% confidence interval (CI): 0.21-2.36) in the ASD group and 0.73 (95% CI: 0.12-4.39) in the DD group compared to the TD group. Conclusions: SSRI exposure was lowest in the ASD group, followed by the DD group, and was highest in the TD group. We are currently in the process of investigating the relationship between pre- and post-natal use of SSRIs and ASD with a larger sample size, the results of which will be reported and discussed.

98 126.13 Validation of Autism Screening Questionnaire or Social Communication Questinnaire, Lifetime version to Portuguese language. R. Lowenthal*[1], F. Sato[2], C. De Paula[3], S. H. B. Ribeiro[1] and M. T. Mercadante[4],

(1)*Universidade Presbiteriana Mackenzie*, (2)*University of São Paulo*, (3)*Mackenzie Presbyterian University*, (4)*Federal University of São Paulo*

Background: The rate of pervasive developmental disorders (PDD) have been described as up to 1%. Although studies do not suggest any modification of this prevalence in relation of ethnical differences, there are no studies describing the prevalence of PDD in cultures different from the northern hemisphere. It´s important to have efficient and validated diagnostic instruments in order to know what is this prevalence.

Objectives: translation, retroversion, cultural adaptation and validation of *Autism Screening Questionnaire* or *Social Communication Questinnaire*, *Lifetime version* to Portuguese language for its use in Brasil.

Methods: a sample of 120 patients was divided in three distinct groups of 40 individuals each: PDD clinical diagnosis, Down syndrome and psychiatric diagnosis. The questionnaire was applied to the persons legally responsible for the patients according to the standards of a self-applicable questionnaire. Psychometric measures of the translated questionnaire in his final version were tested.

Results: Sensibility values of 92.9% and specificity of 95.5% were found, considering a cutoff point of 15 points. The internal validity for the total 40 questions was 0.895, with a variation of 0.6 to 0.8. The reliability values obtained from the test and re-test demonstrated high agreement for most of the questions.

Conclusions: The final version of the instrument translated and adapted to the Brazilian culture, presented fully satisfactory measurement properties, proving to be of easy application and a useful tool for the diagnostic screening of PDD individuals.

99 126.14 Analysis of Prevalence of Pervasive Developmental Disorders in Atibaia - SP- Brazil. S. H. B. Ribeiro*[1], C. De Paula[2], R. Lowenthal[1] and M. T. Mercadante[3], (1)*Universidade Presbiteriana Mackenzie*, (2)*Mackenzie Presbyterian University*, (3)*Federal University of São Paulo*

Background: Pervasive Developmental Disorders (PDD) are characterized by impairments in reciprocal social interaction, language, and communication. The prevalence of PDD has increased in recent years; currently frequencies are 30 to 60 per 10,000. There are no epidemiological studies of PDD prevalence in developing countries.
Objectives: The aim of this study was to realize a pilot study of PDD prevalence in a neighborhood of Atibaia _ SP, Brazil. It also describes the PDD prevalence found.
Methods: To develop this pilot study, it was selected one urban neighborhood with 1470 children, ages 7 to 12. All the PDD services, all public schools in this neighborhood and the Family Health Program team were identified and special meetings were organized with lectures and discussions about PDD. 99 children were indicated; 76 suspect's cases between 7 to 12 years old children were evaluated. All suspected cases were evaluated based on PDD (Autism Screening Questionnaire _ASQ or Social Communication Questionnaire _SCQ) and mental health screenings (Strengths and Difficulties Questionnaire_ SDQ and Self-Report Questionnaire_ SRQ) and the positive cases was evaluated with diagnosis instruments (ADI-R e DSM-IV).
Results: In the screening phase, the PDD prevalence of 0.88% was found, with ratio of males to female 3:1. The 13 positives cases in ASQ (cut off point 15) were evaluated with diagnostic instruments (ADI-R and DSM-IV). 3 subjects matched PDD diagnostic criteria, meaning a prevalence of 0, 20%.
Conclusions: To our knowledge, this is the first study reporting the prevalence of PDD in Latin American countries. The prevalence rates found was similar with others studies. It is important to conduct further studies in order to compare ours findings with others studies.

100 126.15 Is there an Association between ASD and Assisted Reproductive Technology?. P. A. Filipek*[1], K. Thorsen[2], M. M. Abdullah[3], J. Phan[4] and C. Devine[4], (1)*University of California, Irvine (UCI) School of Medicine*,

(2)*UCI School of Social Ecology*, (3)*University of California, Irvine*, (4)*UCI School of Medicine*

Background: Infertile couples have easier access and fewer constraints to have children using assisted reproductive technology (ART), which permits 1.2% of live births in the U.S. and California. We suspected an association between ART and autism (ASD) based on clinical experience.

Objectives: To determine the rate of ART in a clinical practice of children with ASD.

Methods: All new consultations for ASD (N=715) from 2002 through 2006 were reviewed to document: the use of/ type of ART; parental age/ education; and insurance provider.

Results:

- ART^+ represented 10% of the total ASD sample, an 8-fold increase over the expected 1.2%. When only those with commercial insurance (CI) were included (thereby better controlling SES), the rate of ART increased to 14%, a 12-fold increase.
- Forty-five percent of the ART^+ children were singletons, and 42% were twins.
- ART methods included: 21% ovarian stimulation medication alone; 30% *in vitro* fertilization ± intracytoplasmic sperm injection; and 38% a combination of methods.
- The male-to-female ratio in the ASD sample was 3.5-to-1, and in the ART^+ sample was 2.7- to-1.
- The parents of ART^+ children were older ($p<0.002$) with more years of education ($p<0.4$) than the parents of non-ART ASD children.
- The ART^+ children presented for evaluation 10 months younger than did the non-ART ASD children with CI ($p<0.1$).

Conclusions:

- This is the first known report of an apparent association between ART and ASD, with an 8-to-12-fold increase of ART^+ in this clinical ASD sample over that expected in the general population.
- The variable ART methods suggests that *in vitro* manipulation is not the sole causative factor and warrants further research into association of infertility itself and parental age.
- Couples undergoing ART procedures should be informed about the potential association with autism, and the offspring should be closely monitored.

101 126.16 CLOSER SCRUTINY OF THE AUTISM EPIDEMIC. E. C. Ihle*[1], C. Cerros[1], T. Sendowski[1] and B. Siegel[2], (1)*UCSF*, (2)*University of California, San Francisco*

Background: Much attention has been paid to the recent CDC report suggesting an increase in the incidence of autism spectrum disorders (ASDs). Recent data suggest that, in California, causes are unlikely to be solely environmental (Schechter and Grether, 2008). However, it remains unclear whether this change in incidence reflects a true increase in the number of children meeting DSM-IV criteria for autistic disorder (AD) or is an epidemiologic confound. **Objectives:** Children reported by their parents to have a diagnosis of an ASD were evaluated to determine whether this diagnosis withstood further scrutiny. This set of patients included children whose parents suspected that their child had autism based on their own research and gave a positive history during a screening interview, as well as children diagnosed with an ASD by non-ASD specialist clinicians or by the educational system.
Methods: Children (N=190) who presented for diagnostic evaluation were assessed using the DSM-IV diagnostic criteria for AD, ascertained using methods consistent with the California Department of Developmental Services Best Practices Standards (CA DDS, 2002). **Results:** Only 51% of children with referral diagnoses of AD (N=90) received confirmation of AD following assessment. The

49% of children who were not confirmed to have AD received either a different Axis I diagnosis (22% had an ASD but not AD and 20% had a non-ASD diagnosis) or were found to have no Axis I diagnosis (7%).
Conclusions: A large fraction of the children previously viewed as having AD did not meet DSM-IV criteria for AD when re-evaluated using methods focused on raising convergent validity. Thus, in the referral population we sampled, diagnostic errors are likely introduced from various sources. These sources, including media foment and non-specialist diagnosis without best-practices standards, can yield a different diagnostic impression of AD than a diagnosis derived from a standardized, best-practices assessment.

102 126.17 Autism Prevalence Trends Over Time: The Confounding of Changes in Age at Diagnosis. E. Parner*[1], D. E. Schendel[2] and P. Thorsen[1], (1)*Institut of Public Health, University of Aarhus*, (2)*Centers for Disease Control & Prevention*

Background: Several studies have shown an increase over the last two decades in the age-specific prevalence of autism. The apparent increase in autism prevalence may be confounded by changes in the age at diagnosis, in studies with insufficient follow-up time to estimate the lifetime cumulative prevalence of autism.

Objectives: Examine if there is evidence for changes in age at diagnosis on the reported diagnosis of autism in Denmark. Further, to estimate the amount of bias in the reported prevalence of autism caused by changes in the age at diagnosis.

Methods: The study cohort consisted of all children born in Denmark from 1994 through 1999 identified in the Danish Medical Birth Register (approximately 407,000 children). Outcome data consisted of both in- and outpatient diagnoses reported to the Danish National Psychiatric Registry from 1995 through 2006 using the ICD-10 diagnostic coding system (N=2649). The study population was divided into 2 year cohorts to examine the changes in age at diagnosis.

Results: The study confirms increases in the prevalence by age of both autism spectrum disorder and childhood autism seen in other studies. There was, however, evidence for changes in the distribution of age at diagnose. Changes in age at diagnosis and differences in follow-up time between the two-year cohorts accounted for 52% of the apparent increase in Autism Spectrum Disorder (ASD) prevalence at age 3 in the 1996-97 cohort, and 66% of the apparent increase in ASD in the 1998-99 cohort, compared to the 1994-95 cohort.

Conclusions: Shifts in age of diagnosis, especially the substantial acceleration at younger ages, inflated the observed prevalence of autism in young children in the more recent cohorts compared to the oldest cohort.

103 126.18 Changes in Diagnostic Category among Affected Children in the Interactive Autism Network. A. M. Daniels* and P. Law, *Kennedy Krieger Institute*

Background: In the context of a growing number of children diagnosed with autism spectrum disorders, there is a need to better understand characteristics associated with a first ASD diagnosis, how these characteristics may differ by diagnostic subtype and how they may influence a change in ASD diagnosis.

Objectives: To summarize diagnostic characteristics of IAN Research participants by ASD sub-type and to explore factors associated with a change in ASD diagnosis.

Methods: As 9/11/07, self-report data on diagnostic and developmental history were collected from 4,675 affected children through an online instrument entitled the *Child with an ASD* Questionnaire. Bivariate logistic regression techniques were applied to identify factors associated with a change in ASD diagnosis. Multiple logistic regression was used to examine the strength of association between these factors and a change in ASD diagnosis after controlling for potential confounders.

Results: Results of this study show that diagnostic characteristics vary by ASD diagnosis. In addition, approximately 25%

(n=1,138) of all ASD children in IAN Research have a current diagnosis that differs from their first. These children are significantly less likely than their ASD peers to have a first ASD diagnosis of autism or Asperger's syndrome (OR 0.1, 95%CI 0.2-0.45 for autism, OR 0.9, 95%CI 0.2-0.43 for Asperger's syndrome). Furthermore, children whose ASD diagnosis changes are less likely to have been diagnosed by a clinical psychologist or a team of health professionals (OR 0.71, 95%CI 0.54-0.94, OR 0.59, 95%CI 0.44-0.80). These relationships remain statistically significant after controlling for current age, gender, race and other factors.

Conclusions: A change in ASD diagnosis among IAN participants is not uncommon. Findings from this study are of particular clinical and public health significance as they suggest that a change in ASD diagnosis depends upon both the symptomatology of the child and the context in which he/she is diagnosed.

104 126.19 The Study to Explore Early Development (SEED): a multi-site epidemiologic study by the Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE) Network. T. CADDRE Network*, *Centers for Disease Control and Prevention*

Background: In response to The Children's Health Act of 2000, the Centers for Disease Control and Prevention (CDC) funded five Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE) and a CADDRE Data Coordinating Center; CDC participates as a site in the CADDRE Network.

Objectives: The CADDRE Network designed SEED as a collaborative case-cohort study to address critical gaps in our understanding of potential causes of autism. This presentation provides an overview of SEED research goals, study approach and methods, and preliminary data regarding participant recruitment.

Methods: SEED is designed to investigate etiologic hypotheses related to infection/immune function, hormone function, and genetics, in case subgroups refined by autism phenotype; investigation of the roles of gastrointestinal features and socio-demographic factors in autism etiology and phenotypic variation are also primary research goals. Children with autism will be compared to children identified with other developmental problems and a random sample of all birth cohort children. Target enrollment is 2,700 children (ages 24-60 months, born September 2003 through August 2005) who were born in and currently reside in the 6 study site areas. Protocol development included site-specific advisory boards, parent focus groups, and scientific peer review to review study goals, design, materials, and feasibility.

Results: SEED implementation began December 2007. Data collection includes: 1) primary caregiver interviews and self-administered questionnaires, 2) medical record abstraction, 3) child developmental evaluation and physical exam, and 4) bio-sampling from biological parents and child.

Conclusions: SEED is the largest collaborative study of the causes of autism planned to date and will address a critical missing component in autism research: large, representative population-based studies that can answer multiple, high priority questions needed to determine the causes of and develop prevention strategies for this complex disorder.

105 126.20 Designed strategy for a prevalence study in Europe: EAIS proposal. M. Posada*[1], P. García-Primo[1], C. Martín-Arribas[1], M. J. Ferrari[1], L. Boada[1], E. García-Andrés[1] and A. Ramirez[2], (1)*RARE DISEASES RESEARCH INSTITUTE*, (2)*Children Therapy Centre - The Hope Project*

Background:
Rapid changes in prevalence of Autism Spectrum Disorders (ASD), from 4/10,000 to 66/ 10000 children in the last 20 years, have alerted the scientific community. Although the criteria for and awareness of autism definitions have changed over the years, these changes do not explain major differences in reported prevalence over time. One of the aims of the EAIS project, co-funded by the European

Commission, is to design a model for a harmonized and valid prevalence study to be used in European countries where insufficient information about prevalence is available.
Objectives:
To design a harmonized European Protocol for Autism Prevalence (EPAP).

Methods:
A general strategy including steps such as a general survey on ASD services and data accessibility, expert consultations, a checklist and a pilot feasibility study have been designed. This whole process has produced different drafts and reviews with several expert inputs until the final document has been achieved.

Results:
It is suggested to use a cross-sectional study, targeting children living within the participant European regions with age range from 6 to 10 years. The case definition is a child who fits the DSM-IV criteria codes F84.. Education, health and social services, both public and private, as well as parents' organizations, will be used as sources of information. Case ascertainment procedure will be organized in three different stages such as identification of potential cases, first approach to diagnosis and confirmation of the diagnosis. Specific details of the study as well as difficulties and limitations are also discussed. Eleven European countries have already shown their interest in participating in the pilot phase of this strategy.

Conclusions:

Due to European countries' different cultures, traditions and service provider organizations, a pilot feasibility study is needed in order to test the real possibilities of developing the prevalence estimate strategy, to guarantee a successful outcome.

106 126.21 Social Communication Competence and Functional Adaptation in a General Population of Children. D. H. Skuse*[1], W. Mandy[1], K. Lawrence[1], L. L. Miller[2], A. Emond[2] and J. Golding[2], (1)*Institute of Child Health*, (2)*University of Bristol*

Background: The incidence of autism seems to be increasing. Population estimates of prevalence may underestimate autistic characteristics of lesser severity, for two main reasons. First, cases are usually ascertained from secondary screening, based on initial selection of children with severe and obvious symptoms. Consequently, mild or moderate deficits in social and communicative competence may be missed, especially if associated with marked comorbidity such as conduct problems and ADHD. Second, methods of ascertainment are designed to maximise the distinction between valid cases of autism, defined according to conventional criteria, and to exclude conditions that do not quite reach diagnostic significance.

Objectives: The proportion of schoolchildren with mild deficits in social and communicative competence far exceeds the number diagnosed with an autistic spectrum disorder (ASD). We aimed to ascertain both the population distribution of such deficits, and their association with functional adaptation, in middle childhood.

Methods: Parents of children (7-8 years) in ALSPAC, the prospective Avon Longitudinal Study of Parents and Children, completed the Social and Communication Disorders Checklist (SCDC) (n=8094). We correlated severity of impairment with: i) cognitive abilities; ii) independent clinical diagnoses of ASD; iii) teacher ratings of maladaptive behaviour.

Results: SCDC scores were continuously distributed in the general population; boys had mean scores 30% higher than girls. Cases of ASD were predicted with a specificity of 91% and a sensitivity of 88%. Deficits in social and communicative competence were associated with functional impairment at school, especially in domains of ADHD and Conduct Disorders

Conclusions: Social and communicative deficits are of prognostic significance, in terms of behavioural adjustment at school, for both boys and girls. Their high prevalence in the general population emphasises the potential importance of measuring such traits, and evaluating their significance for management, among clinically referred children who do not meet diagnostic criteria for an ASD.

107 126.22 HOW CASE DEFINITIONS IMPACT PREVALENCE ESTIMATES OF AUTISM SPECTRUM DISORDERS. M. Y. Kaiser*, J. S. Durocher, V. Gonzalez and M. Alessandri, *University of Miami*

Background: There is the feeling that the prevalence of Autism Spectrum Disorders (ASDs) has been increasing in recent years. However, most US-based studies used different case definitions and a variety of age groups. In 2007, the Centers for Disease Control and Prevention (CDC) published prevalence estimates of 1 in 150 eight-year old children with ASD across 14 different sites all using the same case definition. This case definition was based on review of historical records and required evidence consistent with DSM-IV diagnostic criteria.

Objectives: To determine if applying different case definitions of ASD to the same group of children impacts prevalence estimates.

Methods: Four case definitions of ASD were applied to a sample of 127 children: 1) a parent-reported diagnosis of ASD, 2) first diagnosis given, 3) score on the SCQ, and 4) CDC record review case definition. Each case definition was applied to two age groups: 58 children ages 4-5 years and 69 children ages 6-7 years.

Results: Prevalence estimates differed by case definition. For 4-5 year olds, the prevalence estimates of ASD per 1000 were: 1) 1.40 using a parent-reported diagnosis, 2) .96 using ASD as the first diagnosis, 3) .99 using SCQ cutoff, and 4) 1.33 using CDC record review standards. Similar results were obtained for 6-7 year olds: 1) 1.66 using a parent-reported diagnosis, 2) 1.18 using ASD as the first diagnosis, 3) 1.33 using SCQ cutoff, and 4) 1.47 using CDC record review standards.

Conclusions: As expected, how studies define ASD has an impact on the resulting prevalence estimates. Estimates ranged from .96 to 1.66 when different definitions were applied to the same group of children. Differences within and across age groups will be discussed in addition to implications for clinical and policy practices.

108 126.23 GENDER DIFFERNCES IN AUTISM SPECTRUM DISORDER CLASSIFICATION WITHIN A COMMUNITY BASED SAMPLE. J. S. Durocher*, M. Y. Kaiser, V. Gonzalez and M. Alessandri, *University of Miami*

Background: The widely accepted gender ratio in Autism Spectrum Disorders (ASDs) is approximately 4:1 (boys:girls). Recent studies suggest rates rangoing from 2.8:1 to 5.5:1 based on review of historical records and as high as 8:1 based on special education placement.

Objectives: To determine gender differences in ASD classification based on case definition and symptom presentation.

Methods: Participants included 197 children (ages 4-9) who participated in a larger prevalence study in south Florida. We examined the gender ratios obtained by applying different case definitions of ASD including: 1) parent-reported ASD diagnosis, 2) first diagnosis received, 3) score on SCQ and 4) historical record review. We also examined agreement between SCQ and record review classifications across gender.

Results: The male:female ratios for three case definitions were similar: 6.5:1 for parent-reported ASD diagnosis, 6.3:1 for ASD as first diagnosis and 6.8:1 for SCQ score. However, the ratio was much higher (8.1:1) using historical record review. The agreement between SCQ and record review classification was 75% for boys, but only 63% for girls.

Conclusions: Results indicate that gender ratios are affected by case definition and may be higher than previously reported. It may also be that girls are under-identified using certain criteria. In order to further explore these findings, we will also examine differences in symptom presentation, school eligibility and type and source of first diagnosis. Implications for policy and clinical practice will also be discussed.

109 126.24 Informatics for the National Study to Explore Early Development (SEED). J. E. Siebert, J. D. Bonner*, M. F. Kuhn, P. A.

Thompson, K. L. Marable, G. B. Jensen, T. L. Holland, S. J. Sharp and M. H. Rahbar, *Michigan State University*

Background:
The national *Study to Explore Early Development* (Seed) is a multi-year multi-site autism study of several thousand families which commenced enrollment December 2007. SEED will be the largest study to date elucidating the etiology of autism in the US. Michigan State University serves as the data coordinating center, and develops and hosts the *CADDRE Information System* (CIS). This poster exhibit presents the implementation of the CIS, and an assessment of the initial 5 months of SEED experience with CIS.

Objectives:
- Implement a secure, centralized, web-based, automated workflow system to improve study quality by standardizing workflows and processes across all study sites and providing end-to-end data management.
- Assess the performance of the CIS.

Methods:
Use Case Analysis identified the functional requirements. Workflow automation is driven by individual- and role-based dynamic task lists and a flexible event generation system. An Entity-Attribute-Value data collector provides rapid deployment of forms and phone interviews (CATI), meta-data and codebook management. Integration with *Internet System for Assessing Autistic Children* (ISAAC, Autism Speaks) supports data collection of copyrighted instruments and automated scoring. Personally identifying information is encrypted in the database. Internet communications are encrypted.

Results:
CIS supports all study activities: batch import, subject recruitment tracing and tracking, mailings, incentives, reimbursements, barcodes, data entry (double-data entry and CATI), instrument scoring, biosample management, medical record abstraction and request tracking, scheduling, QC workflows, core laboratory integration, data management tools, and many study management and QC reports. Over 25,000 study data elements are now captured in the CIS. Metrics detailing the CIS performance over the first 5 months of study production are presented.

Conclusions:
The workflow-oriented CIS represents a modern multi-site study information system that enforces standardized study procedures with the expectation of improved data quality and consistent protocol execution.

Sponsor: *Centers for Disease Control and Prevention* USA

110 126.25 LINKING TOXICOLOGY LITERATURE TO AUTISM RESEARCH: A BIBLIOMETRIC CONTRIBUTION TO A TRANSLATIONAL RESEARCH CHALLENGE. M. Herbert*[1], A. P. Ringer[1] and M. A. Corrales[2], (1)*Mass Gen Hosp/Harvard Med School*, (2)*US Environmental Protection Agency (identification only)*

Background: While autism spectrum disorders likely arise from gene-environment interactions, environmental risk factors are greatly underrepresented in ASD literature, with the possible exception of articles on thimerosal and vaccines.

Objectives: To quantify the share of autism research literature devoted to various types of chemical substances, such as endogenous biological substances, exogenous potential risk factors, and medications. Furthermore, to present a tabular and graphical overview of chemicals in toxicology or epidemiology literature that have been associated with biological effects relevant to autism.

Methods: 1) All autism literature indexed in PubMed was searched for publications relating autism to chemical substances, and substances were classified as medications, pollutants, or other, and then subclassified. 2) Literature in toxicology and epidemiology potentially relevant to autism was identified, based on a) risk factors for behavioral or cognitive symptoms of autism, and b) risk factors for physiological or molecular features of autism.

Results: Most autism literature that focuses on the molecular level addresses pharmaceuticals or genetics. There is almost no investigation of

potential chemical risk factors beyond thimerosal and vaccines. Conversely, although substantial toxicology and epidemiology literature identifies chemical risk factors for features found in autism, (e.g. altered monoamine levels, PPI deficit, hyperactivity, anxiety) almost none of this literature is explicitly focused on autism. For example, since the 1980s, endosulfan has been known to affect serotonin, GABA receptors, and dopamine, but it has been investigated in connection with autism only very recently in one small study. Similar observations relate to the immune system.

Conclusions: Translational linkage of knowledge about exogenous substances that may cause or contribute to autism-pertinent endpoints will require expansion of substance-related research in autism guided by existing literatures in toxicology and epidemiology, as well as inclusion of more specifically autism-related endpoints in toxicology and epidemiology.

127 A Strategic Plan for Autism Research

Speaker: T. Insel*National Institutes of Health*

Invited Educational Symposia Program

128 Reflections on the Mirror Neuron Hypothesis of Autism: Lighting the Way Forward

Organizer: J. H. G. Williams*University of Aberdeen*

Speakers: C. Keysers[1]L. Oberman[2]J. Grezes[3]J. H. G. Williams[4]I. Smith[5](1)*University Medical Center Groningen*, (2)*Beth Israel Deaconess Medical Center*, (3)*Ecole Normale Supérieure*, (4)*University of Aberdeen*, (5)*Dalhousie University*

Recognizing commonalities in action and behaviour between ourselves and others may be a very important prerequisite for social understanding and development. It is important for understanding when and how other people will behave as we do and is a starting point for learning from others by watching them. This capacity may be impaired in autism. Such ideas first gave rise to the self-other matching hypothesis of autism, and later, the mirror neuron hypothesis of autism. The last few years have seen much interest in mirror neurons and studies in human and non-human primates. This symposium will consider the roles of mirror neurons and other brain areas in self-other matching functions, including empathy, imitation, joint attention, mentalizing and auditory-visual integration. Finally, the relevance of this work to clinical practice will be discussed.

128.1 Introductory Remarks.

128.2 From Mirror Neurons to Empathy and Autism. C. Keysers*[1], J. A. C. J. Bastiaansen[2], V. Gazzola[1] and M. A. Thioux[1], (1)*University Medical Center Groningen*, (2)*Lentis*

How do we understand other people's thoughts and feelings? We will show how in monkeys, mirror neurons transform the sight and the sound of goal directed actions performed by other individuals into corresponding motor programs. We will show that in humans as well, the vision and the sound of goal directed actions activates regions involved in the execution of similar actions. We will then show that observing dynamic facial expressions triggers activity in regions of the premotor cortex irrespective of the type of expression (emotional or neutral). This phenomenon probably corresponds to the neural correlate of facial mimicry. If the facial expression is emotional, the activity spreads to the anterior insula involved in experiencing similar emotions, a phenomenon probably akin to emotional contagion. Participants that score higher on psychological measures of empathy activate their premotor and emotion regions more strongly while perceiving the actions and emotions of other individuals. To conclude, we will briefly show data that suggests that high functioning adults with autism spectrum disorders activate the premotor and emotional regions more strongly than matched control subjects in response to dynamic facial expressions. This last finding, that will be described in more detail in a separate contribution at the same conference, seems to challenge the idea that mirroring is grossly

and generally impaired in autism, and may point towards an alternative explanation according to which dynamic facial expressions may cause an overreaction of the autistic brain that renders social interactions unpleasant.

128.3 Electrophysiological indexes of mirroring in ASD and neurotypical individuals. L. Oberman*, *Beth Israel Deaconess Medical Center*

Long before the term "mirror neuron" was coined in the mid 1990's evidence for a shared motor observation-execution mechanism could be found in the human EEG and EMG literature. Studies dating back to 1954 find that, similar to mirror neurons, EEG mu oscillations respond specifically to self-performed, observed and imagined actions (Cochin, Barthelemy, Lejeune, Roux, & Martineau, 1998; Gastaut&Bert, 1954; Pineda et al., 2000). Behavioral and EMG Studies as early as those performed by Darwin indicate that when individuals are in the presence of others, the observer tends to synchronize his or her movements to match those of the others (Condon & Ogston, 1967; Darwin, 1872/1965; Kendon, 1970). Upon the discovery of the mirror neuron system (MNS) in the macaque by Rizzolatti and colleagues (Di Pellegrino et al., 1992) using single-unit electrophysiology, researchers began to wonder if these newly discovered neurons may underlie the electrophysiological findings from decades prior. This presentation will discuss recent studies investigating the MNS in typically developing individuals as well as individuals with ASD through the use of EEG and EMG. These electrophysiological indices provide a noninvasive, inexpensive option that is well suited for use with clinical populations. Findings suggest that there is a dysfunction in the MNS in ASD, however, our studies suggest that this dysfunction is not likely to be primary, but rather an indirect consequence of abnormalities in developmental mechanisms involved in cortical plasticity.

128.4 Understanding non verbal signals in social interactions. J. Grezes*, *Ecole Normale Supérieure*

Social exchange is a critical component of everyday life. It depends on an ability to predict and infer the mental states of others, such as their emotions, beliefs and intentions, from the perception of their motor behaviours. Impaired use of these nonverbal social signals is a core feature in autistic spectrum disorder. There are currently many lines of research on the possible origin of these problems in social communication. Some authors think that the social deficit could be a consequence of amygdala, fusiform and / or superior temporal sulcus dysfunction leading to functional abnormalities that impair the ability to detect socially relevant visual cues. Another model speculates that this impairment could be the consequence of a malfunctioning mirror system generating a deficit in the ability to represent the actions of others. In this presentation, we will review and present neuroimaging studies that explored the neural basis of everyday human competence to understand the actions, intentions and emotions of others. The aims are to clarify to what extent this ability rely on the mirror neuron system, to assess inter-individual differences in these processes and finally to address the questions of the interactions between the mirror neuron and the emotional systems.

128.5 Contributions of mirror neurons to imitation and joint attention. J. H. G. Williams*, *University of Aberdeen*

The role of the 'mirror neuron system' (MNS) in social learning is likely to be complex, and attempts to place mirror neurons at the centre of a single primary deficit model are unlikely to be helpful. Rather, the contributions of the MNS to social learning, occur in concert with other brain functions and vary according to the social cognitive function and action features. Exploring the different ways that the MNS contributes to these functions, and how they are disrupted in autism, is more likely to be fruitful. For example, MNS functioning in imitation as a form of motor learning, may differ from the way it functions in 'automatic' imitation or emotional contagion. MNS involvement in joint attention and attention to social stimuli is likely to differ further. This may impact upon different roles for the MNS in belief understanding and empathy.
In this presentation, two networks will be discussed. The first network concerns the contribution of the MNS to the motor learning network during imitation. The second network concerns the contribution of MNS to joint

attention and perceptual sensitivity to others' actions. Both networks are likely to rely on connectivity with the orbitofrontal cortex and amygdala, but perhaps with differential recruitment of parietal cortex and Broca's area. Brain areas serving 'theory of mind', cognitive integration and biological motion processing are likely to be differentially networked with the mirror neuron system in imitation learning and joint attention.

128.6 Are mirror neurons relevant to clinical practice?. I. Smith*, *Dalhousie University*

The discussant will address the implications of mirror neuron system research for clinical practice in autistic spectrum disorders. To what extent do the findings or theories generated by mirror neuron research illuminate clinical phenomena observed in persons with ASD? Do they have any more direct implications for practice? For example, do mirror neuron system accounts of impaired imitation and empathy enhance clinicians' ability to understand, assess or treat ASD? Discussion will focus in particular on the developmental nature of ASD.

Roundtable Program

129 How to choose between diagnostic tools?

Moderator: H. McConachie*Newcastle University*

Speakers: A. S. Le Couteur[1]J. Gould[2]D. H. Skuse[3]S. J. Wheelwright[4]S. Risi[5]D. Bishop[6](1)*Newcastle University*, (2)*National Autistic Society*, (3)*Institute of Child Health*, (4)*University of Cambridge*, (5)*University of Michigan*, (6)*University of Oxford*

The aim of the session is to consider the strengths and weaknesses of the main diagnostic instruments currently in use in the field of autism. Five contributors will each present information about the measure they have been involved in developing. They will briefly describe its theoretical framework, aims, scope, development process, and data on training of assessors, usage, and validity from recent research. The discussant is asked to sum up the strengths and weaknesses of the instruments with reference to research and to clinical practice. The discussant will then facilitate large-group consideration of what should be the 'gold standard' diagnostic tools and process followed in applications for major research funding in studies with clinical and non-clinical samples. (Currently ADOS and ADI-R are the essential tools in NIH National Database for Autism Research.) If time allows, there may be consideration of what should be the minimum diagnostic process described as followed in studies submitted for publication.

Oral Presentations Program

130 Clinical Phenotype 2

130.1 Maternal Resolution of the Child's ASD Diagnosis: Relationship with Maternal Emotional Availability and Child Attachment. S. Dolev*[1], D. Oppenheim[2], N. Koren-Karie[2] and N. Yirmiya[3], (1)*The Hebrew University of Jerusalem & Oranim Teacher's College*, (2)*Haifa University*, (3)*Department of Psychology and School of Education, The Hebrew University of Jerusalem*

Background: Receiving a diagnosis of ASD for one's child is a painful experience for parents, one that requires that they realign their thoughts, feelings, and expectations regarding the child. Such realignment, also referred to as "resolution" of the diagnosis, is necessary in order to provide caregiving that is matched to the child's needs and challenges. Resolution is therefore hypothesized to foster maternal emotionally-available behavior toward the child and secure child-parent attachment.

Objectives: To examine whether indeed mothers' resolution of the ASD diagnosis of their children is related to their emotional availability during play interactions with their children and to secure child-mother attachments.

Methods: 45 boys diagnosed with AD or PDD-NOS (ages 32-69 months) and their mothers participated in the study. Mothers' resolution of their children's diagnoses was assessed using the *Reaction to Diagnosis Interview*. Mothers' emotional availability was assessed using the *Emotional Availability Scales* applied to three play interactions. Finally, the attachment of the children to the mothers was

assessed using the *Strange Situation Procedure*.

Results: Mothers who were resolved with regard to their children's diagnosis were more sensitive to their children's signals and structured their interactions better than mothers who were unresolved. Additionally, children of resolved mothers were more likely to be securely attached than children of unresolved mothers. These associations held over and above the effects of the severity of children's diagnosis (AD vs. PDD-NOS) and level of functioning (low vs. high).

Conclusions: Maternal resolution of the child's diagnosis is associated with (a) more optimal caregiving behavior in mothers of young children with ASD and (b) secure child-mother attachment. These findings have important implications for our understanding of the socio-emotional development of young children with ASD. Clinically the findings stress the importance of helping parents come to terms with their children's ASD diagnosis.

130.2 Altered tryptophan metabolism in autistic children may account for the paradox of elevated plasma serotonin and depressed central serotonergic function. A. Boasso*[1], D. Fuchs[2], S. J. Spence[3], A. Thurm[3], G. M. Shearer[1] and S. E. Swedo[3], (1)*National Institutes of Health - National Cancer Institute*, (2)*Innsbruck Medical University*, (3)*National Institutes of Health - National Institute of Mental Health*

Background: 30-50% of autistic children show increased blood levels of the neurotransmitter serotonin, despite depressed serotonergic function in the central nervous system (CNS). Serotonin is synthesized in the CNS and in the gut from the essential amino acid tryptophan, which can be also degraded into kynurenine. Blood serotonin derives from the gut and, in contrast to tryptophan, cannot cross the blood-brain barrier (BBB).
Objectives: We investigated alterations of the tryptophan-kynurenine catabolic pathway in autistic children.
Methods: Blood (N=22) and cerebrospinal fluid (CSF) (N=11) samples were collected from autistic children (AUT) ages 2-6 years. Blood samples from age-matched typically-developing children (TD; N=16) and from children with developmental delay not associated with autism (DD; N=4) were also collected. We measured plasma and CSF tryptophan and kynurenine, as well as leukocyte mRNA expression of the tryptophan-to-kynurenine catabolizing enzyme indoleamine 2,3 dioxygenase (IDO) and of its inducer interferon-g.
Results: Plasma and CSF tryptophan were directly correlated (P=0.19), consistent with the permeability of the BBB to the amino acid. Kynurenine was undetectable in CSF (<0.4mmol/L). Plasma tryptophan was significantly reduced in the AUT, but not DD, groups compared to TD ($p=4.6x10^{-5}$ and $5.1x10^{-5}$). Surprisingly, plasma kynurenine levels were also reduced in the AUT group compared to TD (p=0.003). No differences were observed for IDO and interferon-g expression, suggesting that the reduction of tryptophan was not due to IDO-mediated degradation.
Conclusions: Low plasma tryptophan may result in its limited availability for serotonin production in the CNS, negatively affecting serotonergic function in young children with autism. Reduced plasma kynurenine suggests that tryptophan may be preferentially diverted to other pathways in the periphery, most likely toward gut-associated production of serotonin, which does not cross the BBB nor contribute to serotonergic function in the CNS.

130.3 Relationship between ASD Diagnosis and Developmental, Psychiatric, Medical, and Concurrent Diagnoses or Symptoms in Children Age 8 Years in 2002. S. E. Levy*[1], L. C. Lee[2], E. Giarelli[3], L. Schieve[4], R. S. Kirby[5], C. Cuniff[6], J. A. Reaven[7], J. Nicholas[8], J. Pinto-Martin[3] and C. E. Rice[4], (1)*Children's Hospital of Philadelphia*, (2)*Johns Hopkins Univ. School of Public Health*, (3)*University of Pennsylvania*, (4)*National Center on Birth Defects and Developmental Disabilities*, (5)*University of Alabama at Birmingham*, (6)*University of Arizona College of Medicine*, (7)*University of Colorado Health Sciences Center*, (8)*Medical University of South Carolina*

Background: Few studies have examined the population-based prevalence of concurrent medical, developmental, and/or psychiatric conditions in children with ASD; however,

studies of referred populations support high frequencies.

Objectives: To examine concurrent diagnoses and symptoms in a population-based sample of 8-year-old children.

Methods: Data were collected by 13 surveillance programs in the Autism and Developmental Disabilities Monitoring (ADDM) Network. Information was abstracted from existing clinical and education evaluation records of 8 year-old children with an indication of an ASD or related condition and reviewed by trained clinicians. This study included 2568 children who met the surveillance case definition for ASD; 73% had been classified with autism or ASD previously.

Results: Eighty-one percent of study children were male; 63% white, 23% black, 14% Hispanic, Asian, or not stated. ASD was classified before age 3 years for 13%, between ages 3-5 years for 23%, after age 5 years for 29%, and age was not specified for 8%. No previous ASD diagnosis or educational eligibility was recorded in evaluation records for 27%, but they had behavioral descriptions consistent with DSM-IV-TR criteria for ASD (and in 41%, suspicion of ASD was also noted). Overall, the prevalence of ³1 concurrent non-ASD developmental diagnoses was 83%, ³1 psychiatric diagnoses was 10%, ³1 medical diagnoses or symptoms was 18%, and a possibly causative genetic or neurologic diagnosis was 4%. For any type of concurrent diagnoses 14.8% of children had none, 59.6% had one and 25.7% had 2 or more. Children with ASD classification based on behavioral description (not a previously documented clinician diagnosis) were more likely to have all four types of concurrent diagnoses than children with a previously documented diagnosis or classification.

Conclusions: Improved understanding of high frequency of co-occurring conditions among children with ASD has implications for understanding etiology, recognition and appropriate treatment of ASD.

130.4 THE AUTISM DIAGNOSTIC OBSERVATION SCHEDULE (ADOS): STANDARDIZING SCORES FOR A MEASURE OF ASD SEVERITY. K. Gotham*, S. Risi and C. Lord, *University of Michigan Autism and Communication Disorders Center*

Background: At IMFAR 2006, we reported our work in standardizing raw ADOS total scores from a large dataset to approximate a severity metric for the construct of 'Autism' as it is measured on this instrument. We are now approaching this pursuit with changed methodology.

Objectives: To estimate severity of autism using ADOS scores that have been normalized to reduce the effects of verbal level, chronological age, and IQ.

Methods: Analyses were conducted using ADOS and psychometric data for 1415 children aged 2 to 16 years, some with repeated assessments for a total of 2195 cases. The ASD sample (N=1786 cases) was divided into cells determined by chronological age and language level. Previously, calibrated scores were generated based on percentiles of raw ADOS totals within each cell. In the revised approach, severity scores were based on raw total percentiles corresponding to each diagnostic classification within each age/language cell.

Results: Preliminary findings indicate that new calibrated scores (1) allow comparison of assessments across raters, modules, and time; (2) provide a means of assessing the relationship between severity in ASD and verbal and nonverbal IQ; and (3) may offer another option for identifying homogeneous groups of individuals with ASD for genetic and neurobiological research.

Conclusions: Calibrated severity scores should be replicated in large independent samples, and tested for validity in predicting outcome (treatment responsiveness, school achievement and placement, eventual independence, etc.) in children with ASD.

130.5 Racial and Ethnic Disparities in the Identification of Children with Autism Spectrum Disorders. D. S. Mandell*[1], L. D. Wiggins[2], L. A. Carpenter[3], C. DiGuiseppi[4], M. Durkin[5], E. Giarelli[6], M. J. Morrier[7], J. S. Nicholas[3], J. Pinto-Martin[6], P. Shattuck[8], K. C. Thomas[9], M. Yeargin-Allsopp[10] and R. S. Kirby[11], (1)*University of Pennsylvania School*

of Medicine, (2)*Centers for Disease Control and Prevention*, (3)*Medical University of South Carolina*, (4)*University of Colorado, Denver*, (5)*University of Wisconsin-Madison*, (6)*University of Pennsylvania*, (7)*Emory University*, (8)*Washington University*, (9)*University of North Carolina at Chapel Hill*, (10)*Centers for Disease Control & Prevention*, (11)*University of Alabama at Birmingham*

Background: Delayed and missed diagnosis of ASD may be exacerbated among medically underserved ethnic and racial minorities. Studies examining racial and ethnic differences in the age and accuracy of identification of ASD have produced mixed results, but are limited in that they relied on clinical samples in which subjects already had a putative diagnosis of ASD, rather than relying on population-based samples.

Objectives: to examine racial and ethnic disparities in the recognition of ASD in a population-based sample

Methods: Within a multi-site surveillance network, 2,568 8-year-old children were identified as meeting research criteria for ASD through screening and abstraction of evaluation records from multiple sources. Using logistic regression with random effects for site, we estimated the association between race/ethnicity and documented ASD, adjusting for sex, intelligence quotient (IQ), birth weight and maternal education.

Results: 58% of the sample had a documented ASD. In adjusted analyses, children who were black (odds ratio [OR] = 0.78; 95% confidence interval, 0.64 to 0.96), Hispanic (OR = 0.75; 0.55 to 0.99) or other ethnicity (OR = 0.65; 0.44 to 0.97) were less likely than white children to have a documented ASD. The extent of disparities varied as a function of the interaction of intellectual disability and race/ethnicity.

Conclusions: This study demonstrates racial and ethnic disparities in the recognition of ASD. The presence of intellectual disability among children wtih ASD may affect clinicians' and educators' further assessment. Our findings suggest the need for continued professional and caregiver education.

130.6 Identifying Very Early Behavioral Predictors of Autism Spectrum Disorder (ASD) in NICU Infants. J. M. Gardner*, B. Z. Karmel, L. D. Swensen, I. L. Cohen, E. M. Lennon, P. M. Kittler, R. L. Freedland, M. J. Flory and E. London, *NYS Institute for Basic Research in Developmental Disabilities*

Background: Infants with obstetric/neonatal complications may be at higher risk for ASD. Our longitudinal studies evaluate development of attention, motor, and regulatory mechanisms from birth in NICU infants. Evaluation of records from 1995-present indicated ~1.5% of our population with ASD, with higher % after 2000 (1% vs 2%, $p<.5$); ~1/3 diagnosed at IBR, 2/3 by education/community resources.

Objectives: To identify useful behavioral predictors of ASD during early infancy.

Methods: NICU infants later diagnosed with ASD (n=37) were compared to non-ASD (n=2342) children on a range of behaviors from birth to 3 1/2 years.

Results: ASD children were predominantly male, with higher-educated mothers. They were born at lower gestational age and birthweight, but did not differ on intrauterine growth, Apgar Scores, or CNS involvement. In analyses controlling gender, CNS severity, and maternal education, ASD children exhibited a pattern of behavioral deficits starting in the newborn period. Their neonatal neurobehavior at 1 month (adjusted) showed higher incidences of visual asymmetry, increased hypertonicity in arms, but better head extension (p's<.1). They also had poorer arousal modulation of visual attention at 4 months (adjusted) ($p<.001$), showing greater stimulus seeking more similar to younger or cocaine-exposed infants. Bayley-II motor and mental scores were lower starting at 7 and 10 months, respectively. After 2 years, deficits were found, with increased incidence of middle/high arm guard during gait analyses, and with lower scores on Griffiths Mental Development Scales.

Conclusions: As early as newborns, infants later diagnosed with ASD may form a distinct sub-population within NICU-assigned babies, with atypical development of visual, motor,

and regulatory processes compared to other high-risk infants. Furthermore, disintegration on standardized testing may be expected as early as 7 months, which typically only occurs in infants with the most severe CNS pathology. These differences may be indicative of precursors to ASD at older ages.

130.7 Associations of Postural Knowledge and Basic Motor Skill With Dyspraxia In Autism: Implication for Abnormalities in Distributed Connectivity and Motor Learning. L. R. Dowell, E. M. Mahone and S. H. Mostofsky*, *Kennedy Krieger Institute*

Background: Children with autism often have difficulty performing skilled movements. This "dyspraxia" remains significant after accounting for basic motor skill deficits (Dziuk et al., 2007). Performance of skilled movements also requires knowledge of spatial and temporal representations of the movement, mediated by parietal regions, and transcoding of these spatial representations into movement plans, mediated by premotor circuits. Objectives: The goals of this study were: (1) to determine whether autism is associated with impaired representational knowledge of skilled movements ("postural knowledge") and (2) to examine the combined contributions of postural knowledge and basic motor skill to dyspraxia in autism. Methods: 34 children with HFA and 37 typically-developing (TD) children, ages 8-13, completed: (1) a postural knowledge test (PKT), a praxis discrimination test assessing knowledge of transitive/intransitive postures (2) a childhood examination of basic motor skills (the PANESS), and (3) a praxis examination including gestures to command, imitation, and tool-use. Results: Children with HFA showed worse postural knowledge than TD controls ($F=5.350$, $p=.2$). Hierarchical regression further revealed, that after controlling for age and IQ, both basic motor skill ($\Delta R2=.11$ $p=.004$) and postural knowledge ($\Delta R2=0.16$ $p<0.0001$) were significant predictors of praxis performance; nevertheless, the HFA group continued to show significantly poorer praxis than controls after accounting for these abilities ($\Delta R2=0.19$, $p<0.0001$). Conclusions: The findings suggest that dyspraxia in autism is associated with both impaired formation of spatial representation, as well as transcoding and execution, of skilled movements. This would be consistent with a model in which distributed abnormality across parietal, premotor and motor circuitry, and/or connectivity between these regions, contributes to dyspraxia in autism. The findings might also be explained by a developmental model in which impaired acquisition (learning) leads to anomalous formation of both spatial and motor representations of skilled movements, as well as impaired execution.

130.8 Immune Comorbidities in Children with Autism Spectrum Disorders. L. A. Croen*[1], L. L. Tee[1], B. Fireman[1], A. Leong[1], L. F. Barcellos[2] and P. Bernal[1], (1)*Kaiser Permanente*, (2)*UC Berkeley School of Public Health*

Background: Immune system disturbances have been reported in several clinical studies of autism, and the presence of immune-related illnesses are frequently described by parents and providers. However, population-based data on the prevalence of immune comorbidities among children with autism are lacking.
Objectives: To determine the prevalence of immune comorbidities in individuals with autism, investigate whether these conditions occur more often than expected, and explore the timing of onset in relation to the autism diagnosis.
Methods: We conducted an observational study among the membership of Kaiser Permanente (KP) in Northern California. Individuals born from 1980 to 2003 with a minimum of one year KP membership were eligible for inclusion. All children with at least two autism diagnoses recorded in outpatient records between the ages of 3-18 were identified (n=5,565). A comparison group of children without autism was randomly sampled at a ratio of 5 to 1, matched to case children on year of birth, sex, and length of KP membership (n=27,825). The main outcomes - asthma, allergies, and autoimmune diseases - were identified from KP inpatient and outpatient databases. Chi-square tests were used to evaluate case-control differences.

Results: Overall, immune-related conditions were diagnosed with equal frequency among children with autism and controls (28.6% vs. 27.6%, P=0.11). However, allergies and

autoimmune diseases were diagnosed significantly more often among children with autism than controls (allergy: 20.6% vs. 17.7%, P<0.0001; autoimmune disease: 1% vs. 0.76%, P=0.4), and asthma was diagnosed significantly less often (13.7% vs. 15.9%, P<0.0001). Psoriasis was the most frequently diagnosed autoimmune condition among children with autism, and it occurred over twice as often in cases as controls (0.34% vs. 0.15%, P<0.0018).

Conclusions: These results support previous observations that children with autism have somewhat elevated rates of specific immune-related comorbidities, and improve our understanding of the biomedical correlates of the autism phenotype.

Oral Presentations Program

131 Human Genetic Studies

131.1 Further Evidence Supporting Oxytocin Receptor in an Irish Sample. K. Tansey*, R. Anney, L. E. Cochrane, M. Gill and L. Gallagher, *Trinity College Dublin, Ireland*

Background: The neuropeptides oxytocin and vasopressin have recently been implicated in the aetiology of autism. Both have effects on behaviour and physiology especially in relation to social bonding. Furthermore, both are modulated by the sex hormones, which heighten their candidacy for a role in autism where the ratio of affected males to affected females is highly skewed (4:1). **Objectives:** To examine the genetic variation within the oxytocin and vasopressin receptor in the Irish autism sample. **Methods:** Tagging SNPs in the oxytocin receptor (OXTR) and VNTRs in the arginine vasopressin receptor 1A (AVPR1A) were analyzed in the Irish autism sample, a sample of 179 parent-child trios. **Results:** Prior to correction for multiple testing, associations between OXTR and autism were found with 3 markers (rs11720238 p=0.31, rs7632287 p=0.0076, and rs4564970 p=0.0091). Two SNPs in OXTR showed association with a high functioning subset of the sample after a multiple permutation testing (rs11720238 p= 0.25 and rs7632287 p=0.0042) based on a cluster analysis of the clinical sample. **Conclusions:** These results confirm the importance of oxytocin receptor in the aetiology of autism.

131.2 Autism Associated Alleles Affect the Regulation of the Homeobox Gene, ENGRAILED 2. R. Benayed[1], J. Choi[1], P. G. Matteson[1], N. Gharani[2], S. Kamdar[1], V. Vieland[3], L. Brzustowicz[2] and J. H. Millonig*[1], (1)*UMDNJ-Robert Wood Johnson Medical School*, (2)*Rutgers University*, (3)*The Research Institute at Nationwide Children's Hospital*

Background: Our previous analysis demonstrated that two intronic SNPs (rs1861972 and rs1861973) in the homeobox transcription factor, ENGRAILED 2 (EN2), are significantly associated both individually and as a haplotype with Autism Spectrum Disorder (ASD). This was observed in three separate datasets indicating that EN2 is a likely ASD susceptibility gene (Gharani et al., 2004; Benayed et al., 2005). Objectives: The goal of our study was two-fold: to identify candidate risk alleles by extending our linkage disequilibrium (LD) map and testing these candidates for function by standard molecular genetic approaches. Methods: To extend our LD map additional EN2 polymorphisms were typed and publicly available Hapmap data analyzed. Candidate risk alleles were then tested for functional differences by luciferase assays and EMSAs. Results: The LD mapping determined that the associated SNPs are not in high LD (r2<.370) with any typed polymorphisms, identifying rs1861972 and rs1861973 as candidate risk alleles. The EN2 intron was then tested for transcriptional activity by transfecting appropriate luciferase constructs in three different cell types: primary mouse cerebellar neurons, a neuronal cell line (PC12) and a non-neuronal cell line (HEK293T). This analysis demonstrated that the EN2 intron acts as a transcriptional repressor in all three cell types (P<.00005; two tailed paired Student's T test). To test for functional differences between haplotypes, both versions of the intron were cloned into luciferase constructs with two different promoters and transfected into the same three cell types. In all cases the autism-associated alleles result in weaker repressor activity (P<.005). EMSAs were performed for both SNPs individually and uncovered differential binding of proteins to both associated alleles,

providing a molecular mechanism for the transcriptional difference. . Conclusions: These studies present additional evidence that the associated EN2 haplotype is functional and a likely common genetic risk factor for ASD.

131.3 Association of familial autism with imprinted locus on 7q32. E. Korvatska* and G. D. Schellenberg, *University of Washington*

Background: A strong genetic component of autism is being approached by linkage analysis, candidate gene association studies, and, most recently, by analysis of copy-number variations and whole-genome associations. Given multiple linkage signals found across the human genome, most findings cannot be replicated on different populations. Linkage to 7q is by far the most robust finding in autism. Recently, linkage signal on 7q32 was replicated in two independent studies including ours.

Objectives: To search for susceptibility genes within the large genetic interval (20 cM) identified by linkage we performed association analysis of selected candidate genes.

Methods: 350 multiplex autistic families were subjected to transmission disequilibrium test (TDT) analysis.

Results: We detected an association with ~220 kb interval situated right under the linkage peak. Signals arose from multiple SNPs comprising several haploblocks with the largest one extending over 100 kb. The associated region contains 5 protein-coding genes, and 4 of which are expressed in the brain. At least 3 of 5 candidate genes are imprinted in human and mouse. Mutations affecting coding sequences/splice sites of 7q32 candidate genes have been searched by sequencing of 100 autists and 100 control individuals.

Conclusions: We identified a new candidate region for autism on 7q32. The associated locus contains several imprinted genes. The involvement of epigenetic component - altered imprinting in autism may explain increasing incidence of the disorder.

131.4 Genetic analyses of serotonergic factors in autism. K. Nakamura*[1], A. Ayyappan[1], K. Yamada[2], S. Suda[1], M. Tsujii[3], Y. Iwayama[2], T. Miyachi[1], H. Matsuzaki[4], K. Tsuchiya[1], T. Sugiyama[5], N. Takei[1], T. Yoshikawa[2] and N. Mori[1], (1)*Hamamatsu University School of Medicine*, (2)*RIKEN Brain Science Institute*, (3)*Chukyo University*, (4)*Graduate School of Medicine, Osaka University*, (5)*Aichi Chilren's Health and Medical Center*

Background: autism is a pervasive developmental disorder diagnosed in early childhood. Abnormalities of serotonergic neurotransmission have been reported in autism. Serotonin transporter (SERT) modulates serotonin levels, and is a major therapeutic target in autism. Factors that regulate SERT expression might be implicated in the pathophysiology of autism.

Objectives: SERT expression in *Drosophila* is reported to be regulated by the roundabout axon guidance molecule, *robo*; ROBO proteins (ROBO1, 2, 3, and 4) play a vital role in mammalian neurodevelopment also. We examined the associations of *ROBO* genes with autism, in a trios association study. Further, we compared the mRNA expressions of *ROBO* genes in the autistic patients and control subjects.

Methods: DNA samples from trio families recruited to the AGRE were used for this study; 252 trio families, with male offspring scored for autism, were selected. Genotypes were determined in ABI PRISM 7900HT Sequence Detection System. One-way analysis of variance was used to examine the variability in the distribution of ADI-R phenotypic data. We further compared the mRNA expressions of *ROBO* genes in the lymphocytes of 19 drug-naïve autistic patients and 20 matched controls.

Results: four SNPs of *ROBO3* (rs3923890, p=0.23; rs7925879, p=0.17; rs4606490, p=0.33 and rs3802905, p=0.49) and a single SNP of *ROBO4* (rs6590109, p=0.009) showed significant associations with autism, by transmission disequilibrium test; the A/A genotype of rs3923890 showed lower ADI-R_A scores, which reflect social interaction. Significant haplotype associations were also observed for *ROBO3* and *ROBO4*. Expressions of *ROBO1* (p=0.18) and *ROBO2* (p=0.23) were significantly reduced in the autistic group; the possibility of using the altered expressions of

ROBO as peripheral markers for autism, may be explored.

Conclusions:we suggest a possible role of ROBO in the pathogenesis of autism. Abnormalities of ROBO may lead to autism either by interfering with serotonergic system, or by disrupting neurodevelopment.

131.5 A PPP1R1B Polymorphism is Associated with Risk for Autism Spectrum Disorders in Male-only Affected Sib-pair Families. J. A. Hettinger*[1], X. Liu[1], M. Hudson[2], R. C. Michaelis[3], C. E. Schwartz[4], M. E. S. Lewis[5] and J. J. A. Holden[1], (1)*Queen's University*, (2)*Queen's Univerity*, (3)*Western Carolina University*, (4)*Greenwood Genetic Center*, (5)*University of British Columbia*

Background: Dopamine (DA) modulates learning, executive functions, emotional processing and social cognition, all of which are impaired in individuals with autism spectrum disorders (ASDs). The dopamine- and cAMP-regulated phosphoprotein M_r 32kDa (DARPP-32) is encoded by the *PPP1R1B* gene, which is located at chromosome 17q12, and is expressed in dopaminoceptive (DAceptive) neurons. DARPP-32 is differentially phosphorylated or dephosphorylated by D1-like or D2-like dopamine receptors with the phosphorylated state of the protein determining the downstream physiological effects of DA receptor activation.

Objectives: To determine whether the *PPP1R1B* gene is associated with susceptibility to ASDs.

Methods: Because our previous findings in DA-related genes (*DRD1* and *DRD2*) suggested that the dopaminergic system may be affected in families with only affected males , we examined 3 polymorphisms (rs1495099G/C, rs907094T/C and rs3764352A/G) in the *PPP1R1B* gene in 112 male-only affected sib-pair families and a comparison group of 443 males and females. We performed single marker and haplotype case-control comparisons as well as family-based tests including quantitative transmission disequilibrium tests (QTDT).

Results: There was an increased frequency of rs1495099 C alleles (P=0.001) and CC genotypes (P=0.001) in affected males compared to our comparison group. Family-based tests performed under a recessive model showed over-transmission of the C allele (P=0.0009). QTDT analyses showed associations between rs1495099 C and more severe problems with social interaction (P=0.0016) and nonverbal communication (P=0.0046), as well as increased stereotypic behaviours (P=0.0072) as determined using Autism Diagnostic Interview-Revised subdomain scores.

Conclusions: Our findings support a role for the *PPP1R1B* gene in conferring risk for autism in families with only affected males and suggest that the rs1495099 C allele, or functional variants in linkage disequilibrium with this polymorphism, cause changes either in *PPP1R1B* expression or DARPP-32 function in DAceptive neurons in brain regions which have a role in social interaction, communication and the pathophysiology of stereotypies.

131.6 GENOMIC INSTABILITY IN POST-MORTEM AUTISTIC BRAINS AND CORRELATION WITH GENE EXPRESSION LEVELS. R. Sacco*[1], B. Boone[2], K. Garbett[3], C. Lintas[1], K. Mirnics[3], S. Levy[2], P. Levitt[3] and A. M. Persico[1], (1)*Univ. Campus Bio-Medico*, (2)*Vanderbilt Microarray Shared Resource*, (3)*Vanderbilt Univ.*

Background: Increased frequencies of segmental copy number variations (CNVs) in the human genome have been associated with autism.

Objectives: to assess the frequency and genomic location of segmental CNVs in neocortical tissue samples from autistic patients and matched controls, and to assess its degree of correlation with gene expression.

Methods: CNV analysis was performed on genomic DNA extracted from postmortem temporocortical tissue specimens (BA 41/42) belonging to 11 patient-control pairs, using the GeneChip Mapping Arrays 250K arrays (Affymetrix). Genome-wide expression was assessed in 6 of these 11 pairs, using the Human Genome 133 plus arrays (Affymetrix). SNP intensity data (log2 ratios) were analyzed using the CNAG software.

Results: false negative rates average 23% and 20%, while false positives are at 2.52% and 2.47% for nsp-array and sty-arrays, respectively. There is no significant difference between patients and controls in percentage of duplicated or deleted SNPs, although there appear to be genomic regions that are selectively duplicated/deleted in autistic patients or in controls. Expression profiling of the superior temporal gyrus of six autistic subjects and matched controls reveals increased transcript levels of many immune system related genes. CNV-gene expression correlations are being assessed.

Conclusions:The reliability of our CNV analysis appears quite satisfactory. No widespread increase in genomic instability is found in our postmortem brain sample of autistic patients. The genomic location of CNVs may be more relevant to autism vulnerability than their quantitative representation. Assessments of CNV-gene expression correlations will be important to understand the pathophysiology of CNV contributions to autism pathogenesis.

131.7 CNV Regions Associated with Autism in a Large Icelandic Cohort. R. Fossdal*[1], S. Steinberg[1], P. Magnusson[2], B. Lauth[2], O. O. Gudmundsson[2], S. Hreidarsson[3], E. Saemundsen[3], G. Bjornsdottir[1], H. Einarsdottir[1], H. Stefansson[1], J. Gulcher[1], K. Kristjansson[1], T. E. Thorgeirsson[1] and K. Stefansson[1], (1)*deCODE genetics Inc.*, (2)*Landspitali University Hospital*, (3)*State Diagnostic and Counseling Center*

Background: A number of rare chromosomal events have been identified as causal factors for autism spectrum disorders. The genotyping of a large population sample provides increased power for the detection of new rare events associated with autism.

Objectives: This study aims at detecting de novo and transmitted CNV regions associated with autism in order to increase the specificity of other genetic analysis methods used to detect susceptibility variants.

Methods: A search for copy number variants conferring risk of autism was carried out through a population study of autistic individuals ascertained through the State Diagnostic Counseling Center and the Department of Child and Adolescent Psychiatry in Iceland. To identify and characterize de novo and transmitted CNVs associated with autism, a total of 27,436 Icelandic individuals genotyped at deCODE genetics for 317,503 SNPs using the HumanHap300 BeadChip (Illumina) were examined for increases and decreases in copy number using a Hidden Markov Model applied to normalized intensity data. The data set included 26,532 Icelandic controls, 334 probands and 570 parents of the autistic individuals.

Results: We identified more than 20 genomic regions containing large CNVs. Some of these regions were known to harbour CNVs previously identified in autistic individuals e.g. chromosome 1q, 2q, 15q, 16p, 17p and 22q. A few novel regions were detected. All regions were examined for association with autism in the Icelandic cohort.

Conclusions: Studies focusing on CNVs can find regions associated with autistic phenotypes increasing the specificity of other genetic analysis methods used to detect susceptibility variants.

131.8 Family-based genome-wide association study in autism. D. Ma*[1], I. Konidari[1], J. Jaworski[1], P. Whitehead[1], H. H. Wright[2], R. K. Abramson[2], J. Haines[3], M. Cuccaro[1], J. Gilbert[1] and M. Pericak-Vance[1], (1)*Miami institute of human genomics*, (2)*Univ. S. Carolina Sch. Med.*, (3)*Center for Human Genetics*

Background: Autism has been regarded as the most heritable neuropsychiatric disorder. However, no single major gene has been identified conclusively through linkage or association studies during the past decade suggesting an extensive genetic heterogeneity in its etiology. Recently, several studies have implicated de novo copy number variations in autism.
Objectives: To comprehensively examine the association between genomic structure variations (SNP and copy number) and autistic risk
Methods: The Miami Institute for Human Genomics is processing a genome screen on a completely independent dataset using the Illumina 1-M beadchip. We completed a preliminary analysis of the first 189/600 trios.

All genotypes were called in beadstudio and Plink was used for the TDT analysis. A total number of 189 trios (sample call rate>98%) and 793,380 SNPs per sample (call frequency>95%, genTrain score>0.4 and not in copy number region) are included.
Results: Our results show no SNPs meet a genome-wide significance at this stage. Over 428 SNPs gave a P-value less than 0.001, and these are spread across the genome. Among the top 10 significant SNPs (based on their empirical p-values), none of them fall within previously reported candidate regions or genes.
Conclusions: These data further suggest that the genetic etiology of autism is complex and that no single polymorphism carries a large effect.

Oral Presentations Program

132 Autism Model Systems

132.1 A Genetically Accurate Mouse Model of Autism: Disease-linked Point Mutation in Neuroligin-3 Produces Autism-like Behavior in Mice. K. Tabuchi, J. Blundell, M. R. Etherton, R. Hammer, X. Liu, T. Sudhof and 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. One of these mutations, the R451C substitution in neuroligin-3, alters a conserved residue in the extracellular esterase-homology domain of neuroligin-3 in patients with autism or Asperger Syndrome. In addition, mutations in the neuroligin binding partners, neurexin-1 and shank-3, have also found in patients with ASDs. Thus, mutations in three gene families that encode neuroligins or their interacting proteins are associated with familial ASDs.
Objectives: To create and characterize a genetically accurate mouse model of autism.
Methods: We have introduced the R451C-substitution in neuroligin-3 into mice by homologous recombination. All experiments were performed blind to genotype on 19 male neuroligin-3 R451C knockin mice and 19 wild-type, littermate controls. A thorough array of behavioral tests relevant to autism and cognitive function, whole cell synaptic electrophysiology, electron microscopy, Western blot for synaptic proteins, and immunohistochemistry for synaptic proteins were performed.
Results: R451C-mutant knockin mice showed selective impairment in social interaction while other behavioral domains including anxiety, locomotor activity, coordination, and pain sensitivity were spared. Interestingly, the mutants exhibited a significant enhancement in spatial learning abilities in the Morris water maze.
Unexpectedly, these behavioral changes were accompanied by an increase in inhibitory synaptic transmission in the cortex, with no apparent effect on excitatory synapses. Deletion of neuroligin-3, in contrast, did not cause such changes, indicating that the R451C-substitution likely represents a gain-of-function mutation.
Conclusions: The neuroligin-3 R451C knockin mice may represent the first genetically accurate model of autism not associated with a broader neuropsychiatric syndrome. Furthermore, in agreement with recent findings of decreased cortical excitability in mouse models of Rett syndrome, increased inhibitory synaptic transmission may contribute to human ASDs (Tabuchi et al, *Science*, 2007).

132.2 Generation and characterization of Neuroligin-3 knock down mice for Autism Research. G. Y. Wen*, Y. W. Hwang, M. H. Lee, C. Corbo, E. C. Jenkins, S. R. Guariglia and W. T. Brown, *New York State Institute for Basic Research in Developmental Disabilities*

Background: The cause of autism may be due to synaptic abnormalities. Neuroligins are present in the postsynaptic membranes of neurons and play a crucial role in the synaptic transmission. Neuroligin-3 is known to be mutated in rare cases with autism spectrum disorders (ASD).

Objectives: To investigate the possible involvement of Neuroligins in autism, neuroligin-3 (NL-3) knock down (KD) mice have been generated and characterized.

Methods: Microinjection of a NL-3 RNAi gene construct into embryos of CD-1 mice was

performed. PCR, Western blot and behavioral assessments were analyzed.

Results: NL-3 KD mice survived without premature mortality. Genotyping of the NL-3 KD mice using PCR confirmed the construct. Phenotyping by Western blot using two different antibodies to NL-3 revealed a 42-72% knock-down reduction in NL-3 in hippocampal regions of these NL-3 KD mice. Behavioral assessments of eight NL-3 KD mice compared to 10 control mice both at 33 days using an elevated plus maze showed a significant difference (p=0.005) in anxiety and emotional expression. However, open field test at 32 days showed no difference in social interaction. Morris water maze testing at 35 days showed no difference in spatial memory. A PCR positive line of NL-3 KD CD-1 mice was bred with C57BL mice as a backcross transferring the NL-3 RNAi DNA gene into this widely used inbred strain. Ultrasonic vocalization between 11 days old pups and their mother (1 PCR positive mouse, 2 PCR negative mice) of NL-3 KD C57BL mice showed delayed and reduced communication.

Conclusions: Neuroligin-3 knock down mice manifest behavioral changes in anxiety and emotionality expression consistent with those of ASD. This knock down approach may be a useful model of autism.

132.3 Forebrain Development of Serotonin and Norepinephrine Neurotransmitter Systems is Abnormally Regulated in the Engrailed 2 (En2) Mutant Mouse. L. Lin*[1], P. Sonsalla[1], S. Kamdar[2], J. H. Millonig[2] and E. DiCicco-Bloom[1], (1)*Robert Wood Johnson Medical School*, (2)*UMDNJ-Robert Wood Johnson Medical School*

Background: ENGRAILED 2 (EN2) is a cerebellar patterning gene that has been reproducibly associated with autism spectrum disorders (ASD) in multiple datasets, and cerebella of En2 knock out mice (KO) phenocopy aspects of the human neuropathology. Prenatally, En2 is expressed in the mid- and hindbrain regions of the brainstem where monoamine-containing neurons that project to the forebrain develop. Since changes in serotonin levels, transmitter system maturation, and transmitter re-uptake genes are associated with ASD, we examined monoamine transmitters in this genetic model of autism.

Objectives: Define the effects of En2 deletion on development of monoamine neurotransmitters during brain development.

Methods: Brain regions including cerebral cortex, hippocampus, amygdala, midbrain and pons/medulla were dissected from postnatal day 21 (P21) wild type and En2 KO mice. Tissues were sonicated in buffer, acidified and centrifuged and levels of transmitters and metabolites were assessed by HPLC in supernatants in parallel with known standards. Other tissue homogenates were assayed by western blotting.

Results: At P21, the levels of serotonin and its metabolite, 5HIAA, were reduced 20-40% in the pons/medulla, midbrain, hippocampus and amygdala, but not cerebral cortex. Deficits in serotonin levels were paralleled by reductions in protein levels of its rate limiting biosynthetic enzyme, tryptophan hydroxylase, by western blotting. In contrast, levels of norepinephrine were elevated in the brainstem but markedly reduced in hippocampus and cortex, without change in amygdala. Finally, we observed no differences in GABA or glutamate in these regions, indicating selectivity of En2 effects on forebrain projecting systems.

Conclusions: En2 gene expression is required for normal development of brainstem monoamine-containing neurons that project to the forebrain, providing one mechanism by which this hindbrain patterning gene may contribute to altered brain growth and social, cognitive and repetitive behaviors observed in ASD.

132.4 Serotonin Transporter Function and Prenatal Stress Interact to Modulate Sociability in Mice. R. M. Smith*[1], K. S. Edwards[1], M. R. Tilley[1], H. H. Gu[1], B. S. Givens[1] and D. Q. Beversdorf[2], (1)*The Ohio State University*, (2)*University of Missouri*

Background: Multiple studies have reported that prenatal stress is a possible risk factor for the development of autism spectrum disorder (ASD). In rodents, adult rats exposed to

prenatal stress display a significant reduction in sociability, a diagnostic hallmark for ASD in humans. Genes that contribute to stress reactivity may, therefore, exacerbate prenatal stress-mediated behavioral changes in the adult offspring. Humans with the short allele of an insertion/deletion polymorphism of the SLC6A4 gene, which reduces the expression and function of the serotonin transporter (SERT), display increased stress reactivity. Some studies also link this gene locus and specific polymorphism to ASD. Heterozygous SERT knockout mice (SERT +/-) show reductions in SERT function and expression similar to the human short polymorphism.

Objectives: We wished to examine the role of SERT function and prenatal stress in mice, in order to determine whether they interact to produce reductions in social behavior in the adult offspring.

Methods: We subjected pregnant SERT +/- dams to chronic variable stress and subsequently tested the adult offspring for sociability using a 3-chamber social approach task (Nadler et al., 2004).

Results: Offspring male SERT +/- mice exposed to prenatal stress displayed reduced social novelty-seeking behavior, as they spent significantly less time socially interacting with a novel versus familiar mouse. Wild-type and unstressed SERT +/- male mice displayed typical social novelty-seeking behavior.

Conclusions: Our findings indicate that prenatal stress may interact with reduced SERT function to produce changes in sociability consistent with those observed in ASD. Given previous research implicating the SERT gene locus and prenatal stress as possible risk factors for ASD, our findings provide evidence for a possible interaction between these environmental and genetic factors that contribute to the production of autistic-like behavior in mice.

132.5 Activity-dependent changes in MeCP2 sub-nuclear localization. M. K. Singleton*[1], D. H. Yasui[1], Y. Gwye[1], K. N. Thatcher[1], A. Kumar[2], N. C. Schanen[2] and J. M. LaSalle[1], (1)*University of California, Davis*, (2)*University of Delaware*

Background: Mutations in the methyl CpG binding protein 2 (*MECP2*) gene cause Rett Syndrome (RTT), a devastating autism-spectrum disorder that manifests almost exclusively in females and is characterized by a normal early development with a regression in development between the ages of 6-18 months of age. The gene for MeCP2 is located on the X-chromosome and is mutated in a number of neurodevelopmental disorders. Alternative splicing of *Mecp2* exon 2 results in MeCP2 isoforms with different translational start sites and unique N-termini.

Objectives: The two MeCP2 isoforms (e1 and e2) have been investigated in mouse neuronal cultures using immunofluorescence (IF) and laser scanning cytometry (LSC) to detect changes in the expression level and localization of each isoform following potassium chloride (KCl) induced neuronal activity.

Methods: Primary neuronal cultures were established from embryonic (E14-E17) mice and cultured for 3-5 days *in vitro* in the presence or absence of 50 mM KCl from 10 minutes to 48hrs to observe short and long-term depolarization effects. Mouse 3T3 cells stably transfected with *MECP2e1* or *MECP2e2* were used to confirm isoform-specific antibodies. The co-localization of the MeCP2 isoforms in neurons was determined with isoform-specific antibodies and markers of different sub-nuclear locations by IF.

Results: The results showed that MeCP2 had a distinct staining pattern with MeCP2 e1 localized primarily in the nuclear matrix while MeCP2 e2 localized primarily to large nuclear heterochromatin in mouse brain and neuronal cultures. Results from the activity-dependent experiments showed that KCl treatment led to a redistribution of MeCP2 and a resulting increase in the fluorescent intensity of MeCP2 e1 and the nuclear matrix protein SFPQ/matrin 4 as detected by IF and LSC.

Conclusions: The dynamic changes in sub-nuclear localization of MeCP2 following neuronal stimulation may be important for regulation of downstream targets such as BDNF.

132.6 AUTISTIC-LIKE FEATURES IN A MOUSE MODEL OF MECP2 DUPLICATION SYNDROME CORRELATE WITH ALTERED GENE NETWORKS. R. C. Samaco*[1], C. Mandel-Brehm[1], A. L. Collins[2] and H. Y. Zoghbi[3], (1)*Baylor College of Medicine*, (2)*Duke University Medical Center*, (3)*Baylor College of Medicine and Howard Hughes Medical Institute*

Background: MeCP2 duplication syndrome is a progressive neurological disorder caused by duplications of the transcriptional repressor methyl-CpG binding protein 2. Autism is a recently discovered feature common to patients with MeCP2 duplication syndrome.

Objectives: 1) To determine if the autistic features of MeCP2 duplication syndrome are reproduced by the duplication of *MECP2* alone in mice, and 2) to uncover a molecular mechanism that could explain behavioral abnormalities in the MeCP2 duplication syndrome mouse models.

Methods: Autistic-like features were investigated using behavioral assays for anxiety, social interaction and communication in two mouse models that express a two-fold (*Mecp2*^{Tg1}) or three-fold (*Mecp2*^{Tg3}) increase in endogenous MeCP2. Transcriptional profiling of the cortex and hippocampus from *Mecp2*^{Tg1} mice was performed and gene expression alterations were confirmed by quantitative PCR (qPCR). Gene network analysis of genes confirmed to be altered was used to determine the relevance of altered gene networks to the behavioral abnormalities observed in the MeCP2 duplication syndrome mouse models.

Results: *Mecp2*^{Tg1} and *Mecp2*^{Tg3} mice display heightened anxiety-like behavior, social behavior abnormalities and altered communication. Transcriptional profiling revealed a majority of significantly altered genes to be down-regulated. 28 of 60 gene expression changes were confirmed by qPCR. Preliminary gene network analysis suggests that MeCP2 coordinates complex gene networks that impact each other to serve particular functions relevant to behavior.

Conclusions: An increase in endogenous MeCP2 expression in mice reproduces the autistic features observed in MeCP2 duplication syndrome. The MeCP2 duplication syndrome mouse models are therefore an excellent addition to the current autism mouse models. Furthermore, gene expression profiling has identified novel candidate MeCP2 target genes that may be regulated in gene networks that serve particular functions relevant to autism. Importantly, these data underscore the importance of MeCP2 in the genetic pathways that govern normal anxiety and social behavior.

132.7 A neurodvelopmental rat model showing social interaction deficit and structural features of autism. R. Rajakumar* and R. Nicolson, *London Health Sciences Centre, Department of Psychiatry*

Background: Etiology, primary pathology and mechanisms underlying autism spectrum disorders (ASD) are currently unknown. There is no cure for ASD in the foreseeable future, and available treatment options are limited. Recent evidence indicates that abnormal development of neuronal connections and an altered ratio of excitatory versus inhibitory synapses in the brain may underlie certain abnormalities of ASD. Altered size and packing density of neurons in limbic areas including amygdala has also been described in postmortem brains of autism. ASD is characterized by deficits in social interaction for which no specific pharmacological treatment is currently available. However, evidence indicates that group behavioral therapy might be beneficial in certain cases of ASD. Objectives:

Methods: We are presenting a rat model in which pathfinding of cerebral corticopetal fibers are targeted by lesioning the subplate cells of the developing cerebral cortex. Results: Lesioned animals show increased ratio of excitatory:inhibitory synapses in the cerebral cortex, and increased volume of basolateral and lateral subnuclei of the amygdala showing densely packed small neurons. Moreover, lesioned rats show deficits in social interaction. Interestingly, this abnormality is significantly improved by raising rats as lesioned + control pairs in comparison to raising them as lesioned + lesioned pairs. Conclusions: Present rat model may facilitate identifying mechanisms underlying social interaction deficits, and particularly the neurobiological basis of

improvement seen in lesioned animals following raising them paired with normal animals.

132.8 Pediatric Vaccines Influence Primate Behavior, and Amygdala Growth and Opioid Ligand Binding. L. Hewitson*[1], B. Lopresti[1], C. Stott[2], J. Tomko[1], L. Houser[1], E. Klein[1], C. Castro[1], G. Sackett[3], S. Gupta[4], D. Atwood[5], L. Blue[5], E. R. White[5] and A. Wakefield[2], (1)*University of Pittsburgh*, (2)*Thoughtful House Center for Children*, (3)*Washington National Primate Research Center*, (4)*University of California - Irvine*, (5)*University of Kentucky*

Background: Macaques are commonly used in pre-clinical vaccine safety testing, but the combined childhood vaccine regimen, rather than individual vaccines, has not been studied. Childhood vaccines are a possible causal factor in autism, and abnormal behaviors and anomalous amygdala growth are potentially inter-related features of this condition.

Objectives: The objective of this study was to compare early infant cognition and behavior with amygdala size and opioid binding in rhesus macaques receiving the recommended childhood vaccines (1994-1999), the majority of which contained the bactericidal preservative ethylmercurithiosalicylic acid (thimerosal).

Methods: Macaques were administered the recommended infant vaccines, adjusted for age and thimerosal dose (exposed; N=13), or saline (unexposed; N=3). Primate development, cognition and social behavior were assessed for both vaccinated and unvaccinated infants using standardized tests developed at the Washington National Primate Research Center. Amygdala growth and binding were measured serially by MRI and by the binding of the non-selective opioid antagonist [11C]diprenorphine, measured by PET, respectively, before (T1) and after (T2) the administration of the measles-mumps-rubella vaccine (MMR).

Results: Compared with unexposed animals, significant neurodevelopmental deficits were evident for exposed animals in survival reflexes, tests of color discrimination and reversal, and learning sets. Differences in behaviors were observed between exposed and unexposed animals and within the exposed group before and after MMR vaccination. Compared with unexposed animals, exposed animals showed attenuation of amygdala growth and differences in the amygdala binding of [11C]diprenorphine. Interaction models identified significant associations between specific aberrant social and non-social behaviors, isotope binding, and vaccine exposure.

Conclusions: This animal model, which examines for the first time, behavioral, functional, and neuromorphometric consequences of the childhood vaccine regimen, mimics certain neurological abnormalities of autism. The findings raise important safety issues while providing a potential model for examining aspects of causation and disease pathogenesis in acquired disorders of behavior and development.

Oral Presentations Program

133 Epidemiology 2

133.1 Update on European Autism Information System Project. A. Ramirez*, *Chiren Therapy Centre - The Hope Project*

Background: There is no Europe-wide epidemiological information on prevalence or financial burden of ASD, due to a lack of methodological consistency. There is also inconsistency in early diagnosis and therefore access to appropriate intervention and treatment in many EU Member States.

Objectives: The European Autism Information System (EAIS) Project proposes to develop harmonised tools for early detection, systematic data collection, prevalence and financial burden estimates, for use across Europe. A distance learning platform will be created to make these tools available.

Methods: Partners from the EAIS project, representing six EU Member States, reviewed methods and tools currently used for early detection, systematic data collection, prevalence and financial burden estimation and have consulted with ASD organisations across Europe to develop harmonised tools,

taking into account cultural and language variation. CDC is working with the EAIS project in an advisory role and provides important lessons from their ASD surveillance experience.

Results: Harmonised tools developed by the EAIS project include: systematic data collection system and estimation of ASD prevalence in Europe protocol. Tools still being developed include protocol for estimation of financial burden of ASD in Europe and early diagnosis video tool. The need for widespread consultation to encompass regional, cultural and linguistic variation, financial support for training of personnel and validation of the tools in pilot areas have all been highlighted.

Conclusions: Harmonised tools for early detection, systematic data collection, prevalence and financial burden estimates are necessary to assess the current ASD situation in Europe and monitor trends in the future. The EAIS project is concluding the development of such tools. These tools should now be validated in pilot areas across Europe.

133.2 MODIFIED CHECK LIST AUTISM IN TODDLERS: SPANISH VERSION AND VALIDATION (MCHAT/ES). R. Canal-Bedía[1], P. García-Primo[2], L. Boada[2], A. Martinez[1], E. García-Andrés[2], M. J. Ferrari[2], R. Palomo[3], C. Martín-Arribas[2], L. Herraez[1], A. Muñoz[3], L. Velayos[3] and M. Posada*[2], (1)*SALAMANCA UNIVERSITY*, (2)*Carlos III Health Institute*, (3)*Equipo IRIDIA*

Background: Although retrospective reports suggest that most parents identify ASD symptoms before 18 months of age and that a diagnosis of autism can be reliably made between 2 and 3 years of age, ASD diagnoses are often delayed until mid-childhood. The M-CHAT (Robins et. Al, 2001), a 23-item parent-report checklist has been designed as a screening tool to detect high risk ASD children but there is not enough information about the feasibility and validity of this tool in a population-based study, Objectives: To analyze the validity of the Spanish version of the MCHAT for early detection of ASD in a Spanish population. Methods: The MCHAT was translated into Spanish and a cross-cultural adaptation was performed (MCHAT/ES). A population-based ASD screening programme using MCHAT/ES version was established in three Spanish regions. Parents of 18 months and/or 24 months aged children were asked to fill in this questionnaire at the outpatient health services (compulsory vaccination programme and well-child check-up programme respectively) (SP). For validation purposes, children referred (CR) for early intervention services with either ASD diagnosis or non-ASD developmental disorder were included to enrich the sample. The original MCHAT criteria and a refining procedure for the phone call were adopted after agreement with the MCHAT authors, Results: A total of 5,188 children were included. 29 ASD children, (10 from SP and the other 9 from CR), 71 non ASD developmental disorders (28 from SP and 43 from CR). Both sensitivity and specificity showed high values only if both questionnaire and a systematic phone call were used. Conclusions: The MCHAT/ES shows promise as a screening tool for developmental disorders in an unselected population. However, the cut-off point when only the questionnaire is used should be raised This work is an important contribution to ongoing research into identification of ASD at a young age.

133.3 Risk for Autism is Increased with Paternal Age in an Iranian Population Sample. R. Sasanfar[1], A. Tolouei[2], S. Haddad[3] and S. L. Santangelo*[1], (1)*Harvard Medical School*, (2)*Special Education Organization of Iran*, (3)*Center for Human Genetic Research*

Background:

The etiology of idiopathic autism is still unclear and, despite its strong heritability, few susceptibility genes have been identified. Evidence from several epidemiological studies has implicated paternal age as a risk factor for autism. Recently implemented population screening for autism in Iran allowed us to conduct a large-scale epidemiological study.

Objectives:

To determine whether increasing paternal age is associated with increased risk for autism in an Iranian population sample.

Methods:

The sample consists of 747,403 controls and 229 autism spectrum disorder (ASD) cases obtained from the Special Education Organization of Iran. Cases and controls were 5-12 years of age. ASD diagnoses were made according to DSM-IV criteria and standard diagnostic instruments. Analyses used logistic regression, adjusting for maternal age, paternal and maternal education, birth order, consanguinity, and sex.

Results:

We found a significantly increased risk for ASD with increasing paternal age. Compared with a paternal age of 30 and under, the odds ratio (OR) for paternal age 36-40 was 2.20 (95% CI: 1.9, 4.45), while the OR for paternal age greater than 40 was 2.67; 95% CI: 1.7, 6.64). Paternal age category 31-35 also showed a similar but non-significant trend for increased risk (OR: 1.55; 95% CI: 0.90, 2.67). There was no increased risk for autism with increasing maternal age.

Conclusions:

In this Iranian population sample, paternal age greater than 35 was associated with an approximately 2-3 fold increase in the risk for autism. This effect was independent of maternal age, paternal and maternal education, birth order, consanguinity, and sex. There are several possible explanations for these results, such as that mutations are more likely to occur or accumulate in the germ line DNA of older men, and/or genes transmitted by older fathers may be improperly imprinted, leading to abnormal functioning of these genes.

133.4 Evidence of autism in a psychiatrically hospitalized sample. L. J. Lawer*, E. S. Brodkin and D. S. Mandell, *University of Pennsylvania*

Background: The similarity of the symptoms of ASD with other psychiatric disorders, and the fact that misdiagnosis may lead to inappropriate treatment, has led to interest in the prevalence of ASD in psychiatric populations. The four studies in this area have estimated the prevalence of ASD in adult psychiatric samples to be between 0.6% and 5.3%.

Objectives: To determine the potential prevalence of ASD among psychiatric inpatients and characteristics that discriminate between adults likely to have ASD and other psychiatric disorders.

Methods: The sample included 350 out of 396 patients in one state psychiatric hospital in Pennsylvania. Nursing staff completed the Social Responsiveness Scale (SRS) for each subject. Chart reviews were conducted to examine functioning and medical history. T-tests and chi-square tests were used to examine differences in clinical presentation, putative diagnoses, and medical history among patients scoring above 100 on the SRS (a score highly specific for autistic disorder in the general population) and patients scoring below 100.

Results: Twenty-one percent of patients received an SRS score over 100. They were significantly more likely than other patients to be diagnosed with undifferentiated schizophrenia (30% vs. 22%) and have indication in their charts of childhood onset or a "long history" of psychiatric problems (68% vs. 50%), not starting high school (20% vs. 8%), abnormal movements (20% vs. 10%), gastro-intestinal problems (34% vs. 23%), and mental retardation (15% vs. 5%). Analyses of differences in medication use and self-injurious behaviors are ongoing.

Conclusions:While not conclusive regarding the prevalence of ASD in a psychiatric inpatient sample, these findings are provocative and suggest the need for further research. We currently are conducting patient and family interviews to augment existing data. Improved diagnostic assessment for adults with ASD, especially those that discriminate ASD from the negative symptoms of schizophrenia, may have important treatment implications.

133.5 AGE AND USE OF THE EARLY CLASSIFICATION OF THE AUTISM SPECTRUM DISORDERS (ASDs) IN MULTIPLE AREAS OF THE UNITED STATES. C. Rice*[1], J. Baio[1], A. Washington[1], J. Nicholas[2], L. King[2], L. C. Lee[3] and S. Pettygrove[4], (1)*Centers for Disease Control and Prevention*, (2)*Medical University of South Carolina*, (3)*Johns Hopkins Univ.*

School of Public Health, (4)*University of Arizona*

Background: Despite the importance of early identification of children with an ASD, the Autism and Developmental Disabilities Monitoring (ADDM) Network found a median age of diagnosis between 4.5 and 5.5 years of age in 2000 and 2002 in multiple areas of the United States.

Objectives: Provide a follow-up on the age of ASD diagnosis from four sites.

Methods: The ADDM Network monitors the prevalence and population characteristics of 8-year-old children with ASDs. Four sites (portions of Arizona, Georgia, Maryland, and South Carolina) have data for at least 3 time periods. For 2004, 748 8-year-old children with ASD were confirmed via clinician review using the *DSM-IV-TR* criteria from existing evaluation records.

Results: Most children with ASD were receiving special education services: 86% (MD and SC), 91% (GA), 93% (AZ). They also had documented concerns about development before 3 years: 55% (MD), 79% (AZ), 83% (GA), and 85% (SC); however, the median age of earliest documented ASD diagnosis was later: 50 (SC), 60 (GA), 65 (MD), and 67 (AZ) months. From 2000 to 2004, the mdian age of earliest ASD diagnosis increased by a varying 4 to 25 months in 3 sites and decreased by 4 months in SC. However, children with ASD were more likely to have a documented classification (diagnosis or educational eligibility) of an ASD in 3 sites (GA, MD, and SC) from 2000 to 2004: 70% to 86% (GA); 70% to 89% (MD); and 30% to 58% (SC).

Conclusions: Decreases in the age of diagnosis were not found in most sites during the 4 year period; however, more children were being classified with an ASD. Therefore, evaluating progress in improving early identification may need to take into account not only the age of identification, but that more children are receiving a classification of ASD prior to the age of 8 years.

133.6 Early-Life Infection and Autism Spectrum Disorder. H. Ó. Atladóttir*[1], P. Thorsen[1], L. Østergaard[2] and E. Parner[1], (1)*Institute of Public Health, University of Aarhus*, (2)*Skejby Hospital*

Background:
Early-life infection has long been suspected to be a contributing factor in the etiology of neurodevelopment diseases, such as schizophrenia or autism. Previous studies, investigating the association between autism, and congenital or early-life infection have showed inconsistent results.

Objectives:
In this study we investigated the association between autism spectrum disorder in the child, and infections requiring hospitalization in children under the age of 18 months in Denmark.

Methods:
A population based study, using all children born in Denmark from January 1, 1980, through December 31, 2005, identified in the Danish Medical Birth Registry, a total of 1,612,342 children. The cases of autism spectrum disorder were found in the Danish national Psychiatric Register, a total of 7,409 cases. Data on diagnoses of infection was obtained from the Danish National Hospital Register. Data was analyzed using Cox regression model.

Results:
Preliminary results suggested that children admitted in hospital for an infectious disease had a statistically significant higher risk of being diagnosed with autism; these infections included herpes infections, infectious enteritis, pneumonia, upper airway infections, and otitis media. Infections such as conjunctivitis, appendicitis, and tuberculoses did not display a significant association to autism. Children with multiple hospitalizations due to infections displayed even higher risk of being diagnosed with autism.

Conclusions:
There are many possible explanations for the results in this study, 1) these infections could be a part of the etiology of autism, 2) immune response in the child during infection could trigger the development of autism, 3) children with autism could be more susceptible to infections due to an altered immune system,

or 4) the hospitalization of these children could have directed the professionals' attention to developmental deficiencies in the child.

133.7 Environmental Toxicology and Risk Assessment for Autism Phenotypes: A Prospective Study of Children Exposed In Utero to Antiepileptic Drugs. K. M. McVearry*[1], D. R. Brost[2], J. VanMeter[1] and K. J. Meador[3], (1)*Georgetown University Medical Center*, (2)*NIH National Institute of Mental Health*, (3)*University of Florida McKnight Brain Institute*

Background: Despite the momentum of the environmental factor hypothesis, the role of toxins in the pathogenesis of autism is poorly understood. Data from experimental animals with in utero and postnatal exposure to certain GABA agonists, including ethanol and some antiepileptic drugs (AEDs), show altered neurodevelopment for CNS substrates including cell differentiation, neuronal apoptosis, and neuronal migration. Human outcomes from well-controlled studies, however, are needed to identify the risk this class of environmental factors may pose to the development of autism. Objectives: In a prospective teratology study of neurobehavioral outcomes in a pediatric population, we report the incidence of traits associated with autism in preschool children who were exposed in utero to four commonly used antiepileptic drugs. Methods: Subjects are prospectively-enrolled preschool children between 3.5 and 5 years of age (n=54) from mother-child pairs who met stringent inclusionary criteria and are characterized by in utero exposure to carbamazepine, lamotrigine, phenytoin, or valproate monotherapy for the treatment of maternal epilepsy. Neuropsychological assessment, play observation, and clinical reports of traits associated with autism spectrum diagnoses are reported as observation data. Results: Across monotherapy groups, we observed traits associated with autism spectrum disorders, including developmental delay diagnoses (19%; n=10), expressive language deficits (20%; n=11), referral for occupational therapy services (11%; n=6), and extreme perseveration during cognitive tasks (24%; n=13). 17% of the subjects show 3 or more traits (valproate n=3; lamotrigine n=2; carbamazepine n=2; phenytoin n=1). Hand flapping, head banging, non-nutritive chewing, and contamination obsessions are reported as case reports. Conclusions: These outcomes exhibit increased incidence of traits associated with autism spectrum disorders. In humans, antiepileptic drugs may be in utero environmental factors that increase the risk of autism pathogenesis.

133.8 Autism Spectrum Disorders and Antibodies Measured in Neonatal Blood Samples in a California Population. K. Cheslack-Postava*[1], C. Newschaffer[2] and J. K. Grether[3], (1)*Johns Hopkins Bloomberg School of Public Health*, (2)*Drexel University School of Public Health*, (3)*California Department of Public Health*

Background: Previous studies have suggested that CNS-reactive antibodies may be more prevalent among both subjects with autism and their mothers than controls. Fetal or neonatal exposure to such antibodies may affect the developing nervous system. Because it is likely that prenatal factors affect the development of autism, antibody status during gestation may be more relevant to autism risk than that during later life.
Objectives: To determine whether neonatal levels of antigen-specific antibodies are associated with autism risk.
Methods: The authors conducted a population-based case-control study comparing autism cases (n=424) identified through the California Department of Developmental Services (DDS) to birth certificate controls (N=644). A group with idiopathic mental retardation (n= 434) identified through DDS was also included to allow assessment of the specificity of any differences to autism. Serum samples from each subject were obtained in the form of punches removed from neonatal heel-stick cards archived by the Genetic Disease Branch newborn screening program of the California Department of Public Health. IgM and IgG antibodies, including those to nervous system, thyroid, and infectious antigens, were measured using microbead suspension arrays. The effect of each antibody on risk for ASD will be assessed using non-parametric rank-sum scores and multiple logistic regression, adjusting for potential effect modification and

confounding by demographic, birth and diagnostic characteristics.
Results: Laboratory assays have been completed for antigen specific antibodies. Crude and adjusted data will be presented for the following analytes: thyroid peroxidase, thyroglobulin, MBP, GFAP, neurofilament proteins, BDNF, polysialic acid, gangliosides, fetal mouse brain extracts, toxoplasmosis, CMV, HSV1, HSV2, and pneumococcal polysaccharides.
Conclusions: There may be differences in maternal antibody levels between autism cases and controls at birth. The results of this study will help to elucidate the nature of any such differences.

Poster Presentations Program

134 Treatment Posters 2

1 134.1 PIVOTAL RESPONSE TRAINING APPLIED TO A GRAMMATICALLY COMPLEX LANGUAGE: A CASE OF RAPID LANGUAGE DEVELOPMENT IN A FOUR-YEAR-OLD FINNISH-SPEAKING CHILD WITH AUTISM. J. Niemi*, *University of Joensuu*

Background: Pivotal Response Training (PRT) is a naturalistic behavioral (ABA) intervention approach combining traditional behavioral techniques with techniques known to facilitate early social-communicative behavior in typical children.

Objectives: As PRT is very much about language, it seemed appropriate to analyze the language of a child immersed in the PRT program linguistically and grammatically. There is a need for linguistic and especially grammatical studies among the speakers with autism spectrum disorder.

Methods: The subject is a 4-year-old echolalic autistic boy who was administered a total of 32 PRT sessions during a 3-month period. His verbal performance was analyzed from digitalized video recordings of his PRT therapy sessions. The sessions chosen for the present paper were the first two (Phase 1) and the final two sessions (Phase 2) of PRT therapy. The subject's communicative verbal output was labeled as a prompted speech category with three subcategories: correct prompted reply, incorrect prompted reply and no reply. Spontaneous speech was classified into two subcategories: correct spontaneous speech and incorrect spontaneous speech.

Results: The grammatical analysis of the subject's speech shows a radical shift from single-word responses of Phase 1 to more complex structures of Phase 2. Unintended verbal behavior such as imitation, babbling and crying also diminished by Phase 2. Other developments in the subject's spontaneous speech was also observed, e.g., a decrease of incorrect spontaneous speech from 51.1% (28/55) in Phase 1 to 17.8% (18/101) in Phase 2. Quantitatively, the total number of spontaneous speech attempts nearly doubled from 55 in Phase 1 to 101 in Phase 2.

Conclusions: The development from the one-word phrase stage to that of two-word phrases and further follows the path seen in typical children. Two language acquisition models describing the present child's language development will be discussed.

2 134.2 TREATMENT OF CHILDREN WITH PDD SPECTRUM DISORDERS BY COMBINATION OF ATYPICAL AND COX-2 INHIBITOR. (OPEN PRIMARY STUDY OF 6 PATIENTS). M. G. Yeghiyan* and N. Israelyan, *Yerevan State Medical University*

Background: The occurrence of autism has also been discussed in many cases as a consequence of inflammatory processes.The treatment of PDD related behavioral problems with atypical antipsychotics show considerably good effectiveness with more favorable side effect profile. However, antipsychotics in treatment of PDD spectrum, in general act as syndrome oriented therapy and less as a causal therapy. All patients with autism have some core symptoms such as poor social interaction and relationship, verbal and nonverbal communication difficulties, limited interests in activities or play. All mentioned symptoms are based in specific behavioral problems of autism. With early and intensive treatment, most children improve their ability to relate to others, communicate, and help themselves

Objectives: The study was based on the idea that substances with immunomodulatory properties could be used for the treatment of psychiatric disorders such as autism. Methods: We have worked on 6 children who were from 6 to 8 year old (4 boys and 2 girls) with significant bihavioral problems in PDD spectrum. All the patients before participating in study had received risperidon 1- 4 mg. However, due to the lack of effects , the treatment was discontinued. After two weeks of washout, combination of Ziprasidone (Geodon® 20 mg – minimal dose) and Meloxicam, (Movalis ® 3,7 mg- minimum dose) was administrated. Behavior assessment based in symptoms estimation by parents and other caregivers was made at the end of 3 week of the treatment. Simultaneously our team estimated the patients using CGI scale. Results: Significant improvement was registered among 4 out 6 children. No side effects were observed.
Conclusions: Combination of atypical and COX-2 inhibitors may be promising for treatment of behavioral disorders among children with autistic spectrum. However more comprehensive study is needed.

3 134.3 Prescription Patterns Of Psychotropic Medication Among Patients With Autism Spectrum Disorders. E. Duketis*, M. Bundschuh, E. Herbrecht, M. Holtmann, S. Boelte and F. Poustka, *Department of Child and Adolescent Psychiatry, J.W. Goethe University*

Background: Currently no medication is approved to treat the core symptoms of autism spectrum disorders. Nevertheless drug treatment is used as an adjunct therapy in autism targeting stereotypies, aggression, self-injurious behaviour and comorbid disorders. While there is some survey data on psychopharmacological intervention in autism in the United States, little is known about prescription practices in Germany. Objectives: The aim of this study was to survey the frequency and type of psychopharmacological intervention in a clinical sample of patients with autism spectrum disorders. Methods: A retrospective chart review was conducted identifying a clinical sample comprising 530 patients (412 male, 118 female) with autism spectrum disorders (408 with autism, 132 other ASD). The mean age was 12,2 years (SD= 7,6) and the mean IQ was 76,6 (SD= 29,0). Data about the history of past and present psychopharmacological interventions were collected from the medical records and the Autism Diagnostic Interview (ADI-R). Results: 93.6 % of the patients have a history of psychopharmacological treatment. 28% of the sample received pharmacological treatment at the time of data collection (including alternative treatments and herbal remedies). The most frequently prescribed drugs were antipsychotics (12.1 %), stimulants (7.3 %) and anticonvulsants (4.9 %). The strongest predictor for the the prescription of medication was severity of general psychopathology (p= .001) followed by severity of the autistic symptomatology (p =.8). Age, gender, IQ, language development, adaptive functioning and the subtype of the autism diagnosis had no significant influence on the frequency of prescription. Conclusions: The results indicate a comparatively moderate prescription use of psychopharmacological agents in autism. With the antipsychotics as the leading prescription drug we find a substance class whose effectiveness has been well approved in several clinical studies. In contrast to surveys from the United States the use of antidepressants in autism spectrum disorders is less common.

4 134.4 THE LONG TERM EFFECTS OF EARLY INTENSIVE ABA INTERVENTION ON ADAPTIVE BEHAVIOR AND IQ IN ASD – A LONGITUDINAL STUDY ON EVIDENCE BASED TREATMENTS IN ITALY. G. Doneddu*[1], R. Fadda[2], L. Ferretti[3], G. Saba[3], S. Marras[3], M. G. Iacolina[3] and E. Sitzia[3], (1)*Azienda Ospedaliera*, (2)*University of Cagliari*, (3)*Azienda Ospedaliera "G.Brotzu"*

Background: The studies about the effects of intervention in ASD show dramatic improvements thanks to intensive and early intervention but the question of how and why improvements come about is still controversial (Howlin, 1998). Despite the great deal of knowledge about early intervention programs in Autistic Spectrum Disorders, the most of the interventions for individuals with ASD in Italy are still based on anecdotic evidences or clinical judgments. Objectives: This study aims

to evaluate the long term effects of an ABA early intensive (ABA-int), an ABA non intensive (ABA-non int) and an Eclectic intervention on the Vineland Adaptive Behavior Scale (VABS) scores and on the Leiter scores in ASD in Italy.
Methods: 34 participants with ASD (25M; 9F; aver.chron.age=6;7yrs;ds:33; aver.IQ=60). The participants were divided in three groups of intervention: ABA-int (10 hrs of DTT, 5 hrs of speech therapy a week); ABA-non int (5 hrs of DTT, 2 hrs of speech therapy a week); Eclectic. The participants were tested with the VABS and with the Leiter within a 6 months interval (T1-T2) and again after 24 months (T3). At the end of the study, all the participants got an ABA non-int or an eclectic intervention.

Results: After 6 mths: the VABS increased significantly in the ABA-int (1 yr; t=-3,41;df=8;p<0,05) and in the ABA-non int -10 mths (t= -8,61; df= 16; p<0,05). The IQ gained 23 scores in the ABA-int (t=-2,96; df=8; p<0,05) and 12 scores in the ABA non intensive group (t=-2,78;df=16;p<0,05). After 24 mths: the VABS score increased in the ABA-int (1;9 yr; t=-3,67;df=7;p<0,05) and in the ABA-non int (2;4 yrs; t=-5,4; df=14; p<0,05). The IQ scores increased of 21 scores only in the ABA-int (t=-2,6; df=7; p<0,05).
Conclusions: The results highlight a long term effects of ABA-int early intervention in ASD on adaptive skills and IQ.

5 134.5 CAREGIVER-CHILD RELATEDNESS IN AUTISM: WHAT CHANGES WITH INTERVENTION?. J. A. Hobson*[1], P. Hobson[1], S. Gutstein[2], A. Ballarani[1] and K. Bargiota[1], (1)*University College London and Tavistock Clinic, London*, (2)*The Connections Center*

Background:

Children with autism have relatively typical attachment *relationships*, but their personal *relatedness* is atypical.

Objectives:

To assess whether children with autism show changes in relatedness with a parent-based intervention.

Methods:

Participants were 30 boys aged 3-13 years (*M* = 7y; *SD* = 3y), IQ scores 49-125 (*M* = 88.4; *SD* = 21.5), with autism or ASD, and ADOS social-communication scores 7 - 23 (*M* = 14.3; *SD* = 4.3). With their primary caregivers, they received Relationship Development Intervention®.

Two assessments of parent-child play were made by separate raters at treatment onset and later in treatment *M* = 19.6 months (9 – 38 months):

a) Dyadic Coding Scale (Humber & Moss, 2005) for interactions relevant to attachment e.g., communication, appropriate role assumption, mood, enjoyment.

b) Novel ratings of moment-by-moment states of interpersonal relatedness (Observer XT Coding System) on mutually exclusive categories: separate attention (attending to different objects/activities), parallel attention (attending to the same object/activity, but lack of awareness of joint focus), coordinated attention (mutual focus but little communication), or connected attention (joint focus on an object/activity involving mutual communication in relation to shared focus).

Results:

Preliminary results on a pilot sample suggest that dyadic interactions relevant to the attachment *relationship* had not changed with treatment (time 1 overall *M* = 4.70, time 2 *M* = 4.90, with mean scores very similar to dyads with typically developing children). In contrast, there were significant changes in moment-to-moment *relatedness* e.g., time spent in connected states of attention, time 1 *M* = 29%, time 2 *M* = 58% (*p* < .5). Furthermore, time spent in parallel attention *without* mutual communication was significantly related to lower ratings on the Dyadic Coding Scale.

Conclusions:

When children have autism, caregiver-child patterns of interaction may reflect stable attachment *relationships*. However, atypical *relatedness* may change with intervention.

6 134.6 Intrinsic motivation as a mediating variable in the maintenance and transfer of academic performance in children with autism. S. Lynch*, J. Cameron and W. D. Pierce, *University of Alberta*

Background: Research with typically developing individuals has shown that the social context surrounding the administration of rewards has an effect on individuals' intrinsic motivation (IM) (Cameron, Banko, & Pierce, 2001; Deci, Koestner, & Ryan, 1999). Specifically, when individuals are reinforced for achievement in autonomy-supportive contexts (settings that provide opportunities for choice), their IM for academic tasks increases. Choice has also been found to be an important motivator for children with autism in academic programs using explicit contingencies of reinforcement (Koegel et al., 2006; Moes, 1998). However, researchers have yet to examine the effects of choice and reinforcement on the IM of children with autism (once the reward procedures are withdrawn) and the possible generalization of IM to novel academic settings.

Objectives: This research examined the effects of performance-based reinforcers presented in differing social contexts (adult-directed vs. child choice) on the academic IM of children with autism. As such, it was expected that IM for academic tasks would increase, resulting in enhanced maintenance of performance as well as skill generalization to novel settings.

Methods: Three children participated in a within-subject repeated measures design, consisting of multiple baseline and experimental phases. In baseline sessions, children were free to engage in either an academic task or a distracter. During the experimental intervention, children received reinforcers for completing math or language arts tasks in either autonomy-supportive (choice) or adult-directed (no-choice) contexts. Measures of IM include time on task, accuracy, affect, task liking, and incidence of problem behavior.

Results: IM increased, maintained over time, and generalized to novel settings for two of the three children.

Conclusions: This research suggests that when children with autism are offered performance-based reinforcers in contexts that support their autonomy (provide choice) IM for academics are enhanced, and the experimental effect both maintains and generalizes to novel situations.

7 134.7 NUTRITIONAL QUALITY OF THE GLUTEN-FREE AND CASEIN-FREE DIET. P. A. Stewart, S. L. Hyman*, J. Foley, R. Peck, U. Cain, C. Stamm and D. D. Morris, *University of Rochester*

Background: A popular therapy for autism spectrum disorders (ASD) is the gluten-free and casein-free (GFCF) diet which eliminates proteins found in some grains (barley, rye, oats, wheat) and milk. Few prospective studies have evaluated behavioral response to the diet and none have reported on nutritional quality.
Objectives: Prospective documentation of changes in macro and micronutrients and servings of Food Guide Pyramid recommendations ingested by children with ASD between baseline and stable administration of the GFCF diet.
Methods: Preschool children (N=11) in Applied Behavior Analysis programs were recruited for a double blind, placebo controlled challenge study of the GFCF diet. Reported here are initial nutritional data. Three day diet records were collected at baseline and after at least 4 weeks on the GFCF diet with intense weekly nutritional counseling. Diet data was analyzed by *Food Processor* © software. Nutrients were examined as % of RDA and servings per the Food Guide Pyramid.
Results: No group differences on the T test for paired observations were evident in calorie, protein, fat, fiber, carbohydrate, calcium, iron, and vitamins A, D, or C intake after implementation of the diet. Individual children were at risk for deficits in calcium, iron, and vitamins A and D intake. Servings of fruits, vegetables, protein, and sweets/fat all increased on the GFCF diet ($p=.16$, $p=.2$, $p=.3$, $p=.008$ respectively) on the Wilcoxon

Matched Pairs Signed Ranks Test .
Conclusions: Preschool children with ASD can be appropriately nourished on a GFCF diet, however monitoring by a dietitian is strongly recommended. Diet sufficiency was maintained by increasing food variety, use of appropriately fortified foods, and vitamin supplementation. Fortified soy products contributed to protein, calcium and vitamin D adequacy. The effects of nutrition must be considered in evaluation of the behavioral data.
Funded by NIMH PO1HD35466 and National Center for Research Resources (NCRR) NIH UL1RR024160

8 134.8 GrammarTrainer, a software based language intervention. F. Hurewitz*[1] and K. Beals[2], (1)*Drexel University*, (2)*University of Pennsylvania/Autism Language Therapies*

Background: Delays in syntactic language development are found in verbal individuals with autism, with proposals that a third demonstrate comorbid Specific Language Impairment (SLI) (Kjelgaard & Tager-Flusberg, 2001). While interventions informed by linguistic theory can assist people with SLI in achieving longer utterances and enhanced communication (Ebbels, Van del Lely & Dockrell, 2007), it is unclear if such interventions can help learners with autism. Most current language interventions for autism focus on general communicative improvement, often assessed by vocabulary growth, rather than explicitly addressing syntactic delays. GrammarTrainer is a text-based linguistic software program that teaches children to produce sentences of increasing grammatical complexity. It requires learners to actively construct phrases word by word, and provides principled feedback for ungrammatical utterances. As the program tests and corrects students, it keeps a running record of language errors.
Objectives: One reason for a de-emphasis on grammatical remediation is that the syntactic limitations for people with autism are not well documented. We examine an online database created by users of grammarTrainer in order to target the intervention to the needs of the users.
Methods: A database of 22 individuals with autism using grammar trainer was coded for type (syntactic/semantic/pragmatic) and frequency of errors. This error analysis was compared with a subset of the group, 6 individuals, who completed 7 week-long lessons.
Results: For complex utterances such as questions, 34% had syntactic errors, while 55% had pragmatic errors. Common syntax errors include leaving out the auxiliary, verb morphology, and failing to use subj-verb inversion for WH-questions. Pragmatic errors often involved use of the wrong question word. Individuals who completed 7 lessons had a 21% syntax error rate, and 8.3% semantic/pragmatic errors. Posttest syntactic errors less globally affected comprehensibility compared to pretest.
Conclusions: Syntactic and semantic/pragmatic errors are prevalent, and may be responsive to linguistically informed remediation techniques.

9 134.9 Social Validation of Behavior-Analytic Interventions for Persons With Autism-Spectrum Disorders. D. B. McAdam and J. Breidbord*, *University of Rochester*

Background: Although ideal behavior-analytic interventions include socially important goals; methods; and outcomes, consideration of these components is difficult due to their multiple dimensions and the use of non-standardized assessment instruments. Contextual sensitivity of both evaluative criteria and evaluator involvement increases such imprecision, thus preventing sufficient social validation of behavioral treatments for autism.
Objectives: To identify influential evaluations of behavior-analytic treatments for autism and to examine social-validity trends in this sample of recent research in applied behavior analysis.
Methods: Research articles involving at least one participant with autism and the empirical evaluation of behavior-analytic procedures were selected from volumes of JABA and JADD published between 1992 and 2007. Characteristics of a study's participants and intervention were coded. A multidimensional framework (Schlosser, 1999) was used to identify conceptually distinct aspects of social-

validity components (i.e., methods, outcomes) and assessments (e.g., agent, format). Results: The 249 eligible articles from JABA included 17% with an evaluation of treatment acceptability or treatment outcome and 5% that assessed both of these components. Social validation was more common in naturalistic (29%) than in analog (15%) settings. Among 114 eligible articles from JADD, 75% assessed one component of social validity and 42% evaluated acceptability and outcome. Social validation was comparable between naturalistic (77%) and analog (71%) settings. Evaluation of outcomes instead of methods was more common in treatments based on manipulation of antecedents and/or consequences than in skill-acquisition programs, which were based on behavioral principles but often used scales of diagnostic criteria or general behavior as outcome measures. Further analysis shows differences between journals across various study characteristics.
Conclusions: Summary data replicate results of prior JABA reviews and show more-but-different social-validity activity in the smaller set of JADD studies. These trends may reflect increased interest in general measures, instead of discrete target behaviors, for the evaluation of autism-intervention outcomes.

10 134.10 Targeting Restricted and Repetitive Patterns of Behavior in Children with Autism and Asperger Syndrome. C. E. Lin*, R. L. Koegel, Ph.D. and L. K. Koegel, Ph.D., *University of California, Santa Barbara*

Background: The domain of restricted and repetitive patterns of behaviors (RRB) is one of the core diagnostic features of autism and Asperger syndrome. RRB comprise a heterogeneous group of behaviors, but appear to share a common quality of rigidity or "inflexibility." Furthermore, two main sub-categories of RRB have been delineated into lower-order RRB (i.e. motor-sensory behaviors) and higher order RRB (i.e., complex behavioral rigidity). Research on the developmental course of these symptoms highlight the pervasiveness of RRB, especially higher-order behaviors (i.e. restricted interests, insistence on sameness and ritualistic behaviors); the negative impact RRB pose for the individual and family; and reduced symptom improvement in this area in comparison to social and communication gains. Therefore, further research on interventions addressing RRB is warranted and there is evidence that self-management is an effective component of behavioral intervention in improving a variety of core ASD symptoms.

Objectives: To examine the effects of implementing an individualized self-management program to reduce behavioral inflexibility observed in targeted higher-order RRB, generalization of these behavioral gains and child affect.

Methods: A non-concurrent multiple baseline across participants time series research design was implemented with measures collected longitudinally. Following systematically staggered baselines, each participant (age 5-7), diagnosed with Autism Spectrum Disorder (ASD), was provided with a manualized self-management program in an attempt to increase behavioral flexibility.

Results: Application of a self-management program was effective in improving RRB as evidenced by increased percentages of behavioral flexibility following intervention. All participants demonstrated increased flexibility in comparison to baseline and these gains generalized to a variety of settings and activities. Improvements in child affect ratings were also observed.

Conclusions: Self-management is an effective intervention to improve behavioral flexibility related to RRB among children with ASD and has implications for future theoretical, behavioral and neurobiological research in this area.

11 134.11 Effects of music therapy vs. play session with toys on social behaviors in young children with autism: Sub-group analyses based on differences in age, symptom severity and language skills. J. Kim*[1] and T. Wigram[2], (1)*Jinah Kim Music Therapy Center for Research and Practice*, (2)*Aalborg University*

Background: Music therapy is gaining growing recognition as an effective intervention addressing fundamental levels of emotional

communication and social engagement for young children with autism.

Objectives: Considering both toys and musical instruments involve some form of playing together, this explorative study set out to investigate and compare the effects of music therapy and play session with toys on social behaviors in young children with autism. As children with autism display huge variety and individuality across all ages and abilities, it would be clinical relevant to find out what type of interventions are most suited to the different developmental needs of these children. This study takes a further step into addressing these more specific and fundamental issues.

Methods: A randomized controlled study was undertaken employing a repeated measures comparison design, both between conditions and within subjects. Children were randomly assigned to two groups; Group 1 had music therapy first, and then play sessions later. Group 2 had play first, then music therapy. The responsiveness in children was assessed with the Pervasive Developmental Disorder Behavior Inventory (PDDBI), and the Early Social Communication Scales (ESCS). Analyses of sub-groups were also undertaken as follows: 1) verbal vs. non-verbal children; 2) the younger vs. older children; 3) mild to moderate vs. severe autism.

Results: Overall results from the PDDBI and the ESCS indicated that music therapy was more effective at improving pro-social behaviors in children with autism. Younger, less autistic and more verbal children gained more from these trials in both conditions than 'low functioning non-verbal, severely autistic and older children'. Session analysis revealed significant differences between conditions in target behaviours.

Conclusions:Clinical implications are further discussed. One should not, however, overlook the small improvement in low functioning and severely autistic children in comparison to larger changes in the 'more able' group of children.

12 134.12 PHARMACOGENETICS OF RISPERIDONE THERAPY IN AUTISM. C. Correia*[1], J. Almeida[2], P. Santos[3], A. F. Sequeira[1], C. Lobo[2], T. S. Miguel[2], R. Santos[2], G. Oliveira[2] and A. M. Vicente[1], (1)*Instituto Gulbenkian de Ciência/Instituto Nacional de Saúde Dr. Ricardo Jorge*, (2)*Hospital Pediátrico de Coimbra*, (3)*Instituto Gulbenkian de Ciência*

Background: The atypical antipsychotic risperidone is used to control disruptive behaviors associated with autism. Risperidone is mainly metabolized by cytochrome P4502D6, while drug absorption and bioavailability are mediated by glycoprotein P, encoded by *MDR1* gene. As an atypical antipsychotic, risperidone presents a high serotonin 5-HT2A/Dopamine D2 binding ratio.

Objectives: This ongoing pharmacogenetic study aims at the identification of genetic factors underlying the variability in individual response of autistic patients to risperidone therapy.

Methods: Autistic patients (N=41) initiating risperidone therapy were recruited for this study. Drug efficacy and tolerability was monitored at baseline and at specific times after risperidone introduction (one, three, six and twelve months) using the Autism Treatment Evaluation Checklist (ATEC). Safety and tolerability measures included prolactin levels, weight gain and extrapyramidal movements. The influence of genetic variation in candidate genes *CYP2D6*, *DRD2*, *DRD3*, *HT2A*, *HT2C, HTR6, MDR1* and *BDNF* in drug efficacy and safety was analysed.

Results: ATEC scores decreased very significantly during all time intervals ($P<0.0001$), corresponding to an improvement that was more pronounced in the behavioural and sociability domains and generally during the first month of treatment, and significantly correlated with gender. Prolactin levels, weigh, Body Mass Index (BMI) and waist circumference increased most significantly in the first month of treatment. We found an association of *MDR1* T1236C marker with improvement in the speech (P=0.007) and sensory/cognitive (P=0.006) subscales and of *HTR2A* C-1438A>G with speech improvement (P=0.44). *BDNF* genotypes were significantly

associated with BMI, after adjustment for sex and age (*P*=0.007).

Conclusions: Our preliminary results indicate that the *MDR1* and *HTR2A* genes influence response to risperidone, corroborating previous observations that the *MDR1* T1236C and *HTR2A* -A1438G polymorphisms affect, respectively, the availability and binding of the risperidone. BMI variation was associated with *BDNF*, previously implicated in weight regulation, eating behaviour and drug related weight changes.

13 134.13 Anxiety and paranoid ideation in Asperger's syndrome. D. J. Hare*, *University of Manchester*

Background: Epidemiological studies of psychiatric co-morbidity in Asperger's syndrome [AS] indicate depression, anxiety disorders and bipolar disorder as being diagnosable more often than for the general population and represent substantial morbidity (Gillberg & Billstedt, 2000), with up to 7% of individuals with AS having an anxiety disorder. Similarly, persecutory and passivity delusions and delusions of reference also identified in AS (Clarke et al 1999). However, there have been few attempts to develop the types of powerful cognitive behavioural models of such psychopathology as has been achieved to good effect in the non-AS population
Objectives: To review relevant psychological research on anxiety and delusional beliefs in AS to enable the development of an integrative cognitive model of clinical utility
Methods: Five research studies examining anxiety and delusional beliefs in AS (Blackshaw et al 2001; Craig et al 2004; Meraj & Hare 2004; Abell & Hare 2005; Hembry, Harrop & Hare 2007) were identified.

Results: An integrative cognitive model was developed, based on that of Abell & Hare (2005), and tested against available data.

Conclusions: An integrative cognitive-behavioural model of anxiety and delusional beliefs appears to be both feasible and of clinical and experimental utility

14 134.14 Fluoxetine vs. Placebo for Repetitive Behaviors and Global Functioning in Adults with ASDs. L. Soorya*[1], W. Chaplin[2], E. Anagnostou[1], C. Settipani[1] and E. Hollander[1], (1)*Mount Sinai School of Medicine*, (2)*St John's University*

Background: Serotonin reuptake inhibitors are among the most widely utilized psychopharmacological treatments for individuals with ASD, with use increasing 3.5 times in the eight-year period between 1993-2001 (Aman, et al., 2005). The present study represents the first large-scale, double-blind, placebo controlled trial of fluoxetine in adults with autism.

Objectives: The primary objective of this study was to evaluate the effects of fluoxetine on repetitive behaviors in adults with ASDs

Methods: This study utilized a 12-week, randomized, double-blind, parallel-group, placebo-controlled study design. Study medications were dispensed in an identical, double-blind fashion with dosage following a fixed schedule in the first two weeks and thereafter if tolerated participants. Blinded study psychiatrists completed ratings on the outcome measures including the Y-BOCS and CGI during bi-weekly clinic visits.

Results: Forty-eight adults ages 18-65, with a DSM-IV diagnosis of an ASD, confirmed by ADOS and/or ADI, were screened for the study; with 36 participants randomized and included in the analysis. Analysis of dosing patterns suggest the mean endpoint and peak dose for the sample was 64.76 mg (sd=29.9), occurring at week 8. Mixed regression models with observations nested within subjects were used to analyze Y-BOCS Compulsion subscale data. Treatment by linear interaction indicates a significant reduction in compulsion scores of the Y-BOCS across time for the fluoxetine treatment group compared to placebo (z= -2.432, p-.15, d=.527), with endpoint differences yielding a moderate effect size. Independent sample t-tests of the CGI-Improvement-Obsessive Compulsive (CGI-I-OC) scores and CGI-Improvement-Global

(CGI-I-G) at week 12 also suggest significant improvements both CGI-I-OC and CGI-I-G ratings for the treatment group.

Conclusions: The results of this clinical trial suggest fluoxetine is more effective than placebo in the treatment of repetitive behaviors and global functioning in adults with ASDs; and appeared to be well-tolerated with only mild and moderate side effects in the treatment group

15 134.15 Joint Attention Intervention Outcomes: Language and Social Communication in Young Children with Autism. A. M. Mastergeorge*[1], R. J. Musci[2], N. T. Patra[2], D. Thompson[3] and D. Benjamin[3], (1)*University of California, Davis/M.I.N.D. Institute*, (2)*University of California*, (3)*UC Davis, M.I.N.D. Institute*

Background: Joint attention has been a focus of interest in many studies of autism since it is considered to be a deficit skill and a hallmark for social communication and language development. Recent intervention studies have focused on joint attention; however few studies have focused on the parent's role in joint attention interventions. Objectives: The purpose of this study is to investigate joint attention interventions in mother-child contexts in home environments, and to further our understanding of developmental trajectories of joint attention and social communication in young children with autism engaged in a variety of play-based joint attention activities. Methods: Fifteen young children diagnosed with autism (ages 24 to 38 months with a mean age of 33 months) were selected based on a diagnosis of autism within six months of the study onset. Several pre-test, mid-point, and post-test developmental measures were administered including The Early Social Communication Scales (ESCS), the MacArthur Communication Development Inventory, and the Mullen Scales of Early Development. Daily language diaries, weekly social communication and joint attention ratings were collected. All subjects participated in four laboratory visits, and sixteen weeks of home intervention in joint attention and social communication tasks. All home intervention interventions were videotaped and subsequently rated for both maternal and child behaviors using the Mahoney Behavioral Rating Scales. Results: Correlations indicate strong relationships between joint attention and social communication behaviors and developmental outcomes in intervention contexts. Profiles of joint attention shifts across weeks are presented to explicate indicators that may be influencing the rate of progress in joint attention behaviors and subsequent language outcomes. Conclusions: Joint attention focused interventions play a specific role in increasing social communication skills in young children with autism. In particular, these home-based interventions have important implications for both language development and early intervention approaches.

16 134.16 Effect Of Homoeopathic Drugs Therapy in Children with Autism Spectrum Disorder : A Preliminary Study. D. N. Gupta[1], R. Juneja*[2], D. A. K. Malhotra[1], U. Varma[2] and D. R. K. Saxena[1], (1)*Nehru Homeopathic Medical College and Hospital, Univeristy of Delhi*, (2)*Tamana School of Hope and Autism Research Center*

Background:

Homoeopathic therapeutic system treats the autistic spectrum disorder (ASD) children according to symptomatology. Disease labels are not generally used in homeopathic remedial methodologies. Important characteristic symptoms exhibited by individual disorder forms the basis and plays decisive role in selecting homoeopathic medicines and remedial regimen

Objectives:

To evaluate the efficacy of Homeopathy in Autism Spectrum Disorder. To develop a proper homeopathic therapeutic regimen for autisitc children.

Methods:

30 autistic children (Age group: 4 to 14 yrs) were identified on the basis of severity of symptoms, Psychological assessment (DSM IV criteria and CARS and IQ/SQ analysis) and

other Patho-physiological criteria. After medical, clinical assessments and recording of case histories the subjects were divided into two groups on basis of homeopathic regimen administered to them :

Group A: Classical Homoeopathic Medicinal Treatment

Group B: Multi-drug / Frequent repetition of Homoeopathic medicine.

All the cases were then individualized, evaluated, analyzed in detail and repertorized to arrive at the Similimum.

Results:

The homeopathy regimen was started on 17 subjects. Remaining 13 are still undergoing preliminary assessments. Preliminary results showed significant improvement in 7 subjects in respect to their cognitive functions, hyperactivity, nervous agitation, attention span, obeying of verbal and non-verbal commands and increase in general, social and environmental awareness. In 7 cases moderate improvement was observed and rest 5 were reassessed for those showing partial / or non-improvement.

Conclusions:

Preliminary results are showing definite and significant effect of Homoeopathy in the treatment of ASD and their improvement and progress may help in finding out a novel method of curative remedial system. Detailed results of this study will be presented and discussed after the rigorous evaluations of parameters and important and significant conclusions can be drawn.
Some cases showed scepticism in the mode of treatment as it requires a long-term treatment plan. Study is still in progress.

17 134.17 A study of how children with ASD respond inside a virtual reality room. S. Wallace*[1], A. Westbury[1], K. White[1], S. Parsons[2], K. B. White[1] and A. Bailey[1], (1)*University of Oxford*, (2)*University of Birmingham*

Background:

Virtual reality (VR) technology has the potential to educate children with ASD but to date there has been little research into children's responses to the content of VR programs and whether these responses differ from the experiences of typically developing children.

Objectives:

The aim of this study was to measure participant's sense of presence (the feeling of being located inside a virtual world) while they experience scenes projected into a virtual reality room. Our prediction was that the experiences of adolescents with ASD would not differ from those of typically developing adolescents.

Methods:

Ten participants with ASD and 13 typically developing IQ matched controls were shown 3 animated scenes (a busy road; a school playground; a school corridor) inside a virtual reality room and asked to complete simple tasks. The children then filled out the Sense of Presence Inventory (SoPI) from which a total score can be calculated, as well as domain scores for: 1. Spatial Presence, the feeling of being located in the virtual world; 2. Engagement, a sense of involvement with the content; 3. Ecological validity, how natural the content seemed; 4. Adverse effects, a measure of negative physiological responses (e.g. dizziness).

Results:

There were no significant differences between the two groups on total or domain scores from the SoPI. Questions on user-preference showed that 78% of all participants spontaneously reported liking the content or realism of the scenes; 13% reported disliking their physiological responses.

Conclusions:

Adolescents with ASD felt themselves located inside the virtual worlds in the same way as typically developing adolescents and there were no group differences in reports of negative physiological responses nor engagement with the content. These data

show that adolescents with ASD respond typically to this VR technology, going some way to validating its future use in educating children with ASD.

18 134.18 EFFICACY OF A COGNITIVE-BEHAVIORAL GROUP THERAPY PROGRAM ON TAIWANESE SCHOOL-AGE CHILDREN WITH ASPERGER'S DISORDER.

C. C. Chao*[1], M. Y. Hsu[2], Y. Y. Wu[2], L. C. Wang[2], Y. H. Huang[1] and W. Y. Huang[1], (1)*Chang Gung University*, (2)*Chang Gung Memorial Hospital*

Background:Asperger's disorder is characterized by marked difficulties in social interactions, which might be the result of a specific deficit in theory of mind and lack of social skills. Treatment programs based on cognitive-behavioral therapy (CBT) principles have shown effectiveness in improving the theory of mind and social skills for children and adolescents with Asperger's disorder

Objectives:This study intends to examine the efficacy of a cognitive-behavioral group therapy (CBGT) program designed to promote the theory of mind and social skills for Taiwanese school-age children with Asperger's disorder.

Methods:Eight Taiwanese children aged 7-10 years with average intelligence participated in this program which included 10 weekly sessions with 80 minutes each. The behaviors of these participants were evaluated and compared before and after the training. Outcome measures consisted of (1) Australian Scale for Asperger's syndrome; (2) behavior observation; (3) theory of mind task; and (4) Vineland Adaptive Behavior Scales.

Results:Pre-post comparison showed significant decreases in parental ratings in symptom severity (t=-5.59, p<.1), with a significant improvement in their children's social-emotional ability (t=-4.69, p<.1) and communication skills (t=-2.98, p<.1). Behavior observation also indicated improvement in theory of mind ability. However, there were neither significant difference in participants' performance on the theory of mind task nor in teacher's ratings of symptom severity and social skills.

Conclusions:Findings of this study partially support the immediate effect of this CBGT program for Taiwanese children with Asperger's disorder, but with limited generalization effect across situations.

19 134.19 Meta-Evaluation of Comprehensive Model Treatment Programs for Children.

S. Odom*[1], B. Boyd[2], L. Hall[3] and K. Hume[1], (1)*University of North Carolina*, (2)*FPG Child Development Institute*, (3)*San Diego State University*

Background:

With increases in prevalence of ASD, the need to establish comprehensive treatment program models (CTP) is great. A variety of programs exist, but little evidence exists about the quality of the models.

Objectives:

The purpose of this study was to evaluate the critical features of CTPs for children and youth with ASD on six dimensions: 1) Operationalization, 2) Fidelity of treatment, 3) Replication, 4) Outcome data presented, 5) Quality of the research design, and 6) Related evidence from focused intervention studies of component features.

Methods:

Using objective inclusion criteria (i.e., published description, manualization, theoretical or conceptual framework, addressed multiple development domains or core features, intensity), authors identified CTPS through an exhaustive review of the professional literature. A standardized evaluation form containing the six dimensions noted previously was completed by two raters for portfolios of evidence assembled, initial inter-rater agreement was calculated, and final ratings were based on consensus.

Results:

Twenty-eight CTPs were identified and categorized as: ABA Clinic or Home-Based,

ABA Center-Based, ABA-Inclusive, Developmental, and Other. On the poster presentation, evaluation for each of the CTPs on each of the dimensions will be displayed. CTPs were strongest on the Operationalization and Replication strands of the evaluation, with some also providing strong fidelity information. Few CTPs, with several notable exceptions (e.g., Lovaas Institute), provided RCT or quasi-experimental design efficacy data, although several supplemented evidence for efficacy through focused intervention studies of their model components.

Conclusions:

A different models for CTPs have been developed and are cohesive enough to be replicated by service providers, with training. Evidence for the efficacy of these models is emerging, although still lacking for many CTPs. The next step in this program of research needs to be systematic efficacy trials of the most promising models with examination of moderators and mediators of treatment effects.

20 134.20 NOVEL COMMUNITY-BASED EARLY INTERVENTION PROGRAM FOR AUTISM: ONE-YEAR OUTCOMES. I. M. Smith*[1], C. McCleave[2], L. Putnam[2], K. Smith[2], R. Landry[3], D. Chitty[2] and S. E. Bryson[1], (1)*Dalhousie University*, (2)*IWK Health Centre*, (3)*Cape Breton Regional Hospital*

Background: Effectiveness studies of autism early intervention programs are sorely needed; few have examined alternatives to the UCLA model. The Nova Scotia Early Intensive Behavioural Intervention (NS EIBI) model (Bryson et al., 2007) entails implementation of Pivotal Response Treatment (Koegel et al., 1999; Koegel & Koegel, 2006) by parents and one-to-one therapists in community settings.

Objectives: To examine changes in measures of child cognitive, language and behavioural functioning following 12 months of intervention in the NS EIBI model.

Methods: Fifty-six children with ASD below 6 years of age received up to 15 hours/week of 1-to-1 intervention for one year; parents also received training in PRT. Treatment fidelity was monitored. Independent research assessments were conducted at intervention start, and after 6 and 12 months; measures included both direct child assessment and parent report.

Results: Data are available for 53 children (mean age = 4.3 yrs; mean IQ estimate = 53.0, SD= 20.0), 43 of whom (40 males) have completed 12-month assessments. Significant mean gains were observed on estimated IQ (15.4 points), and on receptive and expressive language mental ages (14.4 and 13.3 months, respectively). Concurrently, significant decreases were seen in autism symptoms (Social Responsiveness Scale Total, 8.1 points), and other problem behaviours (CBCL Total, 8.4 points). Consistent with the focus of treatment, Vineland Communication domain standard scores increased significantly (7.9 points), whereas gains in other domains (except Motor) were significant but more modest. Magnitudes of gains were highly (and significantly) dependent on initial IQ for cognitive and language, but not for behavioural measures.

Conclusions:Children who received up to 15 hours/week of 1:1 PRT and whose parents were trained demonstrated substantial gains after one year of intervention. Results suggest that this less intensive ABA-based model enhances specific social-communication skills, as well as producing generalized change captured by IQ and behavioural measures.

21 134.21 ARIPIPRAZOLE IN CHILDREN AND YOUNG ADOLESCENTS WITH PERVASIVE DEVELOPMENTAL DISORDERS: A NATURALISTIC, RETROSPECTIVE STUDY. A. Cosenza*[1], F. Muratori[2], F. Salvadori[1], R. Tancredi[1] and G. Masi[1], (1)*Scientific Institute*, (2)*Scientific Institute "Stella Maris"*

Background: Appropriate use of pharmacotherapy can improve some symptoms in PDD and facilitate other treatment. Antipsychotics are the widely used drugs in PDD. No systematic data exists on the use of the new atypical antipsychotic aripiprazole

Objectives: To describe efficacy and tolerability of aripiprazole monotherapy in children and young adolescents with PDD and severe behavioral disorders.

Methods: 25 patients (17 males and 8 females, age range 4.5 to 15 years, mean age 9.1 ± 3.1 years), enrolled during 2006-2007, diagnosed as PDD according to DSM IV criteria, and followed-up for 3-12 months (mean 6.7 ± 3.7 months) are included. All youths were treated with aripiprazole monotherapy.Outcome measures: CARS, Clinical Global Impression–Improvement (CGI-I) and Children Global Assessment Scale (C-GAS).

Results: Mean CGI Severity Score: 5.84 ± 0.8. Mean dose: 6.7 ± 4.5 mg/day (range 1.25 – 15 mg/day). After the treatment the CARS improved from 42.7 ± 5.3 to 39.4 ± 5.8 (t=4.8, df=24, p=.000). The improvement of the score was only 7.7%, and the effect size was 0.6. The mean CARS score improved from 26.0 ± 6.0 to 29.7 ± 8.5 (t=-3.8, df=24, p=.000), but the improvement was only 14.2%, and the effect size was 0.51. According to the CGI-Improvement Score, only five patients resulted Much or Very Much improved, while 11 patients resulted minimally improved, 6 patients resulted unchanged, and 3 worsened. Fourteen patients experienced agitation during the treatment, in four patients associated with self-injurious behaviors, in five patients associated with insomnia. One patients presented mild extrapyramidal symptoms. Nine patients discontinued the medication during the follow-up, due to side effects and/or lack of efficacy.

Conclusions: In this sample of very severely impaired children and adolescents with PDD, aripiprazole monotherapy resulted only modestly effective for maladaptive behaviors. Behavioral activation and insomnia were the most frequent side effects. Further controlled studies in this age group are warranted.

22 134.22 AN EVALUATION OF BRIEF PARENT TRAINING IN PIVOTAL RESPONSE TREATMENT FOR PRESCHOOLERS WITH AUTISM. J. Coolican*[1] and S. Bryson[2], (1)*Dalhousie University*, (2)*Dalhousie University/IWK Health Centre*

Background: Evidence of improved outcomes with early behavioural intervention has placed the early treatment of autism as a health research priority. However, long waiting lists for treatment preclude timely access, despite recommendations that intervention be provided as early as possible to optimize the children's outcomes. Pivotal Response Treatment (PRT) has been shown to be effective at promoting social-communication in children with autism (e.g., Koegel & Brookman, 2003). Moreover, an integral component of PRT is parent training, as parents are considered to be the primary implementers in the PRT model. To date, research on parent training has focused primarily on a 25-hour program; however some evidence suggests that less intensive training may still be effective.

Objectives: To evaluate the efficacy of brief training in PRT for parents of preschoolers with autism, who were awaiting, or unable to access, more comprehensive treatment.

Methods: Eight preschoolers with ASD and their parents participated in the study using a non-concurrent multiple (across-participants) baseline design. Parents were seen for three 2-hour training sessions on PRT. Measures focusing on parent and child outcomes, using questionnaires and coding of behaviour from video, were obtained before, immediately after, and 2- to 4-months following training.

Results: Parent's fidelity in implementing PRT techniques improved after training. Concurrent with this, the children's production of functional verbal utterances increased following training (mean change from pre- to post- training = 25%, range = 4.5%-57%). These changes also were maintained at follow-up. Overall, parental stress tended to decrease and self-efficacy increased, although these varied across parent participants.

Conclusions: Based on these findings, brief parent training promises to provide an immediate cost-effective intervention that could be adopted widely. Discussion will also focus on qualitative information that provides

insight into how parent training could be improved.

23 134.23 Comparing the Effectiveness of Two Commonly Used Discrete Trial Procedures for Teaching Simple Discriminations for Young Children with Autism Spectrum Disorders. A. Gutierrez*[1], M. N. Hale[1], A. J. Fischer[1], J. S. Durocher[1], M. Alessandri[1] and H. A. O'Brien[2], (1)*University of Miami*, (2)*Nova Southeastern University*

Background:Discrete trial programs are commonly used to teach children with autism new skills. However, there is no universally accepted discrete trial program methodology, and methodological differences between programs are common. For example, when teaching simple receptive discriminations (e.g., "touch _____, " "show me ___") discrete trial programs are commonly discrepant regarding the preferred teaching methodology. One described procedure used to teach simple discriminations, the Simple/Conditional procedure, suggests that novel receptive discriminations be taught by progressing systematically from a simple discrimination training phase (which involves teaching the stimuli in the absence of any distracter stimuli), to a conditional discrimination training phase, (which involves adding a distracter stimuli). An alternative, yet briefer, procedure, the Conditional Only procedure, suggests that receptive discriminations be taught exclusively in the context of conditional discriminations, using distracter stimuli.

Objectives:We compared the differential effectiveness of two commonly used, yet unevaluated procedures. We evaluated the Simple/Conditional teaching procedure and the Conditional Only procedure for teaching a simple receptive discrimination to young children with autism using discrete trials.

Methods:Three children, ages 2-4 were taught to receptively identify picture cards of common items. A single-subject, adapted alternating treatment design was used to evaluate the two procedures. Data was collected on the number of training trials required to reach a mastery criterion. Following training, a 1-month follow-up session was conducted to assess maintenance of learned skills.

Results: The results of this study showed that there was no consistent difference between procedures in the acquisition of or improved maintenance of discrimination skills.

Conclusions: These results suggest that for some children, the use of the common, yet more lengthy, Simple/Conditional procedure may incorporate unnecessary teaching steps, thereby needlessly lengthening the training process.

24 134.24 Using video modeling for teaching social behavior to children with autism. D. A. Crawford*[1], M. Wójcik[2] and A. Budzińska[2], (1)*York University*, (2)*Institute for Child Development*

Background: Behavioral techniques such as video modeling have been shown to improve play skill, social interactions and behavioral functioning in children with autism spectrum disorder. Video modeling depicting exemplary behaviors can be effective in targeting social skills and daily living skills and increase the child's attention to the modeled task.

Objectives: In the present study we examined whether video modeling techniques could increase the social engagement and play skills of three preschool children diagnosed with autism spectrum disorders using DSM-IV criteria with no other known etiology.

Methods: Videotape models engaging in appropriate verbal and motor play with a selected toy were shown to the children. Each videotape displayed a chain of specific behaviors. The sequence of videotapes was extended with subsequent training. No manual or verbal prompts were used. Food reward was provided when the child performed a correct response within a chain of behaviors. Proper target behaviors were recorded. Only repetitive verbal and motor behavior was interrupted.

Results: Our results show that the video modeling intervention was effective in increasing the performance of desired behaviors and led to the rapid acquisition of

both verbal and motor responses. Improvements were most evident in the area of functional and social-communication skills. In addition, we found that improvements were maintained and transferred to other settings after the program was completed.

Conclusions: In summary, the video modeling teaching procedure was found to be an efficient technique to increase the social engagement in children with autism spectrum disorder.

25 134.25 Medication Treatment For Attention Deficit Hyperactivity Disorder In Children With Autism Spectrum Disorders. Classification Problems And Evidence From Literature. E. Paliokosta*[1], A. B. Thomson[2], S. Maltezos[1] and K. Xenitidis[1], (1)*Adult ADHD Service, The Maudsley Hospital*, (2)*Institute of Psychiatry, Kings College London*

Background: Attention-deficit hyperactivity disorder (ADHD) is a heterogeneous constellation of complex neurodevelopmental problems, with prevalence ranging from 1.5% to 7% according to criteria used. In DSM-IV ADHD criteria, Autism Spectrum Disorders (ASD) are exclusionary criteria for ADHD diagnosis however there is increasing evidence that both conditions can co-exist.

Objectives: We will review studies examining the effectiveness of medication treatment for ADHD in people with ASD.

Methods: Electronic Searches will be used to identify all studies of medication for ADHD in people with ASD. The primary outcome studied will be change in symptoms of attention deficit and hyperactivity.

Results: A number of studies provide evidence that first line ADHD treatment (stimulants) can be effective in children with ASD however the response rate is decreased and the adverse effects increased compared to the general population. Risperidone has been studied also and it is considered effective for ADHD symptoms. Atomoxetine, introduced more recently in the treatment of ADHD, was proved well tolerated and effective for reducing ADHD symptoms in a small open label trial and a cross over trial.

Conclusions: Treatment of ADHD symptoms can enhance social and occupational adaptation, prevent aspects of co-morbidity and increase self-esteem and quality of life in children and adults with ASD. Literature suggests that ADHD medication can be effective in the ASD population although Randomized Controlled Trials are still lacking.

26 134.26 LANGUAGE COMPREHENSION IN YOUNG CHILDREN WITH AUTISM SPECTRUM DISORDER: DATA FROM AN EARLY INTERVENTION STUDY. K. Wittemeyer*[1], B. Rogé[1], C. Mantoulan[1] and G. Magerotte[2], (1)*Université Toulouse*, (2)*University of Mons-Hainaut*

Background: Previous studies have demonstrated the efficacy of early intervention in improving communication skills of children with autism spectrum disorder (ASD). Most of these studies have focussed on expressive language outcomes, paying little attention to the role a child's early speech and symbol comprehension has as a foundation for later productive word use. It is therefore essential to assess possible comprehension difficulties and the efficacy of educational strategies to address them.

Objectives: To establish whether an early intervention program based on the NRC's (2001) recommendations can help children with ASD increase their language comprehension skills.

Methods: Two groups of children with ASD were matched on the Griffiths Mental Scales and chronological age (mean age 63 month). The experimental group (N=16) received a global intervention program for 15-20 hours per week following an individualised curriculum. Activities included many opportunities for children to practice effective listening behaviours and develop their receptive vocabulary. The control group (N=11) received standard treatments offered by education and health services. The children's comprehension of labels, instructions and syntactically complex

sentences was evaluated with the Picture Vocabulary Test and the Reynell Comprehension Subscale at baseline and after 1yr of intervention.

Results: The children in the experimental group (EG) improved significantly more than the control group (CG) on the Picture Vocabulary Test, progressing by 17 months (age equivalence) compared to 7 months in the CG. On the Reynell Comprehension Subscale the EG showed a gain of 16 months versus 3 months in the CG.

Conclusions: Children from the EG made significant gains in language comprehension, reducing the magnitude of their developmental delay. Conversely, the comprehension skills of most children from the control group continued to fall behind. A long term aim of our research is to analyse the effect of improvements in language comprehension on children's expressive language skills.

27 134.27 The Behavioural and Developmental Continuum of Autism Interventions: A Systematic Review. V. Smith*, *University of Alberta*

Background: Considering the importance of, and demand for interventions for ASD, and the current rising trend in new programmes, a rigorous synthesis of high quality intervention is needed to inform the clinical community, policy makers, researchers, and families of children with autism. Objectives: To review and synthesize the evidence on the efficacy and effectiveness of the behavioural and developmental continuum of interventions for autism. Methods: Comprehensive searches were conducted in 22 electronic data bases of medical and psychological literature up to May 2007. Other sources of potentially relevant studies included hand searches of relevant journals, reference tracking, and contact with experts. Included studies were clinical trials and observational analytical studies on any behavioural or developmental intervention for individuals diagnosed with autism and published in English. Two independent reviewers assessed study relevance, extracted the data, and assessed the methodological quality of the studies. Results: Evidence on the effectiveness of interventions was provided in 101 studies that were predominantly of poor to moderate methodological quality.The substantial variations among the studies in the the design, the description of the interventions, the type of controls, the type of populations, and the outcomes reported allowed for direct comparisons of only 13 of the 101 studies included in the review. Conclusions: In spite of the many published studies on the subject, there remains deep controversy and no definitive answer regarding the "best" approach to treat the core symptoms and other manifestations of autism. Management decisions need to be guided by individual clinical presentation, needs of the caregivers, and availability of resources for implementation of the intervention. Future studies on effectiveness of these interventions need to be more rigorous.

28 134.28 Barriers to Successful Training in Positive Behavior Support: Predictors of Attrition and Success. M. L. Zona*[1], K. V. Christodulu[2], V. M. Durand[3] and M. Hieneman[3], (1)*The Warren Alpert Medical School of Brown University*, (2)*Center for Autism and Related Disabilities*, (3)*University of South Florida St. Petersburg*

Background: Parents of children with developmental disabilities have been taught to use positive behavior support (PBS) approaches in their homes to successfully reduce and eliminate the challenging behaviors of their children and to help their children live more productive lives (Lucyshyn, Dunlap, & Albin, 2002). Despite the success of these training programs, many parents end treatment prematurely. Limited information is available regarding why these parents may be dropping out.

Objectives: The purpose of the present study was to examine the relationship between barriers to treatment participation, parental pessimism and depression, and attrition from treatment and treatment outcomes.

Methods: The study used a sample from a larger project, The Positive Family Intervention Project (Durand, 2007; see also Durand, Hieneman, Clarke, & Zona, in press), in which

parents with high pessimism scores were randomly assigned to either traditional training in PBS or PBS with the addition of an optimism component. Twenty-five parents of a child with a developmental disability and significant challenging behaviors, ages 3- to 5-years-old, completed pre- and post-intervention questionnaires assessing child behavior levels and support needed and parental pessimism and depression. Pre- and post- video samples of the child's behaviors and treatment attendance were also collected. Finally, both the parent and the therapists completed the Barriers to Treatment Participation Scale (BTPS) following treatment. The present study examined the relationship between these variables across treatment conditions.

Results: Results indicated significant relationships between parental depressive symptoms and child behavior outcomes. In addition, therapist reports of stressors and obstacles to treatment were related to treatment attendance. Results also support the use of parent training programs targeting both child behaviors and parental perceptions to improve child behavior and family outcomes.

Conclusions: Discussion highlights the relationship between parental affect and treatment outcomes. Limitations of the study and future directions for research are also discussed.

29 134.29 Use of Complementary and Alternative Medical Treatments among Individuals with Autism associated with del 15q.
M. Petrongolo*[1], D. S. Mandell[2], K. Lesko[1], B. Finucane[3] and S. E. Levy[1], (1)*Children's Hospital of Philadelphia*, (2)*University of Pennsylvania School of Medicine*, (3)*Elwyn*

Background: Studies report high rates of complementary and alternative medical (CAM) treatments for children with autism. Little is known about child and family characteristics associated with CAM use.
Objectives: The purpose of this study is to compare the frequency and correlates of CAM treatment in individuals whose autism is associated with del 15q with those without a known genetic cause in order to examine factors determining families' choices of treatment.
Methods: Families were recruited for a web based survey posted in the IDEAS (isodicentric exchange and support) newsletter and website. Caregivers' responses to questions about their child's clinical presentation and types of treatment were recorded and encoded into mutually exclusive categories. The prevalence of CAM strategies, patterns of treatment and associated child and family characteristics were compared to results from a previous Pennsylvania survey of caregivers of individuals with ASD without known genetic cause.
Results: 102 families responded (52% response rate), and 82 (80%) reported a family member with del 15q and an ASD. Age ranged 3-26; 57% males; average age of diagnosis of del 15q was 2.8 years. Comorbidities included intellectual disability 74%, seizures 53%, ADHD 29%, allergies 27%, anxiety 24%, GI symptoms 22%, and others. The most commonly used treatment was sensory integration training, followed by music therapy and ABA. At least 50% of families used $\geq$ 1 type of CAM treatment. The most commonly used treatments were anti-infectives, vitamin supplements, GI medications and restrictive diets. Comparison of sample characteristics with the Pennsylvania sample is forthcoming.

Conclusions: Use of CAM in families with children with del 15q is high, despite the fact that the cause of the autism is known. These findings should inform clinicians in counseling and managing families of children with autism with or without genetic disorders who may use CAM.

30 134.30 Collateral Gains in Social Communication Skills. J. Suhrheinrich*[1], A. B. Cunningham[1], L. Schreibman[1], A. C. Stahmer[2], R. L. Koegel[3] and L. K. Koegel[3], (1)*University of California, San Diego*, (2)*Rady Children's Hospital*, (3)*University of California, Santa Barbara*

Background: Pivotal Response Training (PRT) and the Picture Exchange Communication System (PECS) are empirically-based programs for teaching communication skills to

children with autism. Because PRT teaches verbal communication and PECS teaches communication via pictures, research has focused on evaluating gains in these areas. Less is known about collateral gains in early social communication skills.

Objectives: To assess change in child social and communicative behaviors.

Methods: Sixteen children with autism (age 2-4), with 10 or fewer functional words, were randomly assigned to PRT (n=8) or PECS (n=8). Children were matched on pre-treatment age, word use, and developmental level. Children received 258 hours of intervention across 23 weeks. Participants were assessed using the Early Social Communication Scales (ESCS) at pre- and post-treatment.

Results: Participants showed improvements in several behavioral domains. Participants made statistically significant gains in rate of high-level joint attention initiations, social interaction initiations, and use of language coordinated with other requesting behaviors. Participants also increased significantly in frequency of responding to the assessor's bids for joint attention and social invitations. There was no significant difference in verbal requesting between treatment conditions.

Conclusions: These findings suggest that children benefit from collateral gains in social skills and communication skills that are not directly targeted through PECS and PRT. Children in both treatment conditions made gains in use of verbal language to request, which suggests that children are equally likely to learn verbal communication skills when taught through a pictorial communication system. Differences in areas of growth in specific nonverbal social communication domains will be discussed within the context of intervention received.

Poster Presentations Program

135 Communication Posters 2

31 135.1 Problem behaviour or a communication break down?. K. J. ,. Tait*, *University of New England*

Background: This case study was conducted in Brunei Darussalam situated on the north-west of the island of Borneo with major population groupings being Malay and Chinese. Brunei Darussalam has extremely limited educational and allied health services for children with autism. Objectives:To assist a regular class teacher in a remote village to support a child's transition from the prelinguistic to the more symbolic stages of communication development.

Methods:The researcher evaluated teacher use of functional communication training (FCT) to replace and enhance prelinguistic behaviours in a young child with autism. Initially, the communicative functions of the child's prelinguistic behaviours were assessed by teacher interview. Initially, one communication function was identified for the child and an intervention goal to replace the child's existing prelinguistic behaviours was developed in consultation with the child's teacher and parents. After baseline phase, the teacher received training on implementation of FCT. Intervention was designed using a simple A-B time series design. The class teacher was trained by the researcher to teach the child how to use this replacement behaviour using a positive behaviour management strategy.

Results: This study investigated the idiosyncratic behaviours of a young child with autism by combining the theoretical areas of prelinguistic communication and functional behaviour. However, this study went beyond analysing the child's current disruptive behaviour. It examined how one child's regular class teacher interpreted the challenging behaviour of a seven (7) year old male child as communicative. Further, the researcher showed how this initial information could be used to enhance the child's communication skills by teaching a replacement behaviour to the child, through the use of positive behaviour management.

Conclusions: A number of implications for training teachers who work in remote villages in Brunei, and recommendations for the use of functional analysis and communication training to overcome a child's challenging behaviour, will be discussed.

32 135.2 INTERACTIONS OF CHILDREN WITH SEVERE AUTISM. C. L. Pollock*, T. Auburn, J. Clibbens and C. Phillips, *University of Plymouth*

Background:Investigating autism in severe cases is fraught with practical difficulties, which has resulted in a literature that tends to focus on high functioning autism. To fully understand autism it is essential that severe autism is also considered. The methodology of Conversation Analysis (CA) has the potential to further our understanding of severe autism as it emphasises interaction as a mutual accomplishment, meaning that it can provide a powerful framework for the analysis of talk when the language abilities of one or more of the participants is compromised.

Objectives:To demonstrate how the methodology of Conversation Analysis (CA) may be usefully employed to investigate interactions of severely autistic children.

Methods:Nine hours of video was obtained from eleven severely autistic children with a CARS score of 37+. The children were filmed engaging in naturally occurring interactions, both at home and at a special school for children with severe learning difficulties. The video material included therapy, teaching sessions and mother-child interactions. From this data a corpus of requests was isolated, transcribed and analysed using CA methodology.

Results: Children were capable of interacting skillfully with their co-participants and despite profound difficulties with speech and language were able to initiate requests. The analysis demonstrated the importance of shared knowledge between the child and their co-interactant which enabled requests to be mutually understood and accomplished.

Conclusions:This study serves as a reminder that the interactional competencies of severely autistic children can be underestimated. The analysis of the children's interaction, showed for example that they were able to design requests to take into account co-participants' shared knowledge. These competencies raise questions about the nature of the deficits involved in autism. CA has the potential to clarify how the deficits considered central to autism are reflected in the everyday talk-in-interaction of 'low functioning' individuals.

33 135.3 Computer Systems for Children with Severe Autism and Learning Difficulty. S. Y. A. Elzouki* and D. Moore, *Leeds Metropolitan University*

Background: There is much research work concerned with computing as an assistive technology for people with autism. Thus far, however, most of the work has concentrated on people with Asperger Syndrome, with very little concern paid to how such technology might help people with severe autism. The research we will discuss in our proposed presentation is an attempt to begin to redress this imbalance.

Objectives: Conduct an in depth qualitative research concerning the use by children with severe autism of computer technology.

Methods: A longitudinal study over some 14 months was carried out with 8 children in a specialist unit for children with severe autism and learning difficulties, set within a mainstream UK school. A participatory action research approach was adopted. First, a relatively formal baseline study was conducted to establish the extent to which the participants could use a bespoke computer system to identify facial expressions of emotions. Results from this informed the subsequent action research cycles. Each cycle involved creating a simple bespoke system for each child, aimed at their individual level of ability and taking advantage of their individual interests.

Results: Results from the baseline study showed a range of ability to recognise the emotions e.g. one child recognised all expressions while several did not co-operate at all. Results from the action research cycles are interesting but they are too complex to outline here; rather, they will be presented at the conference.

Conclusions: The high number of instances of non-cooperation in the first study indicates the difficulties that working with such children can involve. However, by using systems centred on

their individual interests each child in the study was able to enjoy the computer technology and learn from it. Thus our research gives grounds for optimism for the use of computer technology for people with severe autism.

34 135.4 GESTURES OF INFANTS WITH AUTISM, OTHER DD, AND TYPICAL DEVELOPMENT. L. Watson*[1], E. Crais[1] and G. Baranek[2], (1)*University of North Carolina at Chapel Hill*, (2)*University of North Carolina*

Background:

Gestures may differentiate infants with autism or other developmental disabilities (DD) from typical development (TD), and account for variability in later communication.

Objectives:

Gestures of infants with autism, DD, or TD at Time 1 (9-12 months) and Time 2 (15-18 months) were examined to: (1) determine group differences in behavior regulation (BR), joint attention (JA), and social interaction (SI) gestures; (2) compare developmental trajectories of gestures; and (3) use infant gestures to predict preschool communication.

Methods:

Parents of preschoolers provided home videos of their children as infants. Children's preschool skills were assessed using the Vineland. Representative video segments were coded for BR, JA and SI gestures at Times 1 and 2. At Time 1, n=31 autism, 18 DD, and 30 TD; at Time 2, n=21 autism, 12 DD, and 12 TD; at both time points, n=19 autism, 5 DD, and 12 TD.

Results:

(1) Multivariate analyses yielded significant group effects for BR and JA at Time 1, and for BR, SI, and JA at Time 2. Post-hoc analyses showed infants with autism and DD were similar at Time 1, but differentiated by Time 2. (2) For BR, growth slopes from Time 1 to Time 2 were similar for autism and TD. For SI and JA, slopes were similar for DD and TD, but flatter for autism. (3) For the autism group, gestures at Time 1 accounted for significant variance in preschool Vineland Communication (R^2 =.29, F=3.96, p=.18).

Conclusions:

Limited BR and JA gestures at 9-12 months are associated with both autism and DD. Autism-specific deficits in JA are apparent at 15-18 months. Infants with autism may also be distinguishable by slowed growth of both SI and JA gestures in the first half of the 2nd year. Gestures of infants with autism around one year predict preschool communication.

35 135.5 Impairments in Early Communication Skills in Toddlers with Autism and Williams Syndrome. G. Perminova*, J. Burdukova, A. Kazmin and T. Stroganova, *Moscow State University of Psychology and Education*

Background: Williams syndrome (WS) is a genetic disorder which results in uneven cognitive profile and unlike autism syndrome (AS) is characterized by good social skills. We hypothesized that despite these syndrome-specific contrasting communication skills both genetic syndromes could be linked to the impairments in the ability to initiate triadic co-ordination (joint attention)

Objectives: We examined unique patterns of early social communication skills of young toddlers with AS and WS in comparison to typically developing children (TDC).

Methods: Early Social Communication Scale (ESCS, Peter Mundy, 2003) was administered to 8 children diagnosed with AS (chronological age (43,1±8)), 8 children with WS (43,6±15), and 18 TDC (22,7±7). Mental age was assessed with Bayley Scales(BSID II, 1993) and Psychological Educational Profile (Schopler et al, 1990). Three groups were matched for mental age. Repeated measures ANOVA was used for statistical analysis.

Results: The results showed that in average the early communication scores of autistic children were much lower than those of both TDC and WS children. Despite superficially good social skills, toddlers with WS were only proficient in response to social interaction, whereas similarly to autistic children they were

impaired in their ability to initiate communication with an adult. The unevenness of their communication profile was particularly striking in initiating joint attention skills.

Conclusions:Unlike autistic children, toddlers with WS displayed an uneven profile of their social communication. Despite superior responding to social interaction compared to AS, toddlers with WS were as delayed in the development of protodeclarative acts and triadic interaction as toddlers with autism. Atypical acquisition of early joint attention skills in WS may contribute to their subsequent abnormal cognitive and language development.

36 135.6 GAZE FIXATION PATTERNS IN ASD: A PILOT INVESTIGATION. D. Ostfield*[1], K. Cornish[1], L. Tidmarsh[2] and A. Bertone[1], (1)*McGill University*, (2)*Montreal Children's Hospital*

Background: Children with autism lack social precursors observed in typical development, including a preferential orientation to faces. Consequently, children with autism are less likely to engage in direct eye contact within dyadic interactions that support the acquisition of joint attention skills and referential communication. Thus, atypical sensitivity to gaze may have developmental consequences for social cognition.

Objectives: To pilot a novel, computerized task to compare gaze preferences of children newly diagnosed with an Autism Spectrum Disorder to typically developing (TD) children.

Methods: Children with autistic disorder (diagnosis based on ADOS/ADI) were matched on chronological and developmental age to TD children (mean CA= 30 months; mean MA= 17 months). At time of diagnosis, children were administered the Mullen Scales of Early Learning and the *Gaze Behavior Task*. During this task, a central probe engages the child's attention before each experimental slide. The display then changes to 1 of 4 conditions: eyes closed, gaze directed straight-on, 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: Preliminary findings indicate significant differences in fixation time and orienting responses across gaze orientation and group. Children with autism were less likely to look at faces than TD children. CA matched children made more orienting responses and fixated longer on faces with direct gaze than developmental controls and the ASD group.

Conclusions: Data reported demonstrate that the *Gaze Behavior Task* discriminates typical and atypical populations and detects developmental differences in gaze fixation patterns. Future studies will confirm the current findings among a larger sample and address the longitudinal relationship in autistic populations between gaze sensitivity and joint attention development following a social communication intervention.

37 135.7 Atypical eye gaze reponse to social and non-social motion stimuli in young children with autism. D. Annaz*[1], A. Remington[2], M. Coleman[2], R. Campbell[2], E. Milne[2] and J. Swettenham[2], (1)*University of Edinburgh*, (2)*University College London*

Background:A number of studies have reported that individuals with autism show reduced orienting to faces, voices and other social cues. Recent studies have reported data suggesting that 2 year old children with autism viewing a split screen, with an upright point-light display of biological motion on one side and an inverted point-light display on the other, do not show a visual preference for the biological motion display. If children with autism fail or show reduced gaze to biological motion in early development this could lead to a lack of specialization in brain regions that play an important role in the perception of biological motion

Objectives:To use a preferential-looking motion task to investigate whether children with autism prefer to direct their gaze to social or non-social stimuli when both stimuli are presented simultaneously.

Methods:Current study employs children with autism and TD children (4-7 years old). Children were presented with brief video sequences of point-light displays depicting human walking and spinning top,presented side-by-side. Children were asked to look at the screen, thus task demand was minimal. Eye direction was recorded using specially designed software. Duration of gaze and first eye-movement at each stimulus was analysed.

Results:Preliminary data suggest that TD children make the majority of their first eye-movements into the image containing a person and that they spend much longer time looking at this image. In contrast, approximately 90% of children with autism directed their first gaze at non-social stimuli and made fewer spontaneous fixations on the image containing a walker.

Conclusions:Children with autism demonstrate abnormal patterns of social visual pursuit consistent with previous studies that reported atypical responses to social stimuli such as faces. These results do support the notion that children with autism have a specific problem in processing socially loaded visual stimuli.

38 135.8 THE LANGUAGE PROFICIENCY PROFILE – NONVERBAL (LPP-NV): A MEASURE OF PRELINGUISTIC COMMUNICATION FOR CHILDREN WITH AUTISM. K. McFee*[1], J. M. Bebko[1], K. Wells[1] and J. J. Holden[2], (1)*York University*, (2)*Queen's Univerity*

Background: It is well recognized that individuals with autism display impairments in language and communication. Difficulties include delay or absence of spoken language, inability to direct or follow attention, and impaired use and comprehension of gestures, among others. Moreover, a broad repertoire of communication strategies is used within and across individuals (e.g. American Sign Language, home signs, gestures, speech, and pictures). Current assessment measures may not capture the full range of linguistic or communication abilities within this population. The LPP-NV evaluates a child's overall developing language skills, independent of specific modality of expression or standard language. It focuses on *prelinguistic* levels of development, a stage at which children with autism generally demonstrate first symptoms (e.g. lack of joint attention or absence of pointing). The LPP-NV is a downward extension of the LPP-2, which measures communication at the linguistic level.

Objectives: The present study investigates whether the LPP-NV captures the emerging and heterogeneous communication skills of children with autism. Further, whether this population demonstrates a unique profile of development on the LPP-NV.

Methods: One hundred children diagnosed with autism (ADI-R and DSM-IV) with two words/signs or less are compared to typically developing children, birth to 1.5 years of age. The LPP-NV is completed by primary caregivers, and includes five subscales: Form, Content, Reference, Use, and Cohesion.

Results: Findings explore the validity and reliability of the LPP-NV as a measure of prelinguistic communication for children with autism. Comparisons are made between children with autism and typically developing children to determine population strengths and weaknesses across subscales. Data analysis is currently underway.

Conclusions: The LPP-NV holds potential as an early communication measure that better captures the broad repertoire of strategies used within this population. Utility as an early screening tool and for identifying areas requiring formal intervention is discussed.

39 135.9 Non communication of pain – Pathognomonic of Autism?. A. Abhyankar*, *TEMHS*

Background:

Background: Non communication of pain has been observed clinically in children with Autism spectrum disorder (ASD). However its prevalence and pervasiveness has not been systematically documented.

Objectives:

The aim of the study was to assess the prevalence of clinically observed phenomenon

of non communication of pain (NCP) in children with Autism spectrum disorder (ASD).

Methods:

Method: NCP was assessed based on a parent administered semi structured interview. Parents of 4 groups of children were selected: (a) children with ASD (b) siblings of children with ASD without diagnosis of ASD, (c) children with a diagnosed psychiatric condition other than ASD and (4) children with no psychiatric diagnosis

Results:

Results: Analysis of results revealed that the phenomenon of NCP was specific to ASD.

Conclusions:

The implications of these findings for the diagnosis, screening and clinical management of ASD are discussed.

40 135.10 The Typical Developmental Order of Social-cognitive Behaviors in Toddlers. N. Inada* and Y. Kamio, *National Center of Neurology and Psychiatry, Japan, National Institute of Mental Health*

Background: Delays and deficits in social-cognitive behaviors such as imitation, joint attention and pretend play are important developmental problems that emerge from infancy with autism spectrum disorders (ASD). A comprehensive examination of the developmental course of social-cognitive behaviors in the general population will be useful to compare with those of children with ASD.

Objectives: Our study aimed to verify the normal developmental order of social-cognitive behaviors in the general population at around of 1 year of age.

Methods: The Japanese version of the Modified Checklist for Autism in Toddlers (M-CHAT), a questionnaire composed of 23 items out of which 16 concerned with social-cognitive behavior, was completed by the volunteer parents of 318 non-selected children aged 8-20 months (168 boys and 150 girls; mean age = 13±3 months) with reference to the child's current behavior. We determined the month of age of the target children showing the positive answer for each of the 16 socio-cognitive behavior items with the pass rate of 75% or over.

Results: Enjoying being swung, interest in other children, enjoying peek-a-boo/hide-and-seek, eye contact, responsive social smile, and response to be named before 8-months-old, imitation and trying to attract attention at 11-months-old, point-following, imperative pointing, declarative pointing and pretend play at 12-months-old, showing, gaze-following and social reference at 15-months-old, functional play at 17-months-old in developmental order.

Conclusions: The results revealed the typical developmental order of social-cognitive behaviors observable in toddlers. Based on this, we may be able to determine which developmental trajectories children with ASD would follow. This could provide us with useful information about when and to whom we should start intervention. Sponsor: RISTEX (Research Institute of Science and Technology for Society)

41 135.11 The effect of story format on narrative fluency in autism. E. McGregor*[1] and E. Murphy[2], (1)*University of Edinburgh*, (2)*St. Andrews University*

Background:Even high-functioning children with autism have difficulties with narration. Fluency is associated with greater language and theory of mind skills (Capps, Losh & Thurber, 2000; Tager-Flusberg & Sullivan, 1995), better memory (McGregor, in prep) and putatively, central coherence (Ochs & Solomon, 2004). Moreover, less able children with autism are dependent on narrative provision for video-presented false belief tasks and have difficulty keeping pace with video presentation of naturalistic false belief scenes (McGregor and Bennett, 2007). This suggests some children with autism may need more time to process such event sequences, a factor that has implications for making sense of real events. The present pilot study explores this issue with children with autism and typically developing controls.

Objectives:To establish whether presentation format might affect children's narrative skills and if so, if there are differences for autism and typical development. Poorer narratives for video material than stills in autism would suggest parallel difficulties in keeping pace with day-to-day events, limiting scope for a coherent account.

Methods:Nine children with autism aged 6 – 12 years with a range of language ability and 10 controls are presented on separate occasions with stories with a false belief theme in two formats (video-recording and static picture sequences, constructed from stills from the videos), and are asked to narrate them. Narratives are recorded and analysed for indicators of fluency. Data are compared with those of 10 controls matched for age and 10 matched for language ability.

Results:Interim results indicate a different pattern of narrating for stills versus video, with a possible trade-off between seeing the 'flow' of events with video and controlling the pace of presentation through stills

Conclusions:Final analyses will be discussed.

42 135.12 Gestures and Words in the Early Communication of Infant Siblings of Children with Autism. J. Iverson*[1], S. Poulos-Hopkins[2], B. Winder[2] and R. H. Wozniak[2], (1)*University of Pittsburgh*, (2)*Bryn Mawr College*

Background: Numerous studies have documented impairments in language and gesture in children with ASD; and more recent work has begun to describe similar delays in the later-born siblings of children with Autism.

Objectives: This study focused on production of words, non-word vocalizations, deictic gestures (Reach, Give, Show, Point), and conventional representational gestures (e.g., Yes, No, Bye) in Infant Siblings (Sibs) and no-risk comparison infants (NR).

Methods: Twenty-one Infant Siblings (2 of whom were later diagnosed with Autism) and 18 NR infants (all later-borns) participated in this research. Infants and primary caregivers were videotaped at home for approximately 45 minutes each month between the ages of 5 and 14 months, then at 3-month intervals from 18 to 36 months. Parents completed the MacArthur-Bates Communicative Development Inventory (CDI) at all observations beginning at 8 months. Data presented here focus on the 13- and 18-month sessions.

Results: Findings indicated that: a) as a group and at both 13 and 18 months, relative to NR infants, Sibs exhibited broad delays in overall communicativeness (total production of non-word vocalizations, words, and gestures) and significantly fewer words and deictic gestures; b) at 13 but not 18 months, Sibs also had fewer non-word vocalizations; c) at 13 months the two children who later received an Autism diagnosis were at the bottom of the distribution on all variables; and d) at 18 months these children produced very few gestures of any kind and almost no words. Finally, communication variables at 18 months were significant predictors of 30-month percentile scores on the CDI.

Conclusions: Even at 13 months, variation in gesture and vocalization production may index later diagnostic outcomes. Findings are discussed in terms of their implications for an understanding of individual differences among Infant Siblings, prediction of future ASD diagnosis, and the Broader Autism Phenotype.

43 135.13 Peekaboo games with affected 6-month-old infant siblings of children with autism. M. Gratier*[1], E. Devouche[2] and A. Rozga[3], (1)*Université Paris Ouest (Nanterre - La Defense)*, (2)*Université René Descartes, Paris 5*, (3)*Georgia State University*

Background: Mastering the rules of social interactive games by young infants depends largely on their ability to coordinate vocal utterances with motor behaviour (Bruner, 1977). Peekaboo games involve subtly varied repetition on the part of the mother and anticipation on the part of the infant. In Peekaboo play, typically developping 6-month-old infants vocalize in response to relevant gestures (Rome-Flanders & Ricard, 1992), smile at the game climax (Fogel et al., 2006) and show specific sensitivity to timing and structure (Rochat, Querido & Striano, 1999). It is widely acknowledged that social and

communication difficulties may be powerful predictors for autism (Adrien et al., 1993 ; Yirmiya et al., 2006). Yet, studies of early signs of autism fail to show clear differences in social and communicative behaviour during face-to-face interaction at 6 months (Rozga, 2008 ; Yirmiya et al., 2006). Objectives: To compare the timing of social interaction in mother-infant Peekaboo play between 6-month-old infants later diagnosed with autism and unaffected 6-month old infants. Methods: 15 6-month-old infants later diagnosed with autism (ADOS at 18, 24 and/or 36 months) were compared with 15 unaffected control infants* using acoustic and frame-by-frame analysis techniques. Results: Our analyses are still underway. But preliminary results show that, compared with unaffected counterparts, infants later diagnosed with autism look less towards the upper portion of their mothers' faces when their faces are uncovered but more when their hands are over their faces. Affected infants also appear to smile slightly less overall. Conclusions: This study suggests that difficulty in anticipating subtle variations in the timing of patterned social exchange may be associated with the development of autism. * Note: This study is based on a large-scale longitudinal study of infant siblings of children with autism [UCLA (P.I. : Marian Sigman) and UC Davis M.I.N.D. Institute (PIs : Sally Ozonoff and Sally Rogers)].

44 135.14 Timing and communicative quality of gestures in adolescents with high-functioning autism. A. De Marchena* and I. M. Eigsti, *University of Connecticut*

Background: Gesture use, as a form of non-verbal communication, is a significant area of impairment in autism spectrum disorders (ASD). The quality of gesture and speech integration is an ADOS criterion, and the absence of deictic gestures may be an early marker of ASD. Despite the clinical significance of gestures, they have received scant empirical attention. Previous work suggests that decreased variety in spontaneous gestures may be linked to ASD in infancy, and that children with ASD use fewer gestures than developmentally delayed and typically developing (TD) peers.

Objectives: Gesture is an effective communicative tool that may be an important focus of educational programs for children with ASD. Understanding how children with ASD spontaneously gesture is an important first step for designing such interventions.

Methods: This study examines the spontaneous production of co-speech gestures in a sample of 12 high-functioning adolescents with ASD ages 10-17 during their production of a story narration, compared with chronological age-, gender-, and IQ-matched adolescents with TD. Narratives, drawn from an ADOS 6-picture cartoon series, were analyzed using the McNeill coding system. Precise event timing was calculated using Noldus Observer Pro.

Results: Findings indicate that, for adolescents with ASD, the length of their narration and the frequency of their gestures was comparable to that of their TD peers. However, the *timing* of their gestures and co-occurring speech was poorly synchronized, and gestures added less information about story events (character identity, location of objects in space, etc.).

Conclusions: Though adolescents with ASD gestured at typical rates during a story telling task, their gestures did not exhibit the exquisitely well-timed integration with speech and enhanced informational quality that characterizes typical gestures. Decreased coordination of gesture and speech suggests both a communicative impairment and a weak internal representation of narrative structure expressed both in gesture and speech.

45 135.15 Communication skills training in a child with autism: A case example. M. Mongia*, *All India Institute of Medical Sciences, New Delhi, India*

Background:

Ms A , 5 years old girl child, visited our Child and Adolescent Psychiatry Clinic with her parents. She presented with problems of poor communication, not being able to reciprocate in social situation, inappropriate gesturing and inappropriate non verbal communication skills.

Objectives:

This presentation would describe a successful attempt at training this girl with autism using operant conditioning principles and psychoeducation for parents.

Methods:

The child was trained in communication skills using reinforcement strategy and other relevant behavior therapy principles. The child's strebgths and behaviors were assessed at the outset and her parents were trained to be co-therapists.

Results:

Throught the use of these strategies and through parent education and training, this child with autism was brought to a level of effective communication.

Conclusions:

Comprehensive strategies employed would be detailed in the presentation.

Poster Presentations Program

136 Cognition Posters 2

46 136.1 VISUAL PERCEPTION AND SENSE-MAKING IN INTELLECTUAL DISABILITY, AUTISM SPECTRUM DISORDER, AND DEAFNESS. J. Maljaars*[1], I. Noens[2], R. Verpoorten[3], G. Van Duijn[1] and I. A. Van Berckelaer-Onnes[1], (1)*Leiden University*, (2)*Katholieke Universiteit Leuven*, (3)*Viataal*

Background: The standardization study of the ComFor (Forerunners in Communication – Verpoorten, Noens, & Van Berckelaer-Onnes, 2004) - a clinical instrument measuring visual perception and sense-making at the levels of presentation and representation – has shown that individuals with an intellectual disability (ID) and an autism spectrum disorder (ASD) exhibit a higher discrepancy between presentation and representation scores than individuals with an intellectual disability only. Items with meaningless materials provided the best discrimination between the two samples (Noens & Van Berckelaer-Onnes, 2007).

Objectives: To examine the influence of co-morbid deafness on visual perception and sense-making in individuals with an intellectual disability and an autism spectrum disorder.

Methods: The ComFor was administered from a sample of 200 children and adults with an adaptive level between 24 and 54 months measured with the Vineland Screener 0-6yrs-NL (Scholte et al., in press). The total sample consists of four subgroups: (1) individuals with an ID (*n*=78), (2) individuals with an ID and an ASD (*n*=84), (3) individuals with an ID and deafness (*n*=22), and (4) individuals with an ID, an ASD, and deafness (*n*=16).

Results: Preliminary results indicate that individuals with deafness also show a significantly higher discrepancy between presentation and representation scores compared to hearing individuals with an ID, but not specifically for items with meaningless materials.

Conclusions: Deaf individuals and individuals with ASD both exhibit a higher discrepancy between presentation and representation scores. In ASD, the discrepancy can be understood within the framework of the central coherence theory, whereas in deafness, it might be due to a more generally enhanced visual perception.

47 136.2 Executive Functioning in Optimal Outcome Children. M. Rosenthal*, E. Troyb, M. Helt, K. Tyson, I. M. Eigsti and D. Fein, *University of Connecticut*

Background: Despite the finding that children with autism can and do achieve favorable outcomes (e.g. Lovaas, 1987), much skepticism exists regarding whether or not recovery from ASDs is possible. Likewise, no study has of yet thoroughly investigated this phenomenon or studied possible residual cognitive impairment in these children. Objectives: The current study examines the executive functioning (EF) of a small cohort of children who were once diagnosed with an ASD and have since lost their diagnosis (described as "Optimal Outcome"). Methods: Seven Optimal Outcome children, matched on

age, sex, and IQ to nine of their typically-developing peers, were contrasted on performance on the DKEFS Tower of London, Color-Word Interference, and Verbal Fluency subtests. Results: Results showed no significant differences on performance between the two groups. Conclusions: Preliminary evidence suggests that the EF of children who achieve Optimal Outcomes is similar to that of their typically-developing peers.

48 136.3 The Difference between High-Functioning Autism, Asperger and Attention-Deficit/Hyperactivity Disorder in Theory of Mind Abilities. Y. H. C. Lin*, C. L. Hsu and Y. H. Chen, *Fu-Jen Catholic University*

Background:High-Functioning Autism (HFA), Asperger (AS) and attention deficit/hyperactivity disorder (ADHD) are three types of Pervasive Developmental Disorders (PDD) that are often manifested deficits in social functioning. Numerous researches have tried to investigate the differences between their social cognitive abilities, especially, Theory of Mind (TOM). The results are, however, inconsistent. Possible reasons for the inconsistent research results include the inappropriate selection of the subjects, the incompleteness of the assessment tools and the lack of consideration of compounding variables.

Objectives: Through careful selection of the subjects and revision of the assessment tools, this study intends to examine the differences between each developmental stage of ToM in school-age children with HFA, AS and ADHD in Taipei.

Methods: Fifteen HFA children (mean age=7.47), 15 AS children (mean age=8.13), 15 ADHD children (mean age=9.35) and 15 normal school-age children (mean age=7.47) were recruited from communities, hospitals, and elementary schools in the great Taipei area. Prior to the ToM test, parents were invited to complete the Childhood Autism Screening Questionnaire and the Abnormal Behavioral Screening Questionnaire. All the subjects were given the Chinese version of the WISC-III and a revised ToM test. ANOVA was calculated to exam the significant level

Results: After controlling for IQ, age and sex, the results revealed that children with HFA had significant lower ToM scores than children with AS, ADHD and normal children. The results also showed that children with AS and ADHD did not differ significantly from normal children.

Conclusions:The results indicated that HFA children had deficits in theory of mind abilities whereas children with AS and ADHD can develop theory of mind abilities normally.

49 136.4 Further evidence for episodic memory difficulties in individuals with ASD. S. B. Gaigg*, D. M. Bowler and J. M. Gardiner, *City University, London*

Background:Individuals with ASD experience difficulties with episodic memory and memory for temporal order but not with semantic memory. Healy et al. (2000) demonstrated episodic/semantic memory differences by asking typical individuals to re-order alphabetical lists of the names of US presidents either in their historical order (semantic task) or in the pseudo-random order in which they had just studied them (episodic task). Enhanced pre-recency effects were found for the semantic but not the episodic task. We predicted no difference between ASD and typical groups on the semantic memory task and diminished serial order reconstruction on the episodic task.

Objectives:To compare serial reconstruction memory for episodically and semantically ordered lists of items high-functioning adults with ASD and typical comparison participants.

Methods:23 individuals with ASD and 24 verbal ability matched typical individuals took part. For the episodic task, participants were asked to try to remember seven lists of seven historical figures presented in random order (e.g. Archimedes, Churchill, Columbus, Napoleon…). There was no study phase for the semantic task. Participants were then given the names in alphabetical order and asked to put them in the order in which they had studied them, or, in the semantic task, to place them in their correct historical order.

Results:Both groups showed similar serial position curves for the semantic task, but the ASD group showed diminished reconstruction accuracy on the episodic task, which was confirmed by a significant Task x Group x Serial Position quadratic trend ($F(1,45) = 4.25$, $p < .5$).

Conclusions:The diminished performance on the episodic but not the semantic task for the individuals with ASD confirms their particular difficulty memory for the order of occurrence of personally-experienced events.

50 136.5 Spontaneous Allocation of Attention to Faces in Adults with ASD. D. J. Moore*, L. Reidy, J. Francis, J. Reidy and I. Garner, *Sheffield Hallam University*

Background:

The tendency to engage with faces can be seen from approximately 9 minutes old in typical development (Goren Sarty and Wu, 1975) and this is thought to underlie face processing and social expertise observed in typical adults (Johnson and Morton, 1991). People with Autistic Spectrum Disorders (ASD's) however, have been shown to have deficits in orienting towards social information, compared to typically developing controls (i.e. Dawson et al, 1998, 2004).

Objectives:

This study sought to utilise a methodology not previously applied to an ASD sample to test the proposition that people with ASD's, unlike typically developing controls, fail to orient preferentially to social stimuli in the form of faces.

Methods:

The Visual-Dot-Probe (Mathews, MacLeod and Tata, 1986) was utilised to examine attentional biases for face stimuli. Two images (a face and a non-face stimulus) were presented in the top and bottom halves of a computer screen for 200ms. Participants were asked to respond to the presentation of a probe which appeared in the same spatial location as one of the previously presented pictures. Reaction times were taken as a measure of attentional allocation (reaction times are shorter if the dot replaces the picture the participant was attending to).

Results:

This study found that the control group showed faster reaction times to probes which appeared in the spatial location previously occupied by a face than locations previously occupied by non-face stimuli; This was not the case for the ASD participants who showed no bias towards either class of stimuli.

Conclusions:

These findings suggest that adults with ASD's do not spontaneously allocate attention to face stimuli as typical controls do. Within the framework of Johnson and Morton's (1991) CONSPEC-CONLERN model this may relate to the broader social deficits observed in autism.

51 136.6 Investigating multiple object tracking capacities in autism using a fully immersive virtual environment. E. M. Hahler*[1], D. Tinjust[1], L. Mottron[2] and J. Faubert[1], (1)*Visual Psychophysics and Perception Laboratory, Université de Montréal*, (2)*Université de Montréal*

Background: There is evidence for superior visual search performance in autism (O'Riordan et al., 2001). There is also evidence for reduced perception of motion integration tasks (Bertone et al., 2003). Given these perceptual anomalies, we could presume that the capacity to track multiple moving objects (multiple object tracking or MOT) a task often performed in daily activities, would be different for this population.

Objectives: Evaluate MOT capacities in individuals with autism in a fully immersive virtual environment (FIVE). Investigate if an association exists between attentional mechanisms in autism and the complexity of the MOT task.

Methods: 9 adults with high-functioning autism and 4 age, gender and IQ matched control subjects tracked either 1 or 3 previously indexed target objects in a set of 8 distractor items. Performances were measured

based on speed thresholds, which evaluate the greatest speed at which observers are capable to track the moving objects.

Results: Preliminary results showed a significant difference in speed thresholds for both groups between conditions. As expected, speed thresholds were higher, and thus reflected better performance, for the single object tracking versus the multiple object tracking condition. However, no significant difference was found between the groups for both conditions.

Conclusions: Participants with autism were able to track multiple objects at the same speed than control subjects, even when the task demanded a more complex integration of the tracked objects. While there is much evidence for perceptual anomalies in persons with autism, this does not seem to be the case for this kind of task.

Sponsors: Autism Speaks, NSERC-Essilor Industrial Research Chair

52 136.7 Implicit Learning of Musical, but not Linguistically-Presented, Steady-State Grammars in ASD. J. L. Ward*, *Goldsmiths College, University of London*

Background: The structure of music is learned implicitly in infancy in much the same way as linguistic structure (grammar) is learned. Artificial implicit learning paradigms have demonstrated that both novel musical and novel linguistic structures can be learned quickly and implicitly by typically developing participants. There is no manifest advantage in TD participants' ability to learn the structures in either modality.
In autism, there is a marked preference and skill, explicit from infancy, for musical stimuli over linguistic stimuli. However, learning strategies for each modality have yet to be investigated in individuals with ASD.
Objectives: This experiment examines to what extent children with autism are able to show implicit learning for a grammar that is presented either musically or linguistically.
Methods: Using Reber's Steady-State Grammar to construct a list of pseudo-word strings. All grammatically correct strings were used in the training trial. A five minute interval was allowed between training and testing to allow for consolidation of implicit knowledge. All novel stimuli were used in the testing trial, but half of the pseudo-word strings were grammatical and the other half were agrammatical. Young people with autism were asked, in the test trial, to identify the familiar strings. The experiment was then repeated with musical notes in the place of pseudo-words.
Results: Young people with autism were unable to identify the familiar pseudo-word strings with better-than-chance accuracy, but did achieve better-than-chance results when the stimuli were musical in nature.
Conclusions: Young people with autism demonstrate implicit learning for grammar with musical, but not linguistic stimuli.

53 136.8 Exploring the ability to deceive in children with autism spectrum disorders. A. Li*[1], E. Kelley[1], S. Shallwani[1], L. Haberl[1] and K. Lee[2], (1)*Queen's University*, (2)*University of Toronto*

Background:

To tell a lie, one must be aware that the person to whom one is lying to does not have the same knowledge available to them as they themselves have; that is, individuals must have at least a rudimentary theory of mind in order to attempt to deceive others. Although much research has been conducted on individuals with ASD's theory of mind difficulties, no published empirical research to date has been conducted on individuals with ASD's ability to tell lies.

Objectives:

The purpose of this study is to examine whether children with ASD will tell lies to protect themselves and/or to avoid hurting other's feelings.

Methods:

This study uses a temptation resistance paradigm to examine deception in children with ASD with mental ages between six and ten years. Children play a game where they

are told not to turn around to look at a toy, but are tempted to peek when the experimenter leaves the room. They are then asked if they had peeked. To examine whether these same children will tell "white lies," an undesirable gift paradigm is used: children receive an unattractive prize for winning a game and are asked if they like their prize.

Results:

It is anticipated that children with ASD will peek and lie about it to avoid getting into trouble for doing something that they were asked not to do. However, children with ASD are not expected to be able to tell white-lies to protect someone else's feelings.

Conclusions:

If the results are as expected, this will suggest that children with ASD have a very basic understanding that other individuals may not be privy to the same information that they themselves have. However, these children will likely not have a full-blown theory of mind and level of empathy to anticipate other's hurt feelings.

54 136.9 VIQ = PIQ in children with PDD-NOS. E. I. De Bruin, L. Ten Hoopen* and F. Verheij, *Erasmus MC-Sophia Children's Hospital*

Background: Previous studies in children with autism often show a PIQ > VIQ pattern in children with autism and a VIQ > PIQ pattern in children with Asperger Syndrome. For the milder form of the ASD's, PDD-NOS (which occurs much more frequently), intelligence profiles are unknown. We often presume children with PDD-NOS will show a similar intelligence profile to children with autism. For treatment and prognosis purposes it is important to be aware of possible strenghts and weaknesses in the cognitive profile of these children.

Objectives: Therefore the aim of this study was to compare IQ scores of children with PDD-NOS to those of children with autism and to those of children with Asperger syndrome. A second aim of this study was to assess strenghts and weaknesses in IQ profiles of children with PDD-NOS.

Methods: The WISC was administered to 100 children, aged 6-12 years, with PDD-NOS (n = 76), autism (n = 13) and Asperger syndrome (n = 11).

Results: IQ scores did not differ between the three groups. In children with PDD-NOS, all IQ scores were in the average range, their VIQ = PIQ and their FFD factor was lower than the other Kaufman factors.

Conclusions: The typical autism PIQ > VIQ pattern was not found in children with PDD-NOS. These children have IQ scores in the average range and show a weakness on subtests that measure attention and concentration. IQ scores alone are not sufficient to distinguish between PDD-NOS, autism, and Asperger syndrome.

55 136.10 Impaired temporal reproduction performance in adults with high-functioning autism (HFA). J. S. Martin*[1], D. Bowler[2] and M. Poirier[2], (1)*University of Birmingham*, (2)*City University*

Background: In recent years there has been surprisingly little research examining temporal processing in the autism literature (although see Szelag et al., 2004). However there are a number of reasons to suspect that people with autism may have particular difficulties judging the passage of time. Time processing deficits have been observed in a number of psychiatric and neurological conditions related to autism, and the performance of people with autism spectrum disorders (ASDs) on a range of tasks that relate to the judgement of time is consistent with underlying difficulties in time perception (Boucher et al., 2006).

Objectives: The aim of the present study was to examine the performance of adults with higher functioning autism on a temporal reproduction task. Methods: The present study tested a group of 20 high-functioning adults with autism and 20 matched comparison participants on a temporal reproduction task. Participants were presented with 42 auditory tones ranging from 500 to 4100ms. After each study tone was presented, a second identical

tone was presented which participants were asked to stop (by clicking on a mouse) when it reached the same duration as the study tone.

Results: The tone duration estimates of the ASD group were significantly longer or shorter than the durations of the study tones than were the estimates of the comparison group ($F(1,38)=16.38$, $p=0.00$)). The ASD estimates were also more variable ($F(1,38)=8.5$, $p=0.1$)). Furthermore the AS group showed particular difficulties as the duration of the target tones increased; they tended to underestimate to a much greater degree than the comparison group.

Conclusions: These findings support earlier evidence that temporal processing is impaired in people with ASDs, and suggest that further research using a variety of different experimental methods is necessary in order to further clarify the nature and source of these differences.

56 136.11 The Computational Modeling of Perceptual Biases of Children with ASD in Naturalistic Settings. F. Shic*[1], K. Chawarska[2], D. Lin[2] and B. Scassellati[1], (1)*Yale University*, (2)*Yale University School of Medicine*

Background: Several studies have shown that individuals with ASD exhibit abnormalities in processing visual information. However, because these studies typically employ elementary perceptual stimuli, such as contrast gratings, it is not clear how applicable they are to natural settings.

Objectives: In this study we use computational techniques developed for modeling visual attention in order to compare the utilization of basic perceptual features by children with ASD versus typically-developing controls as these children view naturalistic scenes. We also access higher level contextual influences by manipulating the presented scenes and gauging the impact of the manipulation on feature usage.

Methods: 40 children diagnosed with ASD (age(months): M=45.0, SD=7.6) and 22 typically-developing controls (age(months): M=44.6, SD=5.8) were presented scenes depicting play interactions between a child and an adult. A computational model of visual attention was used to decompose scenes into elementary perceptual features of intensity, orientation, motion, and color. These features were matched to the gaze positions of the children viewing the scenes. Scenes were presented either upright or inverted and with-sound or mute.

Results: Consistent with laboratory results, children with ASD used more intensity information and less motion information than typical controls. In addition, in ASD, the use of motion was positively correlated with VMA and NVMA. Finally, both groups increased usage of intensity information when the scene was inverted and focused more on motion when sound was added.

Conclusions: The results suggest that abnormalities detected in ASD using basic perceptual stimuli in laboratory settings extend to how children with ASD respond to visual stimuli in natural settings. Furthermore, the relationship between motion usage and behavioral indices of functioning offers the possibility that early abnormalities in perception may have developmental or cognitive associations. Finally, the response of both groups to context modulation suggests common mechanisms for reshaping and redirecting visual attention.

57 136.12 Enhanced visual attention and implicit learning of local context in Autism Spectrum Disorders (ASD). A. Kourkoulou*, J. M. Findlay and S. R. Leekam, *University of Durham*

Background: There is much evidence to suggest that individuals with ASD are characterised by a tendency for attention to details and a processing bias towards featural and local information (Frith, 1989; Happé & Frith, 2006). In visual tasks this cognitive style has been claimed to lead to reduced global/contextual processing, but not when individuals are explicitly required to attend to global information (e.g., Plaisted, Sweetenham & Rees, 1999). Objectives: We aimed to investigate whether individuals with ASD show reduced processing of context (local and global) in visual search tasks, when context

learning was either implicit or explicit. Methods: Participants were asked to search for a target which was embedded in a predictive or a non predictive context (Chun & Jiang, 1998) in a series of experiments. Results: Results showed that both individuals with ASD and a control group were able to use predictive contexts whether the context learning was explicit or implicit. It was also found that when the context was implicitly learned, the ASD group outperformed the control group, but only when the local context always predicted the target location. Conclusions: These results suggest that individuals with ASD can attend to and use contextual information both when implicitly and explicitly required to, but they are even better than TD individuals when what they attend and learn is the local context. Results will be discussed in terms of the enhanced perception of individual features hypothesis (Plaisted, Saksida, Alcántara & Weisblatt, 2003).

58 136.13 A longitudinal study with autistic spectrum disorder children following a structured program of emotion understanding. E. Thommen*[1], A. Guidoux[2] and M. Pachoux[3], (1)*University of Fribourg and University of Applied Sciences WesternSwitzerland of Lausanne, Switzerland*, (2)*University of Fribourg and University of Applied Sciences WesternSwitzerland of Lausanne (EESP), Switzerland*, (3)*Ecole pour Enfants Atteints d'Autisme, Lausanne, Switzerland*

Background:In the literature, it has been often demonstrated that children with ASD encounter difficulties in expressing and understanding emotions (Celani et al., 1999; Thommen et al., 2004), in understanding theory of mind (Yirmiya et al, 1998) and in executive functions (Ozonoff, at al 1991). However, the ability of understanding emotions seems to develop over time and Howlin et al. (1999) postulate that educational programs aimed at the development of this ability.

Objectives:The aim of our research is to follow longitudinally the evolution of children with ASD who are following a structured program of emotional teaching in a specialised school.

Methods:An extensive evaluation was carry on through three sessions through one year and a half. Eight children with ASD (7- to 15-years old) participate in the study, all evaluated with WISCIII and diagnosed with DSMIV criterion. 62 children from 4- to 8-years old were examined with the same evaluation as control. The evaluation contains seven tasks : 1) the understanding of emotions (recognition of emotional facial expressions, attribution of emotions to stories, Reilly & Delehanty,1997) and the empathy reaction to distress, 2) the theory of mind (Sally and Ann and "diverse thinking task", Peterson, et al. 2005), 3) and executive functions (2 items from BADS, Wilson at al, 1996).

Results:Our results reveal that children with ASD are able to recognize some of the basic emotions from faces. The exercise made at school seems to be generalized in the research situation. We do not found evolution in others tasks. Comparison with typical developing children shows impairment in executive functions and theory of mind but less in emotional understanding.

Conclusions:The evaluation seems showing acquisition of emotional concept in children with ASD through school structures learning. Discussion will be given on methodological aspects as comparison with typical developmental children and tasks used for the evaluation.

59 136.14 THE RELATIONSHIP BETWEEN CONCEPTUAL CATEGORIZATION AND SOCIAL COGNITION IN AUTISM. G. Vivanti*[1], A. Nadig[2] and S. J. Rogers[3], (1)*The M.I.N.D Institute, University of California at Davis Medical Center*, (2)*McGill University*, (3)*UC Davis*

Background: Children with autism show difficulties in categorization. Recent data suggest that categorizing an object by its function generates a covert motor representation of the goal-directed action evoked by the object. It has been suggested that children with autism show a reduction in covert motor activation in social-cognitive tasks, and this has been related to their social-communicative deficit. Therefore it can be

hypothesized that a common mechanism underlies difficulties in function-based categorization and social communication in autism. Objectives: This study evaluates 2 hypotheses: (1) Children with autism, compared with typically developing children, will demonstrate a reduced tendency to categorize objects by function and an increased tendency to categorize by physical form (2) In both groups the tendency to categorize objects by function rather than physical form will be related to better social-communication abilities Methods: 8- to 12-year old children with autism and typically developing participants matched for IQ and age were asked to give clues about the identity of a hidden object to an adult partner, who guessed what the object was. Each participant gave clues for 15 objects. A trained coder blind to diagnosis coded participants' descriptions as referring to the object's function or physical form. We collected a series of measures of social-cognitive abilities including standardized parent-report questionnaires, imitative tasks and eye-tracking measures of attention to another person's face. Results: Preliminary data suggest that children with autism, relative to the typically-developing group, show an increase in physical form descriptions and a decrease in function descriptions. Physical form descriptions were negatively correlated with measures of social abilities: Children who use less function-based categorization in this task are those who have poorer social abilities, including problems with imitation. Conclusions: Difficulties in categorization in autism concern a specific categorization mode, e.g. function-based categorization. Function-based categorization may share common mechanisms with social-cognition.

60 136.15 Orienting to social and non-social stimuli in the early broader autism phenotype. H. Garwood*[1], T. Gliga[1], M. Elsabbagh[1], A. Volein[1], L. Tucker[1], S. Baron-Cohen[2], P. F. Bolton[3], T. Charman[4], G. Baird[5] and M. Johnson[1], (1)*Centre for Brain and Cognitive Development*, (2)*University of Cambridge*, (3)*Institute of Psychiatry*, (4)*UCL Institute of Child Health*, (5)*Guy's Hospital*

Background: A growing number of studies with infant siblings of children diagnosed with ASD have revealed early behavioural differences in the broader autism phenotype, allowing for a prospective approach to the study of the emergence of autism in infancy.

Objectives: In view of previous findings of atypical eye gaze tracking in children and adults with autism and more recently, in relatives of individuals with autism, the aim of this study was to examine the early autism phenotype in infant siblings of children diagnosed with ASD (Sibs-ASD) compared to controls (Sibs-TD), using the TOBII 1750 eye-tracking system.

Methods: A group of 20 Sibs-ASD (11 females) was compared to a group of 20 controls (10 females) between 6 and 9 months on a free-viewing task displaying static images of social (e.g. faces) and non-social (e.g. cars) stimuli. An eye tracking system (TOBII 1750) was used to register the gaze of the participants.

Results: The two groups did not differ in a number of gaze behaviours including a larger number of fixations and longer durations spent looking at faces, relative to competing stimuli. On the other hand, there was a tendency for some sib-ASD infants to show longer latencies to orient toward faces.

Conclusions: The results suggest differences in orienting toward faces in a subgroup of infant siblings of children with autism. These differences are likely to relate to the broader autism phenotype in this condition and potentially to the emergence of clear symptoms in subsequent years in some infants.

61 136.16 Driving hazard perception in individuals with ASD. E. Sheppard*, D. Ropar, G. Underwood and E. Van Loon, *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. One aspect of driving which might pose a particular

challenge is hazard perception, as many hazards involve the perception or anticipation of a person's intentions and movements. Baron-Cohen (2002) argues that individuals with ASD (and typically developing males to a lesser extent) are relatively poor at empathising, which includes processing of social information.

Objectives:

This study aimed to determine whether individuals with ASD have difficulty identifying driving hazards, and further, whether they have particular difficulty when the hazard is social in nature i.e. contains a human figure.

Methods:

Twenty-three adult males with HFA or AS, and 44 matched comparison participants (21 male, 23 adult female) viewed 10 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. They then identified the hazard verbally.

Results:

Participants with ASD correctly responded to fewer social hazards than the males (U=132, p<.1) and females (U=167, p<.5). However, for non-social hazards, there was no difference between participants with ASD and male comparison participants. Participants with ASD were also slower to respond than female comparison participants (p<.5). Hazard perception performance correlated with scores on the AQ (Baron-Cohen et al., 2001) but not age or IQ.

Conclusions:

Individuals with ASD were slower and less able to identify driving hazards. AQ scores related negatively with success in this task, consistent with Baron-Cohen's EMB theory of autism.

62 136.17 The Effect of Music on Social Attribution in Autism Spectrum Disorders. A. K. Bhatara*[1], E. M. Quintin[2], E. Fombonne[3] and D. J. Levitin[1], (1)*McGill University; Centre for Interdisciplinary Research in Music Media and Technology (CIRMMT)*, (2)*Université du Québec à Montréal*, (3)*McGill University*

Background: High-functioning autistic individuals can show preserved social cognition when evaluated with Theory of Mind tests but exhibit deficits when tested with social attribution tasks.

Objectives: Using a modified social attribution paradigm, we investigated social cognition in a sample of 26 adolescents with autism spectrum disorders (ASD; Mean age = 13.5 years, Mean FSIQ = 97) and 26 matched controls (Mean age = 13.6 years, Mean FSIQ = 108) to assess what effect music, a domain of spared cognition among many individuals with autism, would have on their social attribution.

Methods: Participants were presented with animations that depicted varying levels of implied social interaction. They observed these animations both with and without music and answered the question "What was happening in the cartoon?" We scored responses for intentionality, appropriateness, and length of utterance.

Results: Adolescents with ASD showed an overall reduced tendency to make social attributions in the animations with the most complex social interactions, $t(50) = -2.47$, $p = .17$. However, when stimuli were presented with music, both groups exhibited decreased appropriateness of response, $F(1, 50) = 15.86$, $p < .001$, and tended to use fewer intentionality words when music was present. This effect was greatest for stimuli with the largest amount of social content, $F(2, 100) = 5.55$, $p = .005$.

Conclusions: Adolescents with ASD are impaired in describing complex implied social interactions between abstract figures. However, the addition of a musical soundtrack influenced the social attribution of both groups in the same direction, suggesting that both groups hear the music and integrate the music with the animation in the same way.

63 136.18 PROCESSING OF SOCIAL AND NON-SOCIAL STIMULI IN CHILDREN WITH AUTISM. L. Sepeta*, M. Dapretto, S. Bookheimer and M. Sigman, *UCLA*

Background: Research suggests that while typically developing (TD) individuals process social (e.g., faces) and nonsocial stimuli (e.g., objects) differently, individuals with autism (ASD) process both stimuli in a similar manner. Objectives: To investigate the visual processing patterns of social (happy and fearful faces) vs. non-social (houses) stimuli in individuals with ASD compared to a TD group. We hypothesized that ASD individuals would show similar fixation patterns for both the social and nonsocial stimuli, while the TD group would prefer the social stimuli and fixate differently for faces with different emotional expressions (happy and fear). Methods: A group of high-functioning individuals with ASD (n=10; age 8-19) and a matched TD group (n=10) viewed blocked presentations of houses and faces (happy and fearful). Using an eye-tracking device, looking times and fixation patterns for the stimuli were compared within and between the two groups. Results: Preliminary results indicate that ASDs did not differ in fixation patterns for social and non-social stimuli. Between group analyses showed that ASDs looked less at faces ($p<.1$), particularly the eyes ($p<.5$) than TDs. Suprisingly, TDs spent more time looking at houses than faces ($p<.1$). TD fixation patterns differed across emotions. TDs looked more at the eyes for fearful faces ($p<.5$) and at the mouth for happy faces ($p<.5$). No feature fixation differences were seen across emotions in ASDs. Both groups spent more time looking at faces for fearful compared to happy expressions (TD: $p<0.001$; ASD: $p<.5$). Overall, ASDs focused more on details presented on the right side of the screen rather than the left ($p<.001$), which was not seen in TDs. Further investigation will include analyzing the sequential scan paths for each group. Conclusions: These findings suggest that the ASD and TD groups may process social stimuli differently, and the ASD group displays atypical fixation patterns in general.

64 136.19 Habituation Speed and Novelty Preference to Faces Differ in Toddlers with ASD Compared to Infant Siblings, and Controls. E. J. H. Jones*, J. Greenson, K. Toth, G. Dawson and S. J. Webb, *University of Washington*

Background:

Processing information from faces is a component ability of many of the social skills that are impaired in young children with ASD. Impairments in face processing and recognition may be apparent in the early development of individuals with ASD.

Objectives:

To assess whether toddlers with ASD show specific impairments in face processing and memory, and whether these deficits are related to their ASD symptoms.

Methods:

Four groups were tested: toddlers with ASD, typically developing toddlers, toddlers with developmental delays, and non-symptomatic toddlers with an older sibling with ASD. In addition to diagnostic and developmental testing (including the ADOS, ADI-R Toddler and the Mullen Scales of Early Learning), each toddler took part in four habituation experiments, in a 2 stimulus (face, house) by 2 delay (5 seconds, 5 minutes) design. Toddlers viewed a picture of a face or a house until they met a habituation criterion. After a delay, toddlers viewed the familiar picture and a novel picture. Time to habituate and preference for novelty were calculated.

Results:

Toddlers with ASD took significantly longer to habituate to faces than the other groups ($p<0.5$); both toddlers with ASD and siblings of children with ASD took longer to habituate to houses ($p<0.5$). Toddlers with ASD showed less attention to the novel face than other toddlers after a 5-minute delay ($p<0.5$). Longer habituation times to faces (but not houses) correlated with lower scores on the ADOS and the Mullen ($p<0.5$).

Conclusions:

Slower learning about faces and poorer face memory may be specific features of ASD in

toddlerhood, and are related to social and communicative difficulties in ASD.

66 136.20 Chindren with ASD Do Not Spontaneously Integrate Facial Expression and Gaze Direction. H. Akechi*[1], A. Senju[2], Y. Kikuchi[1], Y. Tojo[3], H. Osanai[4] and T. Hasegawa[1], (1)*The University of Tokyo*, (2)*Birkbeck, University of London*, (3)*Ibaraki University*, (4)*Musashino Higashi Gakuen*

Background: Recent studies with typically developing (TD) individuals demonstrated that the processing of facial expressions is affected by the valence of other social cues such as eye gaze direction (e.g. Adams & Kleck, 2003). In contrast, our previous study has demonstrated that children with autism spectrum disorder (ASD) were not affected by gaze direction when they encode the facial expressions of emotion. However, since individuals with ASD are known to fixate less on others' eyes, it is still unknown whether children with ASD fail to integrate these social cues in a task that helps them to attend to the eyes of the stimuli.
Objectives: To investigate whether children with ASD integrate facial expression and gaze direction from the eye region of the face stimuli.

Methods: Participants consisted of 10 children with ASD (mean age 12.3; range 10-16) and 10 TD children (mean age 11.3; range 10-14), who were matched on IQ. The eye regions of the faces displaying anger or fear were presented for the participants, and they were asked to discriminate the facial expressions. The gaze direction of the stimuli were either directed toward the participant or laterally averted.
Results: Gaze direction of the stimuli modulated the speed of facial expression discrimination in TD children. However, the performance of children with ASD was not affected by the gaze direction of the stimuli. These results replicated our previous study, which used the whole face as the stimuli.
Conclusions: Results suggest that children with ASD do not spontaneously integrate affective or communicative valence of facial expression and gaze direction, even when they attend to others' eyes.

67 136.21 Others' Face Does Not Hold Attention in Children with ASD. Y. Kikuchi*[1], A. Senju[2], H. Akechi[1], Y. Tojo[3], H. Osanai[4] and T. Hasegawa[1], (1)*The University of Tokyo*, (2)*Birkbeck, University of London*, (3)*Ibaraki University*, (4)*Musashino Higashi Gakuen*

Background: Others' faces hold attention longer than non-facial object in typically developed individuals (Bindemann et al., 2005). Although a number of studies revealed that individuals with ASD exhibit an atypical looking behavior toward faces, there have been no studies whether faces hold attention in children with ASD.

Objectives: Using the gap and overlap paradigm, we investigated the attentional disengagement from faces and non-facial objects in children with and without ASD.

Methods: Participants consisted of 9 children with ASD (mean 12.2 years; range 9-15 years) and 9 typically developing children (mean 12.1 years; range 9-14 years) matched on IQ. Children were required to saccade towards the peripheral target which followed the central fixation, and children's eye movements were recorded using electrooculography (EOG). In the gap condition, a central fixation face or object disappeared 200 ms before onset of a peripheral target. In the overlap condition, the central fixation face or object remained until the children's response.

Results: In the gap condition, SRT (saccadic reaction time) was not different between two groups. In the overlap condition, typically developing children took longer SRT for faces compared to children with ASD. In contrast, both groups did not differ in SRT for objects. Moreover, SRT for faces was longer than that for objects in typically developing children, while SRT for both of faces and objects did not differ in children with ASD.

Conclusions: These results suggest that faces hold attention longer than non-facial objects in typically developing children. In contrast, children with ASD do not show such specifically longer attentional dwelling towards others' faces.

68 136.22 The Trees in the Wood: Atypical Drawing Strategies in Children with ASD. R. Fukumoto*[1], A. Senju[2], Y. Tojo[3], H. Osanai[4] and T. Hasegawa[1], (1)*The University of Tokyo*, (2)*Birkbeck, University of London*, (3)*Ibaraki University*, (4)*Musashino Higashi Gakuen*

Background: Children with ASD often manifest superior skills, as well as difficulties, when they draw pictures. Some researchers argued that these drawing skills and/ or difficulties may relate to their perceptual styles which prefer local processing, and others emphasized the contribution of the impairments in executive functions. However, the experimental studies on their drawing skills are still scarce.

Objectives: We investigated whether children with ASD manifest characteristic drawing styles based on local bias when they reproduce drawings in the conditions with varying degrees of memory demands.

Methods: Participants consisted of 17 children with ASD (mean years 13.3; range 9-16) and 17 typically developing children (mean years 12.2; range 9-15), who were matched on IQ. In each trial, participants were required to trace a line drawing and then copy it with or without the view of the original drawing.

Results: In all conditions, children with ASD were more likely to 1) draw the whole outline as a continuous line, 2) draw the same lines or dots more than once, 3) start the drawing from local feature of the picture and, 4) make fewer errors in tracing and copying local features, than did typically developing children. In addition, children with ASD were more likely to 5) start to draw a different part before finish drawing one part when they trace pictures and 6) fail to reproduce the global structure of a picture when they copy it without the view of original drawing.

Conclusions: Results suggest that the children with ASD rely on the strategy to reproduce the local features of drawing and tend to fail to reproduce their global structures, regardless of the degree of memory demands. These results are consistent with the claim that perceptual and/ or motor properties affect drawing skills of children with ASD.

69 136.23 Executive Function Profiles in Children with Autism Spectrum Disorders and Elevated ADHD Symptoms. J. L. Sokoloff[1], D. Shook[2], K. F. Jankowski[1], B. E. Yerys*[1], G. L. Wallace[3], J. James[1], L. Kenealy[1], S. McCracken[1], C. Vaidya[2] and L. Kenworthy[1], (1)*Children's National Medical Center*, (2)*Georgetown University*, (3)*National Institutes for Mental health*

Background:

Both children with Autism Spectrum Disorders (ASD) and children with ADHD exhibit deficits in Executive Function (EF). Currently, DSM-IV excludes a co-morbid diagnosis of these disorders. To date, the EF profile of ASD children with elevated ADHD symptoms (Co-morbid) as compared to ASD children without ADHD symptoms, children with ADHD, and typically developing (TD) children is unknown.

Objectives:

Investigate whether children in the Co-morbid group present unique EF deficits relative to pure ASD and ADHD groups and to a group of TD children.

Methods:

132 school-aged children (TD, N = 57, FSIQ = 117; ASD, N = 31, FSIQ = 111; ADHD, N = 30, FSIQ = 112; Co-morbid, N = 14, FSIQ = 103) were recruited for research studies conducted at Children's National Medical Center. Participants completed an extensive neuropsychological battery and parents reported on everyday EF. Administered measures included Digit Span (working memory); Walk Don't Walk (inhibition); Tower of London (planning and organization); and the BRIEF, a widely used parent report measure of EF.

Results:

In laboratory measures the Co-morbid group performed significantly worse on the working memory measure relative to all other groups. The Co-morbid group performed significantly worse on the inhibition measure relative to the TD group. No significant group differences

were found on the measure of planning/organization. In parent reports the Co-morbid group was rated significantly more impaired on BRIEF measures of working memory and inhibition compared to TD and ASD groups. The Co-morbid group was not rated as impaired relative to other groups on BRIEF measures of planning/organization.

Conclusions:

Our findings suggest the Co-morbid group exhibits a unique EF profile relative to ASD or ADHD alone. These findings indicate a need to further examine co-morbid diagnoses as contributing to the phenotypic heterogeneity on the autism spectrum.

70 136.24 A Point of Departure in the Comparison of Social and Nonsocial Visual Orienting among Persons with Autism Spectrum Disorders. T. Flanagan*[1], D. Brodeur[2] and J. Burack[1], (1)*McGill University*, (2)*Acadia University*

Background: Attentional differences among persons with ASDs are apparent in orienting, which is defined as the simple shifting of attentional focus in response to information in the environment. It is unclear whether these differences point to a global orienting difficulty or to a social orienting impairment as differences are noted in response to social and nonsocial information and since direct comparisons of social and nonsocial orienting are rare and vary in methodologies. Objectives: To compare social and nonsocial visual orienting at two SOA levels among children with ASDs and typically developing children matched on nonverbal MA at 8.5 years. Methods: A Posner-like task was used to avoid cross-modality task demands and to equate the stimuli on visual complexity as these factors may have influenced earlier findings of a social orienting impairment among persons with ASDs. Participants were asked to detect social (face) and nonsocial (mixed face) targets on the basis of social (hand point) and nonsocial (arrow) cues that could appear to the right or left of a central fixation point, under SOA conditions of 175 ms and 650 ms. RTs and error rates were the dependent measures, and the "orienting effect" was the index of the utility of the cues. Results: The typically developing children and the children with ASDs displayed strong orienting effects that were indicative of similar orienting abilities. The 650 ms SOA was facilitative for both groups. Group differences emerged in the interaction of cue type and SOA where both groups demonstrated social orienting, but the children with ASDs only did so at the SOA of 650 ms. Conclusions: The findings from this study do not support a general notion of social orienting impairment among children with ASDs, but rather, suggest that social orienting abilities may be contingent upon processing time for this group.

71 136.25 Visuo-Spatial Construction: Task Specific Performance in Children with Fragile X Syndrome and Autism. C. Ballantyne*[1], M. Nunez[1] and L. Riby[2], (1)*Glasgow Caledonian University*, (2)*University of Northumbria*

Background:

It is well documented that individuals with autism (ASD) are relatively spared in tasks that require visuo-spatial construction abilities. However, research has found the opposite pattern in individuals with fragile X syndrome (FXS). The differences in visuo-spatial construction tasks between these two groups are apparent despite other documented similarities in their cognitive profile, such as deficits in executive function.

Objectives:

The current study employs the Navon task to investigate the visuo-spatial construction abilities in these two groups of children.

Methods:

A FXS group (21 children), a FXS group of 19 children that also fitted the criteria for ASD (AFXS), a group of 20 high functioning autistic children (HFA), 20 low functioning autistic children (LFA) and 80 typically developing children (TYP) took part in the study. Two construction Navon tasks were designed; one in which the children copied the stimuli by drawing it and one where the participants

copied the stimuli by placing magnet cut-outs onto a white board.

Results:

For the drawing tasks, the main predictor of performance for the HFA was chronological age. However, non-verbal mental age predicted the performance of the LFA group. The performance of both FXS groups' indicated that they depended mostly on verbal mental age. The results for the magnet task indicated that HFA and LFA performance was reliant on non- verbal and verbal mental age. However, verbal mental age still predicted the outcome from the two FXS groups.

Conclusions:

The results imply that both versions of the Navon task assessed different aspects of visuo-spatial construction as the participants employed different methods to complete the tasks. These findings indicate that a similar outcome in performance does not necessarily mean the tasks are completed via the same cognitive pathways.

72 136.26 Self-Referenced Memory Processes in Autism. H. A. Henderson*[1], N. Zahka[2], A. P. Inge[2], C. Schwartz[2], C. Hileman[1], N. Kojkowski[1], D. Coman[1] and P. C. Mundy[3], (1)*University of Miami*, (2)*Graduate Student*, (3)*UC Davis*

Background: Atypical self-awareness may be fundamental to social impairments in autism and disturbances in self-related memory processes may be one manifestation of this atypicality. In typically-developing populations, self-relevant information tends to be preferentially encoded and retrieved relative to information relevant to other people or non-person related information.

Objectives: We examined performance on a self-referenced memory (SRM) task for higher functioning children with autism (HFA) and a matched comparison group. Individual differences in performance were examined in relation to social cognitive tests of mentalizing and symptom severity.

Methods: Fifty-six children (28 HFA, 28 comparison; 8-16 years) completed a SRM task in which they read a list of words and decided whether the word described something about themselves, something about a fictional character, or contained a certain number of letters. They then identified from a longer list the words that were 'old' or familiar. Dependent measures were the proportion of words correctly recalled from each of the three encoding conditions. Children completed The Strange Stories Task and The Children's Eyes Test as measures of social cognition. Parents completed the SCQ and ASSQ as measures of symptom severity.

Results: Although older children and comparison children showed preferential recognition of self-referenced words, younger children and HFA children did not, $F(2, 51) = 3.85$, $p = .3$. Instead, HFA children recognized an equal proportion of self and other referenced words. Among children with HFA, enhanced SRM performance was related to lower symptom scores, $r(27) = -.46$, $p = .2$. These associations were not accounted for by performance on the mentalizing tasks.

Conclusions: Children with HFA preferentially encoded person-related information, but did not show the standard enhanced processing of self-relevant information. Individual differences in the tendency or capacity to process self-relevant information may serve to modify the expression of social symptoms in children with autism.

73 136.27 ATYPICAL SPATIAL ASYMMETRY OF FRONTAL TASKS PERFORMANCE IN YOUNG BOYS WITH AUTISM. N. Pushina*[1], M. Tsetlin[1], T. Stroganova[1] and I. Galuta[2], (1)*Psychological Institute of the Russian Academy of Education*, (2)*Moscow State University of Psychology and Education*

Background: Along with the growing body of work on EF deficit in young children with autism there is evidence that the phenomenon of spatial neglect may contribute to their failure to succeed in performance of EF tasks.

Objectives: The study examined the hypothesis that failure to disengage attention to the left spatial location from previously important or relevant information can contribute to the poor performance of autistic children on EF-tasks.

Methods: A group of 21 boys diagnosed with autism (BWA), aged 3 to 7 years, was compared to the same number of age-matched typically developing boys (TDB). Two delayed-response-type tasks were administered: Spatial Reversal task (SR) that taps prepotent response inhibition and Delayed Alternation task (DA) as a measure of working memory. IQ-level was assessed by Kaufman Assessment Battery for Children (K-ABC-I) or Psychoeducational Profile (PEP).

Results: BWA did not exhibit any deficit in inhibition during the performance on the SR task whereas on the DA task BWA performed significantly poorer than TDB. There was the significant difference between BWA and TDB in the age regression slope: the total number of errors decreased as a function of age in BWA while in TDB it remained stable across the age period under the study. Most importantly, BWA, unlike TDB, demonstrated the strong right-sided bias in the performance of both EF tasks. Whereas the number of errors in both SR and DA tasks in TDB was perfectly symmetrical, BWA made significantly more errors when the successfully retrieved bait was shifted from the right to the left side than vise versa.

Conclusions: These data suggest that BWA aged 3 to 7 years have partial deficit of working memory but no impairment of inhibitory control. Asymmetrical performance of both tasks implies that young boys with autism have difficulties with attention disengagement from right to left visual hemi-field.

74 136.28 Perception of Static versus Dynamic Emotional Displays in High Functioning Autism.
J. Yager*[1], K. Hurd[1], A. Rombough[1], D. Worling[2] and I. Grace[1], (1)*Simon Fraser University*, (2)*Westcoast Child Development Group*

Background: Difficulties in emotion perception have been described among individuals with autism; however, the extent and severity of impairment has not been consistently demonstrated. Discrepancies in empirical findings may reflect diverse assessment methods (e.g., static vs. dynamic stimuli) and/or heterogeneity of participants (e.g., varying levels of functioning).

Objectives: We investigate face and emotion perception among children/adolescents with HFA using computer- and videotape-based tasks varying in the emotional cues provided. It is hypothesized that individuals with HFA will demonstrate relatively greater impairment when presented with increasingly dynamic emotional stimuli.

Methods: Children/adolescents with HFA are MA-matched to a TD sample (mean CA = 13.5 yrs; mean IQ = 96). Subtests from the Let's Face It Assessment Battery (Tanaka & Low, 2001) are used to assess face identity/emotion recognition of static facial displays. The Awareness of Social Inference Test (TASIT; McDonald et al., 2003) is used to assess emotion recognition of more dynamic stimuli. Half the TASIT videos are presented without sound (nonverbal face/body cues only) and half with sound (nonverbal and "verbal" cues). Verbal content is emotionally neutral so that "verbal" cues consist only of affective prosody.

Results: Data collection is ongoing and results based on the complete data set will be presented. Preliminary results (based on 12 participants) suggest that, relative to the TD group, individuals with HFA are less accurate in perceiving face identity and emotion cues. Relatively greater discrepancies (between HFA and TD performance) are apparent on tasks involving emotion versus face recognition and dynamic versus static displays.

Conclusions: Individuals with HFA may experience relatively greater difficulty processing emotion versus face identity cues. Emotion cues may prove particularly difficult for individuals with HFA to interpret when presented in more dynamic social contexts (requiring the integration of multiple, transient cues). Implications for methodology and social information processing in autism will be discussed.

75 136.29 The Cognitive Profile of Women with Autism Spectrum Conditions. E. Ingudomnukul*, S. Baron-Cohen and L. Ruta, *University of Cambridge*

Background: Prior research has suggested that individuals with autism spectrum conditions (ASC) display intact or superior skills in systemizing, alongside impairments in empathizing. This cognitive profile has been psychometrically defined as the 'extreme male brain'. However, few of these studies have focused on women with ASC.

Objectives: To investigate whether adult women with ASC display a psychological and cognitive profile similar to adult men with ASC, and to see how they compare to the general population.

Methods: The Autism Spectrum Quotient (AQ), Empathy Quotient (EQ), and Systemizing Quotient-Revised (SQ-R) were used to measure autistic traits, empathizing traits, and systemizing traits, respectively. The 'Reading the Mind in the Eyes' Test, Karolinska Directed Emotional Faces, and Social Stories Questionnaire were used to measure performance in empathizing. A Mental Rotation task, an Embedded Figures task, and the Physical Prediction Questionnaire were used to measure performance relevant to systemizing. These were administered to 36 men with ASC, 29 women with ASC, 49 control men, and 56 control women, matched for age and IQ.

Results: Men and women with ASC scored significantly higher on the AQ, lower on the EQ, and higher on the SQ-R when compared with controls. Men and women with ASC also showed impairments in performance tasks of empathizing compared with controls. However, men with ASC and women with ASC showed differences in systemizing ability which were consistent with the sex differences seen in controls, i.e., men showing an advantage in systemizing over women.

Conclusions: This is the first known study to explore cognitive abilities specifically in women with ASC. These results indicate that men and women with ASC share similar personality traits and deficits in empathizing, but show sex-typical differences in systemizing. Further research is needed to explore these differences in greater depth.

76 136.30 AMELIORATING INHIBITORY CONTROL ABILITIES IN ASD. H. M. Geurts*, *University of Amsterdam*

Background: For treatment purposes it is crucial to disentangle in what circumstances people with ASD encounter difficulties. The executive dysfunctions (ExDys) account of ASD has resulted in numerous studies delineating the precise types of ExDys that people with ASD encounter. However, hardly any study has focused on ways to reduce or overcome these difficulties.

Objectives: To disentangle how deficient processes that lead to the observed deficits in inhibitory control in ASD can be ameliorated.

Methods: In the first experiment 22 boys with ASD, 22 boys with ADHD and 32 typically developing boys (TD) matched on age (8 to 13 years) participated. An Eriksen Flanker task was applied as this inhibitory control task measures the ability to suppress irrelevant information. The task is applied in a neutral and a motivational situation. In the motivational situation, participants were told that they were competing with peers. In the other experiments 18 children with HFA and 22 TD children matched on age, FSIQ, and gender participated. Two Go/NoGo paradigms were applied, one with neutral stimuli and one with emotional stimuli. The stimuli were presented with varying presentation rates to manipulate arousal level of the children.
Results: 1) All groups benefited from motivation: The boys were faster and made fewer errors when they were competing with peers. However, this was mainly due to the improvement in performance in the children with ADHD. The children with ASD still had difficulties with the task. 2) Children with HFA only encounter inhibition deficits when information is presented very fast and consists of emotional stimuli.

Conclusions:The findings will be discussed in terms of the ExDys account of ASD. However, the ExDys account is not sufficient to explain the pattern of results and alternative explanations will be put forward. Moreover, we

will stress the clinical implications of our findings.

77 136.31 Associations Between Conceptual Reasoning and Adaptive Ability in High Functioning Autism. G. Goldstein*[1], D. L. Williams[2] and N. J. Minshew[3], (1)*VA Pittsburgh Healthcare System*, (2)*Duquesne University*, (3)*University of Pittsburgh School of Medicine*

Background: In high functioning autism (HFA) the level of conceptual skills does not generally predict adaptive function suggesting a different relationship between these areas than for typically developing individuals.
Objectives: The hypotheses were 1) that the correlations between conceptual reasoning and adaptive function would differ between autism and control groups, and 2) that only selected aspects of conceptual ability would be correlated with similarly specific aspects of social function.
Methods: A battery of tests was administered to individuals with HFA and demographically and IQ matched normal control participants to assess aspects of conceptual reasoning. Two measures of adaptive function, the Vineland Adaptive Behavior Scales (VABS) and the Behavioural Assessment of the Dysexecutive Syndrome (BADS) were also administered.
Results: With regard to the VABS, there were only a small number of significant correlations between conceptual ability and adaptive function in the autism group whereas there were a larger number of correlated measures in the controls. In the autism group the significant correlations between conceptual measures and the VABS involved the Receptive, Expressive, and Writing subdomains of the Communication Domain. In the case of the BADS, there were numerous statistically significant ($p<.5$) correlations with the measures of conceptual ability in the autism group; however, the BADS Rule Shift subtest received the largest number of significant correlations. In the control group, there were a substantially smaller number of significant correlations between the BADS subtests and the conceptual reasoning tests.
Conclusions: The most robust correlations for the autism group were for the adaptive measures that were primarily related to cognition and communication whereas the most robust correlations for the controls were between cognitive measures and adaptive measures of activities of daily living and interpersonal relationships. It was concluded that in autism adaptive behavior is most closely related to communication ability and cognitive flexibility.

78 136.32 Contextual Learning in Persons with ASD. M. Klinger*, L. Klinger, B. G. Travers and J. Mussey, *University of Alabama*

Background:

We have proposed that individuals with autism spectrum disorder (ASD) have impaired implicit learning (e.g., learning that occurs without awareness; Klinger, Klinger, & Pohlig, 2006). In the present study, we hypothesized that difficulties in contextual learning, a type of implicit learning, would be impaired in ASD.

Objectives:

The present experiment investigated contextual learning in individuals with ASD and a group of age and verbal-ability matched controls. We predicted that individuals with ASD would be impaired in their ability to implicitly use contextual relationships in their environment.

Methods:

Fourteen high-functioning adolescents and young adults with ASD and 13 matched controls completed a visual search task in which the contextual environment predicted the target location. Participants were told to find Jiminy Cricket (the target) as quickly as possible in a matrix of 36 Disney characters presented on a computer. They indicated by a button push the quadrant containing the target. Unknown to participants, target location was predicted by the complex arrangement of the other characters (i.e., the context). Participants completed eight blocks of 48 trials in which the context predicted the target location followed by a block of trials in which the target location was random, and a final predictable block.

Results:

For this task, learning is seen as the difference in reaction time to the final blocks of predictive trials compared to the block of random trials. Participants with typical development showed more contextual learning (+100ms) than participants with ASD (+10ms). This difference was a large (Cohen's d=1.15) and reliable (p=.004).

Conclusions:

These results suggest that persons with ASD have difficulties in learning implicit, contextual relationships in their environment during a visual search task. This impairment may be related to difficulties understanding subtle social cues that characterize ASD.

79 136.33 Verbal Learning in Optimal Outcome Children. K. Tyson*[1], M. A. Rosenthal[1], M. Helt[1], E. Troyb[1], I. M. Eigsti[1], L. Naigles[1], R. T. Schultz[2] and D. Fein[1], (1)*University of Connecticut*, (2)*Children's Hospital of Philadelphia and the University of Pennsylvania*

Background: Although research has demonstrated that some children with autism achieve favorable outcomes (e.g. Lovaas, 1987), few studies have investigated the recovery of children with an ASD or the nature of these children's potential residual verbal learning deficits.

Objectives: The current study examines verbal learning of a small cohort of children once diagnosed with an ASD who have since lost their diagnosis (labeled the Optimal Outcome group).

Methods: Seven Optimal Outcome children were matched on age, sex, and IQ to seven of their typically developing peers. We compared the groups' performance on the California Verbal Learning Test.

Results: On most of the CVLT variables, including Trial 1, Trial 5, Trials1-5, List B, long-delay recall, semantic clustering, and learning slope, the groups did not differ. However, the Optimal Outcome group tended to use serial clustering strategies more than the typical control group (p = .63) and tended to perform worse on a short-delay cued recall task (p = .61). In contrast to the Optimal Outcome group's average performance on both serial clustering and short-delay cued recall, the typical control group's performance was slightly better than average on both these aspects of the CVLT.

Conclusions: These preliminary results suggest that these Optimal Outcome children do not differ from typical peers on most verbal learning characteristics, and score well within the average range on all learning variables.

Poster Presentations Program

137 Neurophysiology Posters

80 137.1 REM sleep EEG Beta Activity Correlates With Performance On The Embedded Figure Test in Typically Developing Individuals, But Not In Autistic Persons. S. Tessier, C. Bolduc, É. Limoges, É. Ménard, L. Mottron and R. Godbout*, *Hôpital Rivière-des-Prairies*

Background: Neuropsychological, EEG and brain imaging studies point toward enhanced low-level visual perception in autism, leading to a more local bias and increased performance in low-level visual stimuli than typically developing individuals. Our group has recently reported a decreased contrast between primary and non-primary visual areas for EEG Beta activity during REM sleep in autistic persons in comparison to typically developing individuals.

Objectives: The present study aimed at verifying if EEG Beta activity during REM sleep correlates with performance in the Embedded Figure Test (EFT), a task that relies on visual search and local perception, and consistently performed at a superior level in autism.

Methods: Eight autistic (21.9 ± 4.3 years) and 11 comparison participants (19.9 ± 4.4 years) were recorded for two consecutive nights. Spectral analysis of REM sleep Beta EEG activity (13.0 to 19.75 Hz) was performed on primary (O1, O2) and non-primary (P7, P8) visual areas. EFT was administered in the morning following night two. Group performance on the EFT task was compared with Mann-Whitney U-tests. The correlation between performance and EEG spectral power

was estimated with Spearman's rho coefficients.

Results: Participants with autism performed better in task completion time than the comparison group on the EFT task ($p<.3$). There was a negative correlation between REM sleep EEG Beta activity and time to complete the EFT task in the comparison only (rho = -0.66; p=0.25), not in the autism group (-0.19; p=0.63).

Conclusions:These results suggest that autistic individuals use an atypical visual cortical network in association with enhanced performance in local perceptions tasks. This represents a new support for the hypothesis that REM sleep EEG Beta activity, in addition to reflecting REM sleep control mechanisms, is also an index of visual processing that can differentiate persons with autism from comparison groups.

81 137.2 Processing of eye gaze and facial expression in children with Autism Spectrum Disorder – an ERP study. E. Parise*[1], A. Handl[1] and T. Striano[2], (1)*Max Planck Institute for Human Cognitive and Brain Sciences*, (2)*Hunter College*

Background: Children with Autism Spectrum Disorder (ASD) are impaired in processing eye gaze and faces. More specifically, it has been suggested that eye gaze processing in children with autism involves different underlying neural mechanisms than in typically developing children.

Objectives: We investigated the electrophysiological neural correlates of eye gaze processing and their interaction with facial expressions in children with ASD and typically developing controls. This paradigm has successfully been used with infants (Striano, Grossman, Kopp, Reid, 2006).

Methods: We measured event-related brain potentials (ERPs) in 7 children with ASD (6.8 - 9.5 years; 1 female) and 7 age and gender matched controls. We presented children with pictures of angry or neutral facial expressions with direct or averted eye gaze. Data analyses were carried out for the face processing ERP component N170.

Results: There were several significant findings:
1. Among children with autism, there was a more negative amplitude for direct compared to averted gaze in the right hemisphere.
2. Compared to the control group, among the children with autism, the N170 peaked later for angry compared to neutral facial expressions.
3. Among the typically developing children, angry faces with direct gaze elicited a greater negativity compared to neutral.

Conclusions: Children diagnosed with autism processed eye gaze and facial expressions differently. First, children with autism showed a different N170 response for eye gaze processing compared to controls. This response is close to the one displayed by infants. Second, children with ASD showed delayed neural processing for angry compared to neutral, whereas typically developing showed increased processing for angry compared to neutral. In general, the findings show a differential pattern of the N170 suggesting delayed development with differential processing for eye gaze and emotion in school-aged children with ASD. These findings may be used to aid in the development of new diagnostic tools.

82 137.3 Foetal testosterone and autistic traits. B. Auyeung*[1], S. Baron-Cohen[1], E. Ashwin[1], R. Knickmeyer[2], K. Taylor[3] and G. Hackett[4], (1)*University of Cambridge*, (2)*University of North Carolina at Chapel Hill*, (3)*Addenbrooke's Hospital*, (4)*Rosie Maternity Hospital*

Background: Studies of amniotic testosterone in humans suggest that foetal testosterone (fT) is related to specific (but not all) sexually dimorphic aspects of cognition and behaviour. It has also been suggested that autism may be an extreme manifestation of specific (but not all) male-typical traits, both in terms of cognition and neuroanatomy. Objectives: To test if fT levels are associated with individual differences in autistic traits, fT levels were measured in amniotic fluid from pregnant women following routine amniocentesis. Methods: Two instruments measuring number of autistic traits (the Childhood Autism Spectrum Test (CAST) and the Child Autism

Spectrum Quotient (AQ-Child)) were completed by these women about their children (*n*=225), ages 6-10 yrs. Results: fT levels were positively associated with higher scores on the CAST and AQ-Child. This relationship was seen within sex as well as when the sexes were combined, suggesting this is an effect of fT rather than of sex. Conclusions: These findings are consistent with the hypothesis that prenatal androgen exposure is related to the number of autistic traits a child exhibits. Present results need to be followed up in a much larger sample to test if clinical cases of autism have elevated fT.

83 137.4 Incidence of overnight EEG abnormality in Down's patients with comorbid diagnosis of autism. M. Chez*, *Sutter Neuroscience Institute, Sacramento; UC Davis Medical Center*

Background: Down's Syndrome may present with autism as a secondary diagnosis.This may be the result of overlap, or it may have another medical cause. The author hypothesized that patients may suffer from occult clinical epilepsy.

Objectives:

Six Down's patients with autism as a secondary diagnosis were studied for an abnormal EEG as the cause of their autistic features. Treatment with valproic acid was also done for an abnormal EEG to see if clinical autistic features could be modified.

Methods:

Six patients with Down's were studied after presenting with onset of autistic features after age 2 years of age. There were 5/6 male patients, and the 1 patient had epilepsy for 1 year with regression. The patients were studied with ambulatory digital EEG for 24 hours. Patients were offered treatment with valproic acid if the EEG was abnormal. The patients were then evaluated for observed improvement in their autistic features and EEG. Valproic acid trough serum levels were maintained > 80mg/ml < 120 mg /ml.

Results:

Epileptiform central-temporal or parietal discharges were seen in 4/5 patients (3male, 1 female). All were given valproic acid therapy and the EEG improved in 2/4 patients restudied at time of abstract submission. Behavior also showed improved autistic patterns.The single patient with seizures had a varient of continuous spike wave in sleep(CSWS).

Conclusions:

Abnormal EEG was seen in 80 percent of these patients. The other patient with seizures had a unique EEG associated with regression called CSWS. All patients to date have responded to treatment with valproic acid and EEG has responded to aggressive treatment in those restudied.The fact that a high percentage of Down's patients had abnormal EEG patterns that may be part of their comorbid autism supports the need for neurological evaluation for occult epilepsy. This would better define the relationship of EEG abnormality, epilepsy, and autistic behaviors in patients with Down's Syndrome.

84 137.5 N2 and Response Inhibition in Children with High-Functioning Autism. L. Mohapatra*[1], C. Schwartz[2], P. C. Mundy[3], H. A. Henderson[1], C. Burnette[4], A. P. Inge[2] and N. Zakha[1], (1)*University of Miami*, (2)*Graduate Student*, (3)*UC Davis*, (4)*Vanderbilt University*

Background: Discrepant findings on whether children with autism display response inhibition deficits may be partially due to the variety of behavioral tasks used to assess inhibition. A more useful way of understanding early cognitive/attentional processess that influence inhibition may be to look at neurophysiological measures. Specifically, the event related potential N2, a measurement of cognitive control or the effortful decision to inhibit a prepotent behavioral response, may be useful in understanding the discrepancy in response inhibition.

Objectives: In the current study we measured the N2 while high-functioning autistic children and age, IQ-matched control children performed a modified Flanker task. We further examined the associations between N2

amplitude and latency and variations in social communication within the HFA sample.

Methods: Behavioral and electrophysiological data from a modified Flanker task were collected from 27 HFA (1 female) and 24 typically developing controls (1 female) ranging in age from 8- to 16-years. Symptom severity was measured using the ASSQ, ADI, and SCQ.

Results: Regarding behavioral performance, HFA children committed more errors than control children after controlling for age and verbal IQ. Electrophysiological performance indicated marginal group differences in N2 amplitude after controlling for age. However, a significant age-related decline in N2 amplitude was observed in the control but no in the HFA group. In addition, greater N2 amplitude was correlated with lower scores on the SCQ for the HFA children. There were no significant group differences in N2 latency.

Conclusions: Behavioral performance indicates that HFA children show impulsivity but not deficits in inhibition. Electrophysiological N2 data, however, suggest that the development of neural processes associated with inhibition may not display the same age-related improvements as in control children. Moreover, N2 in HFA children may be an indicator of stable differences in cognitive effort or control that are associated with social communication deficits.

85 137.6 Visual Evoked Potentials to Checkerboards in Adults with ASD. J. M. Numata, K. Merkle, E. J. H. Jones*, M. Murias, E. Aylward, G. Dawson and S. J. Webb, *University of Washington*

Background: In autism, higher level visual processing abnormalities have long been found; it is unclear what role lower-level "bottom up" visual processing plays in these deficits. In 8 adults with autism, Hadjikhani et al. (2004) found (via fMRI) that early stage visual processing areas were normally organized. Using visual evoked potentials (VEPs), early abnormalities in the visual processing stream have been found in a number of other neurological disorders (e.g., depression, schizophrenia, ADHD). As well, preliminary evidence from our lab suggests alterations in P1 amplitude and latency in children with ASD when viewing faces (Webb et al., 2007).
Objectives: The goal of this study was to examine the early time course of VEPs in individuals with autism to basic checkerboard stimuli.
Methods: In our study, 27 adults with high functioning autism spectrum disorder and 21 age and IQ matched controls were presented with a unilateral flashing checkerboard stimulus while high density VEPs were recorded. The N75, P100, N145 components were analyzed.
Results: Preliminary analyses suggest a high degree of similarity between control and ASD groups in early visual processing; both morphology and topography of the waveforms were similar.
Conclusions: Lack of differences between groups would suggest that abnormalities in higher order visual processing in individuals with autism are not the result of earlier irregularities as assessed by ERPs.
Funding source: NIMH (U54MH066399)

86 137.7 Illusory Contour Effect in Healthy and Autistic Children. A. Prokofyev*[1], E. Orekhova[2], I. Posikera[3], A. Morozov[4], V. Morozov[4], Y. Obukhov[4] and T. Stroganova[3], (1)*Moscow State University of Psychology and Education*, (2)*Institute of Neuroscience and Physiology, Sahlgrenska Academy, Gothenburg University*, (3)*Psychological Institute of the Russian Academy of Education*, (4)*Institute of Radio Engineering and Electronics of the Russian Academy of Sciences*

Background: Autism syndrome is characterized by atypical visuoperceptual processing that is usually interpreted in terms of the reduction in the contextual integration of information. It is assumed that this reduction is related with dysfunction of neural mechanisms of 'intermediate' vision which can be studied using the illusory contour paradigm.

Objectives: The study examined the hypothesis of lower-level processing abnormalities related to perceptual grouping in

boys with autism aged 3 to 6 years. We investigated event-related potentials response to visual elements that either formed perceptually coherent illusory contour or were arranged in a noncoherent way.

Methods: The subjects were 19 boys with autism aged 3-6 years and 19 age-matched typically developing boys. Electroencephalogram (EEG) was recorded from the 19 electrodes (10-20 International System) and digitized at 500 Hz. EEG was registered while the subject passively viewed two types of visual stimuli which were presented pseudorandomly. Non-parametric analysis of the amplitude and latency values of the N1 component was performed for six posterior scalp regions of interest: O1, O2, P3, P4, OZ, PZ.

Results: In typically developing boys, the illusory contour as compared with control stimulus elicited enhanced negativity of N1 peak (illusory contour effect), which has been previously found in adults. The illusory contour effect on N1 amplitude in typically developing boys was most pronounced at parietal areas of the right hemisphere. Boys with autism demonstrated the reliable *inverted* illusory contour effect, that is, more positive N1 amplitude to illusory contour at occipital areas. The latency of N1 peak in response to illusory contour did not differ between two groups of children.

Conclusions: We hypothesized that sensitivity to difference between illusory contour and control figures in boys with autism is based on collinearity processing mechanisms implemented in neural circuitry of primary visual cortex.

87 137.8 ERP CORRELATES OF PERCEPTUAL CLOSURE IN ADULTS WITH HIGH FUNCTIONING AUTISM AND ASPERGER SYNDROME. N. Desire*[1], A. Hosein[2], L. Mottron[1] and B. Jemel[1], (1)*Hopital Riviere des Prairies/University of Montreal*, (2)*Hopital Riviere des Prairies*

Background:
Perceptual closure (Pc) refers to the neural processes responsible for filling-in of missing information that enable object-recognition under partial viewing conditions. Event-related potential (ERPs) studies showed that Pc is not an all-or-none phenomenon but is achieved gradually with progressively less fragmented images until enough visual attributes are present. Given that autism is typically associated with a detail-oriented visual processing style, one could argue that object recognition might rely on different perceptual mechanisms in this condition.

Objectives:

Track the neuronal mechanisms underlying Pc during object identification in High Functioning Autism (HFA) and Asperger Syndrome (AS).

Methods:

11 Adults with HFA, 11 with AS and 11 matched control subjects were shown line-drawing objects and non-objects (scrambled objects) presented according to the ascending method of limits; each picture was gradually revealed in a sequence of seven fragmentation levels, from the most to the least fragmented, up to complete version. EEG was recorded while participants indicated at each fragmentation level if they recognized or not the object. ERPs were averaged at object identification level, at 1-prior and 2-prior identification levels.

Results:

Controls identified objects at a more fragmented level than HFA and AS did. Spatio-temporal analysis of ERPs revealed differential electrical brain activity associated to Pc in the three groups of subjects. In controls, occipito-temporal P2 and frontal/centroparietal late ERPs gradually increased in amplitude with levels of object identification. However, in HFA and AS, early visual P1 showed amplitude differences between levels of identification. Later ERPs showed different patterns of identification level effects suggesting that Pc in autistic participants was achieved in an all-or-none fashion.

Conclusions:

Behavioral data suggest that Pc in autism relies more on the amount of local visual

information than in typical subjects. ERP data indicate that object recognition in autism is mainly stimulus-driven and that Pc does not operate in a gradual manner.

88 137.9 BRAINSTEM TRANSCRIPTION OF SPEECH IN AUTISM SPECTRUM DISORDERS. N. M. Russo*, B. L. Trommer, E. E. Skoe, T. G. Nicol, S. G. Zecker, A. R. Bradlow, J. M. Hornickel and N. Kraus, *Northwestern University*

Background: Language impairment is a hallmark of autism spectrum disorders (ASD) and prosody, represented by pitch contour of speech, is particularly affected. Prior investigations of language representation in ASD have detected deficiencies in speech perception and cortical encoding, but information about lower (brainstem) level processing is lacking. The fidelity of brainstem transcription permits a link between the acoustic components of speech (e.g., consonants/vowels/pitch) with distinct aspects of the evoked response (e.g., timing/frequency information).

Objectives: To determine whether the auditory brainstem responses to speech syllables in children with ASD differ in comparison with typically developing (TD) controls.

Methods: Speech stimuli, including a consonant-vowel speech syllable /da/ and two fully voiced /ya/ syllables, with ascending and descending pitch contours, were delivered monaurally to the right ear to children (7-13 years) with ASD (N=21) and age- and IQ-matched TD children (N=18). All subjects had normal hearing by air threshold audiometry (20 dB HL) and click-evoked wave V latency and normal mental ability.

Results: /da/-evoked potentials showed altered representation of stimulus timing and frequency, reduced fidelity to stimulus, and greater degradation by noise in ASD vs. TD ($p < 0.5$). A subset of the ASD group (N=5) also showed reduced phase locking and pitch tracking in response to /ya/ ($p < 0.2$). A limited number (3/6) of ASD subjects who underwent auditory training demonstrated improved brainstem transcription of speech, whereas ASD subjects without training (N=6) had stable responses over time.

Conclusions: These data provide unique evidence of deficient brainstem processing of speech sounds in ASD, and suggest a relationship between aberrant prosody and impaired subcortical pitch tracking. Because the speech-evoked auditory brainstem response is both passively-elicited and malleable, it may have clinical utility in detection of ASD as well as monitoring responses to intervention.

89 137.10 Auditory-Visual Multisensory Integration in Autism: an ERP study. A. B. Brandwein*[1], T. Altschuler[2], H. Gomes[2], J. Foxe[3] and S. Molholm[3], (1)*The Graduate Center of the City University of New York*, (2)*City College of New York*, (3)*Nathan Kline Institute for Psychiatric Research and City College of New York*

Background: It is widely believed that individuals with autism spectrum disorders (ASD) experience severe difficulties integrating inputs from the various sensory systems (sight, touch, hearing) – the so-called sensory integration theory of autism. While most typically developing individuals appear to integrate multisensory information effortlessly, many individuals with ASD reportedly find the sensory environment overwhelming. It has been hypothesized that a failure to integrate the sensory inputs into meaningful and manageable units is a major component of autism and related neurodevelopmental disorders. However, this has not been rigorously tested and is lacking direct neurophysiological evidence.

Objectives: Our overarching goal is to establish whether multisensory deficits are present in children with ASD and to characterize the neurophysiological basis of these deficits. Here we use high-density electrical mapping to investigate basic auditory-visual integration in children with ASD and children with typical development (TD).

Methods: Children with ASD and TD were matched for age, sex, and intellectual

functioning. All participants were presented with auditory (simple tones) and visual (red circles) stimuli together or alone. The children performed a simple reaction-time task while recordings of electrical brain activity were made. Average ERP waveforms elicited from the auditory-alone condition and the visual-alone condition were summed for each participant. Comparisons were made between the 'sum' ERPs and the 'simultaneous' ERPs in both groups.

Results: Our preliminary findings suggest that the time course and scalp topography of multisensory integration processes are different in the children with ASD compared to the children with TD. In general the children with TD exhibited multisensory interactions that are more similar to those typically seen in adults while the multisensory interactions observed in children with ASD had markedly different temporal and spatial properties.

Conclusions: Our data suggests that different cortical processes and regions are involved in integrating basic auditory-visual information for ASD and TD children.

90 137.11 ELECTROPHYSIOLOGICAL EVIDENCE OF ANOMALOUS AUDITORY-VISUAL INTERACTIONS IN CHILDREN WITH AUTISM. J. Vidal[1], M. H. Giard[2], F. Bonnet-Brilhault[1], C. Barthélémy[1] and N. Bruneau*[1], (1)*University Francois Rabelais de Tours, CHU Bretonneau, INSERM U930*, (2)*INSERM U821*

Background: The development of adapted behaviours requires to perceive the surrounding world as a whole, taking into account the multiple sensory information that permanently stimulate our different senses. The ability to integrate auditory and visual information is essential in communication development, which is particularly impaired in children with autism.
Objectives: The aim of this study was to investigate the electrophysiological patterns of auditory–visual interactions during bimodal event perception in children with autism.
Methods: Event-related potentials were recorded in response to auditory, visual, and bimodal auditory-visual stimuli (synchronously delivered) in two sub-groups of children with autism aged 5 to 10 years (n=9) and aged 11 to 15 years (n=9), compared to 18 age-matched controls with typical development. Auditory-visual interactions were estimated in the difference between the response to the bimodal stimuli and the algebraic sum of the responses to the unimodal stimuli. Statistical significance of the amplitude of this difference was tested using Student's t tests, and topographic analyses of the sensory responses and of the cross-modal interactions were performed using scalp potential and current density mapping.
Results: Autistic children's unisensory responses were overall preserved whatever the age. These unimodal responses were not modulated by the presence of concomitant information from another sensory modality (bimodal conditions) in children with autism, contrary to what was observed in controls. Moreover, interaction effects were observed in nonsensory-specific areas with a reverse lateralization in autistic compared to typically developped children. This pattern was found in both sub-groups of age, underlying the robustness of the effects.
Conclusions: These findings provide evidence for an anomalous pattern of cross-modal interactions in children with autism which may contribute to ongoing difficulties in communication and social interactions in these children.

91 137.12 An ERP study of cross-modal integration of speech in typical development and autism spectrum disorder. O. Megnin*, T. Charman, T. Baldeweg, M. De Haan, A. Flitton and C. Jones, *UCL Institute of Child Health*

Background: Event-related potentials (ERPs) have previously been recorded from 16 adult participants during video presentation of words in one of four conditions: auditory-only (A), visual-only (V), audio-visual with face (AVF), and audio-visual with scrambled face (AVS). Multi-sensory interactions were regarded as significant when [AVF – (A+V)] >0 at a single electrode for a minimum of 24ms duration. The interaction pattern observed was spatially and temporally consistent with a faster, attenuated auditory N1 component. Bimodal stimuli may speed up

and facilitate auditory processing in sensory-specific cortices, as supported by faster reaction times to the AVF target and shorter P3 peak latency. Increased negativity was also observed at FP2 for AVF stimuli. A significant correlation between N1 attenuation and the earlier-onset frontal negativity implies that these responses may reflect top-down modulation with lip movements (which precede auditory onset by a mean of 332ms) being used to constrain predictions about the word that is to be produced. Importantly, the N1 attenuation and frontal negativity is not observed in the other audio-visual condition (auditory + scrambled face).

Objectives: Examine audio-visual integration in a group of high-functioning adolescents with autism spectrum disorder (ASD) and an age and IQ matched control group.

Methods: Apply the same paradigm as used previously with the addition of a visual-only scrambled face condition (VS) to allow comparison of [AVF – (A+V)] and [AVS – (A+VS)].

Results: Preliminary data suggest differences in audio-visual integration in the adolescents with ASD.

Conclusions: There are a number of reasons why we might expect to see differences in an autistic population, including (but not limited to) findings of atypical unimodal auditory processing (e.g. Bomba & Pang, 2004), atypical unimodal visual processing, particularly with regards to face processing (e.g. McPartland et al, 2004), and multi-sensory processing differences (e.g. Bebko, Weiss, Demak, & Gomez, 2006).

92 137.13 ANTERIOR EEG ASYMMETRY IN CHILDREN AND ADOLESCENTS WITH HIGH FUNCTIONING AUTISM. A. P. Inge*[1], P. C. Mundy[2], H. A. Henderson[1], N. E. Zahka[1], C. Schwartz[1], N. Kojkowski[1], C. Hileman[1], D. Coman[3] and L. Mohapatra[1], (1)*University of Miami*, (2)*UC Davis*, (3)*Center for Autism and Related Disabilities*

Background: Differences in motivational predispositions to engage in approach versus withdrawal behaviors, assessed with anterior EEG asymmetry, are related to social variability in children with high functioning autism (HFA). However, the precise nature of this association is unclear and may differ from those in typically developing populations. Specifically, left frontal HFA children display better social interactions consistent with an approach bias, but also report more anxiety typical of a right frontal withdrawal bias.

Objectives: To better understand anterior EEG asymmetry as an indicator of individual differences in motivational biases and comorbid symptoms of anxiety in HFA children, we examined (1) the short-term stability of anterior asymmetry, and (2) the associations between frontal asymmetry and anxious apprehension versus anxious arousal (Heller et al., 2003).

Methods: Sixteen children and adolescents with HFA completed the Multidimensional Anxiety Scale for Children (MASC), which assesses components of anxiety, including those associated with different cognitive processes (i.e., anxious arousal vs. anxious apprehension). EEG data were collected from 18 scalp sites on two occasions over a 6-week interval. EEG asymmetry was computed for homologous electrode pairs (e.g., lnF4-lnF3). More positive scores were indicative of relative left frontal asymmetry.

Results: EEG asymmetry at Time 1 and Time 2 were significantly correlated at the midfrontal site (r = .43, p < .5, df = 15). Left frontal asymmetry was associated with reports of general anxiety but the magnitude and direction of the association did not differ for the anxious arousal versus anxious apprehension dimensions.

Conclusions: These data suggest that EEG asymmetry provides a stable index of bio-behavioral motivation processes in HFA children. However, the results did not support the hypothesis that differences in phenomenology (apprehension versus arousal) could explain the association of anxiety with left asymmetry in HFA children.

93 137.14 An electrophysiological study of spatial attentional orienting toward emotional faces in autism. I. Giraud*[1], N. Désiré[2], A. Hosein[2], L. Mottron[1] and B. Jemel[1], (1)*Hopital Riviere des Prairies/University of Montreal*, (2)*Hopital Rivière des Prairies*

Background:

Threat-related stimuli tend to attract attention, thus eliciting an involuntary orienting of spatial attention towards their location. Target detection is quicker and evokes larger P1 event-related potential (ERP) peak for probes replacing the location of threatening (valid condition) rather than neutral faces (invalid).

Objectives:

investigate the effect and time course of spatial attentional orienting towards fearful faces in High Functioning Autism (HFA) using RTs and ERPs.

Methods:

RTs and ERPs (a 59-channel EEG) were collected from eleven HFA (age= 26.6y, IQ= 103.6) and twelve contol subjects (age= 23.6y, IQ= 109.4) in a go/no-go task, during which a pair of faces (an emotional, fearful or happy, and a neutral face) was briefly presented followed by a bar-probe presented unilaterally on either the left or right visual field. The bar appeared either at the emotional face's location (valid condition) or at the neutral face's location (invalid). Participants were asked to press a response-key only when the bar's orientation matched that of the thicker segment of the fixation cross.

Results:

Controls showed longer RTs on invalid than valid trials following fearful but not happy faces whereas HFAs made slower responses on valid than on invalid trials following both happy and fearful faces. Consistent with these behavioral results, P1 ERP peak elicited by the bar-probe was both larger and shorter for the valid than invalid condition following fearful but not happy faces in controls. No such spatial validity effects on P1 were found in HFA subjects, following both happy and fearful faces.

Conclusions:

Our present study shows that emotional faces divert HFA's attention from their location, leading to longer RTs for valid than invalid trials. However, no spatial validity effects were found on P1 ERPs suggesting that processing of emotional faces does not influence through top-down attentional mechanisms early visual processing in HFA.

94 137.15 EEG STUDY OF THE MIRROR NEURON SYSTEM IN CHILDREN WITH HFA DURING OBSERVATION AND IMITATION OF FACIAL EXPRESSIONS. R. Raymaekers*, J. R. Wiersema and H. Roeyers, *Ghent University*

Background: The mirror neuron system (MNS) is an observation/execution brain system, translating visual input into motor understanding through the activation of the observer's motor system. Disruptions in this neural circuitry can significantly impact social interaction. It has been suggested that empathy may critically depend on one's ability to understand the observed facial expression in terms of one's own motor representations. In light of the fact that deficits in social cognition are a core feature of autism, it is of interest to examine this system in autism. Studies indicate that a decrease in electroencephalogram (EEG) power in the mu frequency band recorded over motor cortex reflects MNS activity during execution and observation of motor actions.
Objectives: To investigate the MNS activity in children with high-functioning autism (HFA) during imitation and observation of facial emotional expressions.
Methods: Normally intelligent children (9 to 13 years) with HFA were compared with typically developing peers. Subjects were asked 1) to watch photographs of facial expressions and 2) to imitate the observed footage, during which mu wave suppression was measured.
Results: Preliminary results indicate that mu suppression is comparable between the HFA and the control group in action-imitation conditions, as well as in action-observation

conditions. Further analyses are currently in progress.
Conclusions: Preliminary findings do no support the hypothesis of an impaired MNS in children with HFA when observing or imitating facial expressions.

95 137.16 NEURAL CORRELATES OF EMOTIONAL FACE PROCESSING IN CHILDREN WITH AUTISM. K. Burner*, S. Webb, K. Merkle, M. Murias and G. Dawson, *University of Washington*

Background: Behavioral and psychophysiological research suggests that emotion processing is impaired in individuals with autism spectrum disorder (ASD). Furthermore, electrophysiological research indicates that 3-4 year old children with ASD fail to differentiate fearful and neutral faces.

Objectives: Examine event-related potentials (ERPs) to emotional faces in high-functioning children with ASD and investigate whether measures of social behavior are correlated with ERP responses.

Methods: Participants included 9-year-old children with ASD (n=28), typically developing children (n=35), and developmentally delayed children (n=15). Children passively viewed 50 exemplars of prototypical fearful and happy facial expressions while continuous EEG was recorded.

Results: Preliminary analysis of this sample included children with ASD and typically developing children. Initial results reveal no differences between groups in response to facial expressions measured by early and late ERP components.

Conclusions: These preliminary data do not reveal a deficit in emotional face processing in high-functioning children with ASD. These results differ from previous findings of emotion-processing deficits in young children with ASD. However, these results may be consistent with studies of high-functioning children with ASD that suggest that these children are utilizing top-down compensatory emotion-processing strategies. Future analyses will compare speed of processing at 3 and 9 years of age to examine potential developmental differences. Further analyses will also examine the relation between emotion processing and social ability, diagnostic severity, communication, and associated conditions.

96 137.17 A Lack of Neurophysiological Responses to Subliminally Presented Fearful Faces in Adults with High-functioning Autism Spectrum Disorders. Y. Kamio*[1], T. Fujita[2] and S. Tobimatsu[2], (1)*National Center of Neurology and Psychiatry, Japan, National Institute of Mental Health*, (2)*Kyushu University*

Background: Recent studies (Bailey et al., 2005; Critchley et al., 2001; Kamio et al., 2006) have suggested that individuals with autism spectrum disorders (ASD) respond to faces differently from typical developing individuals at an automatic level, even when they can perform face tasks well at a conscious level. Since emotionally significant stimuli are automatically processed outside conscious awareness before being integrated with slower and more elaborative processing, abnormalities of automatic face processing are thought to be essential for the various manifestations of social cognition in individuals with ASD.

Objectives: Our study aimed to examine the neurophysiological basis of subliminal face processing at the V1 level in adults with high-functioning ASD (HFASD) and to compare it with that of healthy adults by measuring the earliest event-related potential (ERP).

Methods: Nine adults with HFASD and 10 healthy control adults performed a low-frequency target detection task in which photographs of faces (fearful, neutral) and objects were presented for 20ms with backward pattern masks either upright or inverted. The latency and peak amplitude of N1 were measured at occipital electrodes (Oz).

Results: In the control group, upright fearful faces evoked greater N1 amplitude at around 100 msec than objects did, but the N1 amplitude for fearful faces was reduced when inverted and did not differ from that for objects. On the other hand, such face-specific

responses were not observed in the ASD group.

Conclusions: The findings suggest that individuals with ASD are impaired in the early and automatic processing specific to fearful faces, which was confirmed in individuals with typical development. The explicit social abnormalities observable in individuals with ASD could be explained by such deficits in precognitive face processing.

97 137.18 Psychophysiological responses to wide-open eyes in children with autism spectrum disorders. A. Kylliäinen*[1], S. Wallace[2], A. Bailey[2] and J. K. Hietanen[1], (1)*University of Tampere*, (2)*University of Oxford*

Background: Eye contact avoidance in autism spectrum disorders (ASD) may be a consequence of negative physiological arousal elicited by direct gaze. In addition, wide-open eyes with increased amount of exposed sclera (such as in fearful eyes) may be misinterpreted as threatening by children with ASD.

Objectives: Our main aim was to investigate whether children with ASD become physiologically over-aroused when looking at faces with wide-open eyes. A secondary aim was to study whether face familiarity modulates the arousal responses in children with ASD.

Methods: Participants included 14 children with ASD and 15 age, gender and IQ matched typically developing children. Skin conductance responses (SCR) and heart rate were recorded as participants viewed pictures of three familiar and three unfamiliar faces with eyes closed, eyes normally open or eyes wide-open. The face pictures loomed toward the participants, creating an impression of an approaching person. In order to ensure that the participants were attending to the eyes, they were asked to make a button press after observing an eye blink.

Results: The results indicated that gaze condition affected SCRs in the children with autism, but not in the typically developing children. SCRs were larger in the wide-open eyes condition than in the eyes closed condition in children with autism, but not in typically developing children. Familiar faces elicited larger SCRs than did unfamiliar faces in both groups.

Conclusions: These findings suggest that children with ASD have atypical physiological responses to wide-open eyes directed at them. The data are interpreted in relation to current views suggesting that individuals with ASD show atypical neural and cognitive responses to direct gaze stimuli.

98 137.19 Neural correlates of processing of familiar and unfamiliar visual stimuli in infants at risk for autism spectrum disorders. C. A. Nelson[1], H. Tager-Flusberg[2], V. Vogel-Farley[1], A. Levin*[1], L. M. Casner[3] and N. B. Leezenbaum[2], (1)*Children's Hospital Boston*, (2)*Boston University School of Medicine*, (3)*Boston University*

Background: The median age for diagnosing a child with autism is between 3 and 4, thus limiting opportunities for very early intervention. Some progress has been made in identifying manifestations of autism at around 12 months of age in infant siblings of children with ASD. For example, Zwaigenbaum and colleagues found that by 12 months, high-risk infants who later met diagnosis for ASD scored on at least 7 of 18 behavioral markers on the Autism Observation Scale for Infants (AOSI).
Objectives: One important goal of research is to push back the age at which the earliest signs of autism can be reliably identified in order to maximize opportunities for intervention at optimal developmental stages.
Methods: In the current project we employ high-density event-related potentials (ERPs) and eye tracking to examine risk for ASD among infants at high risk for autism (by virtue of having at least one affected sibling). Infants are being studied at 3, 6, 12 months. Using ERPs and eye tracking, we are examining the discrimination of mother vs. stranger face.
Results: To date we have obtained usable ERP data from 28 children. Preliminary inspection of the data suggests that at 3 and 6 months,

the mid-latency negative component (NC) in both groups is distinguishing mother's vs. stranger's face . However, at 9 months it appears that for the at-risk group the Nc and P400 is faster to mother (and for the NC, larger), whereas the PSW is larger to stranger. The control group Nc is larger to stranger, the PSW is larger to mother and the P400 is faster to stranger. Behavioral data are currently being analyzed.
Conclusions: This project will lay the groundwork to identify early neurobehavioral risk markers in facial processing for ASD and language impairment.

99 137.20 Electrophysiological correlates of processing native and non-native speech contrasts in infants at risk for autism spectrum disorders or language impairment. V. Vogel-Farley*[1], C. A. Nelson[1], H. Tager-Flusberg[2], A. Levin[1], L. M. Casner[3] and N. B. Leezenbaum[2], (1)*Children's Hospital Boston*, (2)*Boston University School of Medicine*, (3)*Boston University*

Background: Recent research has highlighted potential overlap in phenotype between children with autism and those with specific language impairment (SLI). A significant proportion of first-degree relatives of autism probands have language-related learning disabilities, and in a large epidemiological sample, siblings of SLI probands found an elevated risk of ASD. Several researchers have argued that ASD and SLI form overlapping populations with shared phenotypic features and potential genetic etiology. Because the relatively few studies that have directly compared ASD and SLI have all been conducted with older children, it is not known whether there is overlap in the earliest manifestations for each of these disorders in specific symptoms or developmental timing.
Objectives: We hypothesize that neural correlates of key aspects of language and social-communicative development in infants who later go on to show signs of language impairment or ASD emerge during this critical period between 3 and 12 months in both high risk groups.

Methods: In the current longitudinal project we are employing high-density event-related potentials (ERPs) to examine the discrimination of familiar vs. unfamiliar speech contrasts among three groups of infants: (1) infants at risk for ASD (by virtue of 1 or more affected siblings), (2) infants at risk for SLI and (3) low risk infants. Infants are being studied at 3, 6, 9 and 12 months. The auditory ERP task involves a cross-linguistic double-odd ball paradigm design using Hindi as the non-native speech stimuli.

Results: Thus far 30 infants have yielded useable ERP data and preliminary inspection of the data show discrimination between the native and non-native speech sounds at the P1, N250 and the MMN, with the ERP responses being different between the 3 groups.
Conclusions: This exploratory project will lay the methodological foundation using neurobehavioral measures to determine the earliest signs of ASD and SLI in infancy.

100 137.21 An electrophysiological study of auditory-somatosensory integration among persons with Autism Specrum Disorders. S. Molholm*, N. Russo, H. Gomes, A. Brown-Brandwein, T. Altschuler and J. Foxe, *City College of New York*

Background: In spite of the multitude of clinical and anecdotal evidence to suggest that individuals with Autism Spectrum Disorders have sensory atypicalities, few studies have been conducted in which this is assessed directly using objective physiological measures of sensory processing.

Objectives: Here, we present findings from an electrophysiological study in which we measured the brains response to auditory and tactile stimulation.

Methods: 10 participants with ASD (diagnosed on the basis of the ADOS and ADI), and 10 typically developing children matched on the basis of age, IQ and handedness participated in this study. Participants completed a passive task in which auditory and somatosensory stimuli were presented either alone or simultaneously.

Results: Differences between the persons with ASD and typically developing children emerged

with respect to both basic sensory processing, and how the brain integrated the sensory inputs when they were presented together.

Conclusions: These findings are discussed with respect to their implications for theories of autism and the role of sensory processing and multisensory integration.

101 137.22 Electrophysiological Analysis of Empathy and Theory of Mind Function in Children with Autism Spectrum Disorder. J. M. Bai*[1], D. Asher[2], O. R. Aragon[2] and J. A. Pineda[2], (1)*UIUC*, (2)*UCSD*

Background: Previous research has identified the mirror neuron system (MNS) as a collection of neurons involved in the integration of observation and execution into a matching system. MNS activity monitored by EEG has been indexed through power suppression from 8-13Hz (mu rhythms) over the sensorimotor cortex.

Objectives: Typically developing (TD) individuals show mu power suppression during goal oriented actions in observation and execution. Individuals with autism spectrum disorder (ASD) show suppression only in goal oriented actions involving execution and not observation.

Methods: Our research focused upon two methods for analyzing social cognition through observation of visual stimuli, empathy and theory of mind (ToM).

Results: The ToM method revealed results that reinforced a previous study that dissociates ToM into two subcomponents. The empathy study applied to TD children revealed mu power suppression to emotional faces. In contrast, children with ASD showed similar mu power across different conditions. This result suggests that children with ASD do not engage the mirror neuron system in face emotion processing as do TD children. In addition, TD children show higher mu power suppression in the right hemisphere than in the left. However, children with ASD showed no mu power difference between hemispheres.

Conclusions: Therefore, the electrophysiological data collected through these two methods contribute to the theory that children with ASD are deficient in their ability to suppress mu rhythms. These results provide a fundamental basis for an ongoing study that is investigating whether the electrophysiological discrepancies in ASD are functional, structural or both.

102 137.23 NEURAL CORRELATES OF VERBAL AND NONVERBAL SEMANTIC INTEGRATION IN YOUNG CHILDREN WITH AUTISM. J. P. McCleery*[1], R. Ceponiene[1], K. Burner[2], C. Williams[1], M. Kinnear[1], J. Townsend[3] and L. Schreibman[1], (1)*University of California, San Diego*, (2)*University of Washington*, (3)*UC, San Diego*

Background: Previous behavioral and neuroimaging studies have shown that individuals with autism evidence impairments in semantic processing. However, it is not currently known whether these deficits are confined to the verbal domain or represent a more general problem with the processing of semantic information.

Objectives: To investigate verbal and nonverbal semantic integration in high functioning children with autism and typically developing children, aged 4 to 7 years, using high-density event-related potentials (ERPs).

Methods: The two groups were matched on chronological age, developmental age, and gender, and both groups scored in the normal range on standardized tests of language. Stimuli were matching and mismatching picture-word and picture-sound pairs. For example, a picture of a car was presented with (i) the word "car" (word match), (ii) the word "ball" (word mismatch), (iii) the sound of a car engine (sound match), or (iv) the sound of a bouncing ball (sound mismatch). N400 component effects were examined by subtracting matching word and sound ERPs from mismatching word and sound ERPs. Finally, t-tests were performed to determine whether N400 differences were different from zero.

Results: Children in both groups showed semantic mismatch effects in the environmental sound condition (CON Diff =

1.22 microvolts, s.e.=0.62, p<0.5; AUT Diff = 1.12 microvolts, s.e.=0.62, p<0.5). However, only controls showed differentiation of matching versus mismatching words (CON Diff = 1.27 microvolts, s.e.=0.54, p<0.5; AUT Diff = 0.1 microvolts, s.e.=0.55, p=0.49).

Conclusions:Because N400 match versus mismatch effects reflect the automatic detection of semantic mismatches, these results demonstrate that young children with autism exhibit abnormal automatic processing of semantic information at the level of single word meaning. The finding that match versus mismatch effects were normal in the environmental sound condition further suggests that this semantic processing abnormality may be limited to the verbal domain in these children.

103 137.24 Brain Responses to Temporally Novel Sound in Children with Autism: Evidence for Reduced Involvement of the Right Hemisphere. E. V. Orekhova*[1], T. Stroganova[2], A. O. Prokofiev[2], G. Nygren[3], C. Gillberg[3] and M. Elam[1], (1)*Sahlgrenska University Hospital*, (2)*Psychological Institute of the Russian Academy of Education*, (3)*Göteborg University*

Background:
Unresponsiveness to sound is commonly observed in autism and may relate to a reduced capacity for attention orienting.

Objectives:
The present study was aimed at determining whether young children with autism display abnormalities at early stages of automatic allocation of attention to temporally novel sound presented in nonattended channel.

Methods:
Subjects were twenty one 3-8 year old children with autism and twenty one age-matched typically developing children. While watching a silent movie, subjects were presented with pairs of clicks separated by a 0.5 s intra-pair interval, with longer (7-9 s) intervals between pairs. We assess electroencephalographic (EEG) perturbations and event-related potentials (ERP) in response to sounds of different temporal novelty (first and second click in the pair).

Results:
In control children, the early attention-modulated midtemporal N1c wave of EPR and corresponding EEG phase locking and power increase in response to the first click were right-lateralized and were bilaterally higher than in response to the second click. Children with autism demonstrated abnormal first click responses, characterized by reduced N1c amplitude and EEG phase locking in the right midtemporal region, reversed leftward lateralization of the EEG phase locking and absence of the later frontal N2 wave. Their brain responses to the second click were essentially normal. The behavioral and heart rate analysis suggested that the two groups did not differ in respect to baseline arousal or preliminary (in)attention to the click stimuli. Therefore, the between-group differences in response to the first click could be explained by differences in initial orienting response to temporally novel events.

Conclusions:
The impaired right hemispheric processing of temporary and contextually novel information and suboptimal hemispheric lateralization of normally right-lateralized orienting and alerting networks may importantly contribute to development of the social deficits in young children with autism.

104 137.25 LITERATURE MINING FOR BETTER UNDERSTANDING OF AUTISM. M. Macedoni-Luksic*[1], T. Urbancic[2], I. Petric[2] and B. Cestnik[3], (1)*University Medical Centre Ljubljana, Division of Paediatrics*, (2)*University of Nova Gorica*, (3)*Jozef Stefan Institute*

Background: There's an enormous increase of information in the field of autism. It makes an effort to put pieces together into more coherent picture very difficult.

Objectives: We present a literature mining method for searching pairs of papers in disjoint literatures that may contribute to better understanding of complex pathological conditions, such as autism.

Methods: 214 articles about autism in PubMed database, with their entire text published from 1996 to 2006, served as a source of data. Using ontologies construction (OntoGen) we

identified the main concepts of what is already known about autism. Then the RaJoLi (*Ra*re, *Jo*int and *Li*nking) method was used to uncover interesting relations. It consists of four steps:
1. Identification of *n* interesting rare terms C_R_1, C_R_2, …C_R_n in literature about C
2. Search for a joint term A in the literatures about C_R_1, C_R_2, …C_R_n
3. Search for linking terms B1, B2, …., Bm such that for each Bi there exists a pair of articles, one from literature A and one from literature C, both mentioning Bi.
4. Expert evaluation in which it is checked whether obtained pairs of articles contribute to better understanding of C.

Results: *Calcineurin,* a calcium/calmodulin-dependent protein phosphatase and *NF-kappaB,* a transcriptional factor, were discovered as joint terms in the intersection of corresponding literature. Recent studies indicate that calcineurin participates in intracellular signaling pathways, which regulate synaptic plasticity and neural activities. On the other hand, various genes are responsive for activation of the NF-kappaB, including those for cytokines. In this way NF-kappaB can be involved in the complex relationship between immune system and autism.

Conclusions: Further research is needed to give us stronger evidences about calcineurin and NF-kappaB involvement in autism, but in any case, the method could support experts on their way towards discovering hidden relations in data and better understanding of the disorder.
Sponsor: Slovenian Research Agency

105 137.26 Epilepsy Impairs In Vitro Thalamic Signal Processing. M. Anderson*, *Harvard Medical School/ Beth Israel Deaconess Medical Center*

Background: Autism spectrum disorders (ASD) are often associated with subclinical epileptiform discharge (Chez et al. 2006; Hara et al. 2007) and epilepsy correlated with behavioral regression (Humphrey et al. 2006; Jian et al. 2006). These cortical discharges intensely activate thalamus (Blumenfeld et al. 2004; Enev et al. 2007). Since ASD individuals show impaired rapid sensory processing (Tallal and Piercy, 1973; Oram Cardy et al. 2005), we hypothesized that some ASD might result from excessive cortical excitation of thalamus triggering homeostatic changes in thalamus that impair sensory-motor signal processing.

Objectives: Evaluate effects of chronic infantile epilepsy (stargazer, JAXS) and acute epileptiform discharge (pilocarpine) on thalamocortical neuron firing properties and plasma membrane ion currents.

Methods: Studied were performed on mice (2-4 months old) as previously described (Kasten et al., 2007). In coronal brain slices (230-280 mm), single thalamocortical neurons were visualized using infrared DIC optics. Whole-cell patch-clamp recording performed in current or voltage clamp mode.

Results: First, we found rapid phasic and burst firing were impaired, while prolonged firing (> 1 sec) is preserved in thalamic relay neurons of these two distinct mouse models of epilepsy. Second, fast transient K+ currents (< 50 msec) were increased explaining the selective defect in rapid and burst firing. Third, a dominant negative LGI1 (leucine-rich glioma-inactivated) blocked the increase of K+ current.

Conclusions: We define a molecular pathway involving a protein secreted at glutamate synapses, LGI1, and a transient A-type K+ current that mediate epilepsy-induced impairments of rapid signal processing in thalamus. The studies establish a new model of ASD pathogenesis where cortical epileptiform discharges trigger a reversible defect of thalamic sensory-motor signal processing.

106 137.27 EEG Coherence Abnormalities in Autistic Children Triggered by the Processing of Complex Visual Stimuli in Motion. K. M. Martien*[1], P. Grieve[2], J. Isler[2], N. Snidman[3], J. Kagan[3], T. Kenet[4] and M. Herbert[5], (1)*Massachusetts General Hospital-Harvard Medical School*, (2)*Columbia College of*

Physicians and Surgeons, (3)*Harvard University*, (4)*Massachusetts General Hospital*, (5)*Mass Gen Hosp/Harvard Med School*

Background: Autistics show a diminished ability to integrate complex information. This may relate to altered functional connectivity. EEG coherence measures electrocortical synchrony of oscillatory brain rhythms across neural networks, which is hypothesized as a mechanism for functional connectivity, binding of neural activity and integration of cognitive processes. Objectives: We sought to test the hypothesis that there would be greater coherence differences between autistic children and controls in a complex visual input condition when compared to the differences seen in a simple or minimal visual input condition. Methods: Resting EEG was obtained, using a 128 electrode net, for 3 conditions presented for 5 minutes each: 1) complex visual stimulus: a movie, 2) simple visual stimulus: flashes of light in a visual evoked potential (VEP) paradigm, and 3) no visual stimulus: eyes closed/lights out (EC/LO) in 5 children (4.4-9.8yrs): 2 autistic, 2 autistic spectrum (ASD) and 1 typically developing control. Coherence was computed between all channel pairs for each frequency band. Power and coherence were then averaged for each condition. Results: Autistics showed broadly increased low frequency (delta/theta) coherence in the "movie" condition compared to control. Coherence differences for VEP and EC/LO were far less significant. ASD children showed the same effect but to a lesser degree. Interhemispheric higher frequency (alpha) coherence was somewhat decreased in the "movie" condition when compared to VEP and EC/LO condition in preliminary data. Conclusions: Our data suggest that autistic children show coherence abnormalities that are not static but dynamic and produced by exposure to complex visual stimuli in motion. This abnormality appears to be proportionate to the severity of the autism. Whether motion or complexity is the critical factor in producing these coherence differences remains to be determined. These data suggest that processing of complex visual images in motion alters functional connectivity in autism.

138 Repetitive Behaviour Posters

107 138.1 Validation of a clinical scale for restricted and repetitive behaviours in autism spectrum disorders. Y. Bourreau*, S. Roux, M. Gomot, F. Bonnet-Brilhault and C. Barthélémy, *University Francois Rabelais de Tours, CHU Bretonneau, INSERM U930*

Background: Degrees of heterogeneity have been reported in the clinical expression of autistic syndrome, particularly in restricted and repetitive behaviours (RRB). These overwhelming behaviours represent a common problem over the whole autistic spectrum and comprise a wide range of behavioural manifestations that persist over time. Advances are needed in the understanding of this complex and heterogeneous clinical dimension of autism but to date there is no specific and thorough tool to provide accurate and standardized description of these behaviours.

Objectives: The validation of a clinical scale covering the full range of repetitive, restricted and stereotyped activities observed in autism spectrum disorders.

Methods: A checklist comprising 35 items dealing about RRB is used. Each item is scored on a five-point scale, from "never expressed" to "severely expressed and very characteristic of the person". Reliability and validity studies were performed on a sample consisting of more than 100 children, adolescents and young adults with autism or pervasive developmental disorders. These studies involved the participation of 15 centers.

Results: The scale has good inter-rater reliability and internal consistency. Content validity study, using principal component analysis, allowed the identification of 6 relevant main dimensions of RRB, i.e. "insistence on sameness", "sensory stereotypies", "motor stereotypies", "modulation of temper", "self-focused behaviours", and "vocal stereotypies".

Conclusions: The scale shows good psychometric properties and confirms the heterogeneity of RRB in autism spectrum disorders. The description of clusters of RRB

helps identification of more homogeneous subgroups of patients, possibly related to different psychopathological or physiopathological underlying factors.

108 138.2 FRONTOSTRIATAL FUNCTIONS EXAMINED WITH OCULOMOTOR TASKS ARE ASSOCIATED WITH RESTRICTED AND REPETITIVE BEHAVIORS IN AUTISM.
M. W. Mosconi*[1], A. Seidenfeld[1], M. Kay[1], S. Guter[2], L. D. Stanford[1] and J. A. Sweeney[1], (1)*University of Illinois at Chicago*, (2)*Institute for Juvenile Research*

Background: Impaired executive functions are evident in autism and likely reflect frontostriatal dysfunction. These impairments, which include failure to disengage attention and inhibit prepotent responses, may contribute to problems of cognitive inflexibility, impulsivity, and repetitive behaviors. Oculomotor tasks provide sensitive methods for assessing executive functions in a translational framework.

Objectives: To investigate attentional disengagement and response inhibition in individuals with autism, and determine whether deficits in these functions are associated with repetitive behaviors.

Methods: Eighteen individuals with autism and 15 age- and IQ- matched healthy control individuals performed a visually guided prosaccade task and an antisaccade task. During the prosaccade task, participants fixate on a central cross-hair and make reflexive saccades to novel peripheral targets. During the antisaccade task, participants are instructed to inhibit attention to novel peripheral targets and instead make a saccade to the mirror location of the target. Each task included gap and overlap conditions. 'Gap' trials were characterized by extinction of the cross-hair at central fixation 200 ms *prior* to presentation of a peripheral stimulus. 'Overlap' trials were characterized by extinction of the cross-hair at central fixation 200 ms *after* presentation of a peripheral stimulus. The latency and accuracy of prosaccades were examined. Antisaccade error rates (the failure to inhibit prepotent responses) and latency of antisaccades were examined. Repetitive behaviors were measured with the Autism Diagnostic Inventory – Revised.

Results: Individuals with autism showed prolonged latencies in shifting attention on overlap prosaccade trials, and more antisaccade errors on both conditions of the antisaccade task. Both increased latency on overlap trials of the prosaccade task and increased errors on the antisaccade task were associated with levels of repetitive behavior.

Conclusions: These results indicate that disturbances in the ability to disengage attention and voluntarily inhibit prepotent responses may underlie repetitive and stereotyped behaviors in autism.

109 138.3 Repetitive Behaviors and Intense Interests in High-Functioning ASD.
L. Anthony*[1], G. Wallace[2], B. Yerys[1], J. James[1], S. McCracken[3], A. DellaRosa[1], B. Harrison[1] and L. Kenworthy[1], (1)*Children's National Medical Center, George Washington University*, (2)*National Institutes for Mental health*, (3)*Children's National Medical Center*

Background: Although repetitive behaviors and restricted interests are part of the diagnostic criteria for both Asperger's Syndrome and high-functioning autism (AS/HFA), most investigations into these behaviors are with autism and/or mental retardation.

Objectives: 1) To determine how well the Repetitive Behavior Scale (RBS) and the Interests Scale discriminate between AS/HFA and typically developing (TD) controls, and 2) to explore relationships between repetitive and other behaviors.

Methods: Participants were recruited for multimodal research studies conducted at Children's National Medical Center/Georgetown University and the NIMH. Participants completed an extensive battery that included diagnostic measures (ADI-R, ADOS for AS/HFA subjects only), cognitive (WASI), the RBS, the Interests Scale, the Behavior Rating Inventory of Executive Functioning (BRIEF), and the Social Responsiveness Scale (SRS). Study measures were obtained from 63 youth with

AS/HFA (mean age 12.8, range 7.3-22; 54 male; mean FSIQ=112, sd=18) and 26 TD children (mean age=10.4, range 7.3-13.8; 18 male; mean FSIQ=118, sd=11).

Results: AS/HFA individuals had more repetitive behaviors (F=50.34, df=86, p=.000) and more intense interests (F=10.27, df=53, p=.002) than TD children. Children with AS/HFA did not have a greater number of interests than TD children, though qualitative analyses suggest different areas of interests. The topographies of the repetitive behaviors and intense interests will be presented. Controlling for FSIQ, scores on the RBS were related to intensity of interests (r=.51, p=.000), ADI-R Repetitive Behaviors (r=.57, p=.000), the Global Executive Composite on the BRIEF (r=.67, p=.000), and SRS total score (r=.81, p=.000). RBS scores were not correlated with scores on the ADOS. The Interests Scale was related to the ADOS diagnostic algorithm score (r=-.48, p=.2), the BRIEF GEC (r=.82, p=.000), and the SRS (r=.63, p=.000).

Conclusions: The RBS and the Interests Scale capture core symptoms associated with AS/HFA and are strongly related to each other, autistic traits, communication skills, and executive functioning.

110 138.4 REPETITIVE BEHAVIORS AND SALIVARY CORTISOL IN CHILDREN WITH AUTISM SPECTRUM DISORDERS: PILOT STUDY. R. Gabriels*[1], K. Holt[1], J. Agnew[1], A. Reynolds[1], K. Sherwood[2], M. Goldstein[2], Z. Pan[1] and M. Laudenslager[2], (1)*The Children's Hospital/University of Colorado Denver School of Medicine*, (2)*University of Colorado Denver School of Medicine*

Background: Restricted, repetitive and stereotyped behaviors, interests and activities (RBs) are diagnostic features of autism spectrum disorders (ASD), yet their presence varies greatly. Animal research suggests a relationship between the presence of increased motor stereotypies and lower levels of the stress hormone cortisol. Studies of children with Fragile X found that higher cortisol levels are associated with more internalizing behaviors while lower levels are associated with frequent eye-gaze aversion behaviors.

Objectives: Examine the relationship between frequency/severity of RBs and cortisol levels in pre-pubescent children diagnosed with an ASD, while controlling for sleep quality.

Methods: Two groups of ASD children (ages 3 to 9 years) with **high (n = 7) vs. low (n = 6)** RBs were recruited. Cut-off scores for inclusion were defined by taking the upper and lower quartiles of RBS-R total scores from the lead author's study of 52 ASD subjects. Caregivers completed the RBS-R prior to collecting salivary cortisol samples from their child four times daily (waking, 30 minutes after waking, before lunch and before dinner) for three days and completed sleep diaries. Child's current autism diagnostic symptoms, adaptive behaviors, puberty and medication status, full-scale IQ score, and socioeconomic status were also collected**.**

Results: For each of the four time points, cortisol levels were averaged across three days and these average values were entered into a repeated measures ANOVA. Results of this analysis show a trend towards the high RB group having lower cortisol levels than the low RB group ($F(1, 11) = 3.5$, $p = 0.95$).

Conclusions: We hypothesize that the RBs observed in the ASD population are self-soothing. Salivary cortisol may prove helpful in elucidating the etiology of repetitive behaviors and therefore assist in designing appropriate treatments.

Sponsor: Developmental Psychobiology Endowment Fund, University of Colorado of Denver School of Medicine, Denver CO

111 138.5 REPETITIVE BEHAVIORS IN AUTISM: ASSOCIATED SKILLS AND BEHAVIORS. K. C. Dominick* and H. Tager-Flusberg, *Boston University School of Medicine*

Background: Autism is characterized by varying levels of social and communicative impairment as well as repetitive behaviors and restricted interests. Several factors have been related to the expression of repetitive behaviors in both children with mental

retardation and children with autism spectrum disorders including age, IQ, language ability, adaptive behavior, the severity of social communicative symptoms, sensory processing and anxiety.

Objectives: To examine the relationship between repetitive behaviors and other relevant behaviors and symptoms. In addition, we explore the relationship of different types of repetitive behaviors to one other.

Methods: The severity of repetitive behaviors was measured using the Repetitive Behavior Scale – Revised, which allows for careful measurement of six subtypes of repetitive behaviors: stereotyped behavior, self-injurious behavior, compulsive behavior, ritualistic behavior, sameness behavior, and restricted behavior. The total severity of repetitive behavior and the severity of each subscale were examined in relation to age, IQ, language, adaptive behaviors, sensory processing, social behavior and anxiety using the DAS/KBIT/WASI, PPVT, EVT, Vineland Adaptive Behavior Scales, Baranek Sensory Supplement, Dunn Short Sensory Profile, Social Reciprocity Scale and the Beck Anxiety Inventory.

Results: Preliminary analysis shows a significant relationship between the severity of repetitive behaviors and sensory processing ($r_{s(95)}$=.59, p<.0001) as well as social deficits ($r_{s(88)}$=.48, p<.0001). All subscale behaviors were related to sensory processing and all but self-injurious behavior were related to social deficits. Self-injury was related to anxiety symptoms ($r_{s(50)}$=.31, p=.28).

Conclusions: These results indicate that the total severity of repetitive behaviors is related to both sensory processing and social skills. However, when the construct is further divided into independent subscales we see that some behaviors show a different pattern of relationships. Self-injurious behavior was only related to sensory processing and was unique in its relationship to anxiety.

112 138.6 Arousal Modulation during Engagement in Stereotypical and Repetitive Behaviours (SRB's). S. D. Noyce*[1] and D. Messer[2], (1)*London South Bank University*, (2)*Open University*

Background:

While SRBs are a defining aspect of autism, the occurrence and function of such behaviours is often neglected. One view is that SRBs are linked to arousal mechanisms, which can be traced back to the theories of Leuba (1955) and Hutt (1963). Furthermore, despite the lack of empirical evidence, Guess & Carr (1991) have included this concept in their three stage model of SRB's.

Objectives:

To investigate the connection between engagement in SRB's and arousal. Data from two empirical studies will be presented.

Methods:

Both studies recorded salient contextual and behavioural data over multiple observation sessions. In the first, the occurrence of spontaneous eye blink rate (SEBR) (Monster, Chan & O'Connor 1978) was recorded as an indirect non-intrusive measure of arousal. In the second study, direct physiological and endocrine assessments were made of both sympathetic nervous system arousal (skin conductance response (SCR)), and HPA activity (salivary cortisol assaying). Participants in both studies were male aged 6-11yrs and attended a behavioural school, where the research was conducted.

Results:

Study 1: Analysis shows that while there was only limited variation in SEBR across task activity, arousal was shown to vary significantly during engagement in certain SRB's. Arousal levels were noted to change prior to, during and after engagement. The magnitude of difference being more pronounced for physical type behaviours.

Study 2: The data supports the earlier findings of the SEBR study, suggesting that changes in arousal status corresponds with engagement in SRB's.

Conclusions:

It is suggested therefore, that a sub-group of SRBs may provide a means of modulating psychological and physiological arousal. The results also suggest that arousal thresholds (minimal & maximal) may serve as antecedents for certain behaviours.

113 138.7 IS THERE A SUBGROUP OF CHILDREN WITH ASD WHO HAVE HIGH RATES OF REPETITIVE BEHAVIORS AND HIGH RATES OF SENSORY INTERESTS/RESPONSE ABNORMALITIES?. A. V. Hall*[1], R. K. Abramson[2], R. Gabriels[3], J. Agnew[3] and H. H. Wright[4], (1)*Univ. S. Carolina Sch. Public Health*, (2)*Univ. S. Carolina Sch. Med.*, (3)*The Children's Hospital/University of Colorado Health Sciences Center*, (4)*University of South Carolina*

Background: High rates of restrictive/repetitive and stereotyped behaviors (RBs) and abnormal sensory response have been reported in children with autism spectrum disorders (ASD). Research has suggested that some individuals with an ASD engage in RBs as a reaction to a sensory experience.
Objectives: The aim of this study is to independently confirm the existence of a subgroup of ASD subjects with high rates of RBs and sensory interest/response abnormalities.
Methods: As part of a genetic study of autism, the Repetitive Behavior Scale-Revised (RBS-R) and ADI-R data on 134 individuals with autism were gathered. The sample was divided into quartiles with an RBS-R total score of >41 for upper quartile. A sensory response index was derived from totaling the current scores from ADI-R sensory items (sensory interests, idiosyncratic negative response to stimuli, and noise sensitivity). The relationship between the RBS-R total score and ADI-R sensory index within each subgroup (High-RB vs. Low-RB) were examined. T-tests were used to determine differences between subgroups.
Results: 38 individuals were in the High (upper quartile) RB subgroup and 96 individuals in the Low (lower three quartiles) RB subgroup. High-RB subgroup showed a significant correlation (r=.351,p=.3) between the RBS-R total and ADI-R sensory index. These variables were uncorrelated in the Low-RB subgroup (r=.169,p=.100). The High-RB subgroup differed significantly from the Low subgroup on ADI-R social and communication algorithm total scores, t = 2.205, p = 0.29 and t = 2.298, p = 0.23 respectively.
Conclusions: Results suggests there is a subgroup of individuals diagnosed with autism who have both high rates of RBs and sensory interest/response abnormalities. Finally, further research examining whether these two characteristics within autism constitute a consistent phenotypic subgroup is indicated. This research may have long-term significance for better understanding the genetic etiology of ASD.
This project was supported by 2R01 NS16768-09.

114 138.8 What is the relationship between cognitive flexibility and insistence on sameness behaviour in autism?. W. Mandy*[1], J. Gilmour[1], S. Kamboj[1] and D. H. Skuse[2], (1)*University College London*, (2)*Institute of Child Health*

Background: Recent evidence suggests that domains of autistic impairment often occur independently, in the absence of other elements of the syndrome. This raises the possibility that autism is a disorder of multiple underlying impairments, not explicable by one underlying abnormality. Particular impairments may be associated with specific behavioural domains. One domain of interest is 'Insistence on Sameness', an empirically derived, heritable dimension that is a component of the repetitive, stereotyped behaviour element of the autism triad. It has been suggested that executive function difficulties underlie some of the repetitive interests and behaviours seen in autism.

Objectives: We aimed to investigate whether cognitive inflexibility was associated with one specific element of autistic behaviour, insistence on sameness (IS), but not with the other elements of the syndrome. In a general sense, we aimed to test a 'multiple underlying impairments' model of autism.

Methods: Cognitive inflexibility was measured using three tests of set-shifting (The Wisconsin Card Sort Test, the California Trail Making Test

and the Intradimensional/Extradimensional Shift Task) in a sample of 46 young people with an autism spectrum disorder and a verbal IQ in the normal range. IS was measured using a parent-report questionnaire, the Repetitive Behaviour Scale – Revised, and social-communication impairment was quantified using the 3Di, a comprehensive, semi-structured parent interview.

Results: No correlation was found between IS and social-communication impairments. One set-shifting measure (trail making) showed a moderate correlation with IS in the direction predicted when a one-tailed test was used. There was no relationship between this measure of set-shifting and social-communication impairment.

Conclusions:These findings suggest that cognitive inflexibility is associated with greater IS in children with an ASD, but not with social-communication impairments. They offer support for the idea that the social-communication and repetitive behaviour components of autism may represent separate dimensions with distinct underlying susceptibilities.

115 138.9 Memory, Rule, And Arithmetic In Calendar Calculation: What Can We Learn From A Proto-Savant?. M. A. Thioux*[1], C. Klaiman[2] and R. Schultz[3], (1)*University Medical Center Groningen*, (2)*Children's Health Council*, (3)*Yale Child Study Center*

Background: Recently, we proposed that calendar calculation skills could rely on a large fund of memorized date-weekday associations, in combination with some knowledge of the rules of calendars and simple arithmetic. Objectives: One prediction of the model is that it should be possible to find savants who have little knowledge of rules but have already memorized a set of date-weekday associations. Methods: We investigated calendar calculation skills in AVK, a 18 year-old autistic female with a full scale IQ of 90. Calendar calculation tests were designed to assess the patient's ability to name weekdays, and to evaluate her knowledge of calendar rules. Results: AVK was able to name weekdays in a range of 10 years with an accuracy significantly above chance. The number of correct responses was high for the current year and the year when AVK became first interested in calendars, but dropped quickly below chance for years further in the past or in the future. She had very little knowledge of the rules of calendars. She was unable to match years that are 28, 11, or 6 years apart and have the same calendar. She knew the one-year-one-day rule be failed to adjust her calculation in the case of leap years. AVK was also unable to deduce a weekday from knowing the weekday of a date of the same year but of a different month. She showed no evidence of visual memory of calendars as she was unable to match them with a year of the same structure. Conclusions: Savant skills might very well develop with practice. Elsewhere we have predicted that skills don't reach an exceptional level unless dates constitute a restricted area of interest for a significant amount of time. Memorizing date-weekday associations is probably the first step undertaken by young savants.

Keynote Address Program

139 The Broader Autism Phenotype and the new genetics of familial and non-familial autism

Speaker: J. N. Constantino*Washington University School of Medicine*

New discoveries in molecular genetics are changing the landscape of our understanding of the causes of autism. In familial autism, it is common (significantly more so than in the general population) for clinically-unaffected male family members to exhibit features of what is known as the broader autism phenotype (BAP). This may not be true for females or for non-familial autism. The implications of the BAP for understanding the biology of autism are potentially profound. This presentation will cover recent scientific findings on the clinical, genetic, neurobiologic and epidemiologic features of the BAP, how it relates to other autism endophenotypes, and how quantitative characterization of the BAP can aid in the search

for core genetic and neurobiologic components of autistic syndromes.

139.1 Introductory Remarks: Simons Foundation.

139.2 Keynote Address.

Invited Educational Symposia Program

140 Investigating Links Between Autism and the Environment

Organizer: C. Newschaffer*Drexel University School of Public Health*

Speakers: E. Roberts[1]B. Eskenazi[2]I. Hertz-Picciotto[3]A. M. Persico[4](1)*California Department of Public Health*, (2)*University of California Berkeley*, (3)*University of California at Davis*, (4)*Univ. Campus Bio-Medico*

Although it has been known for decades that there is a strong heritable component to autism risk, interest is also now very high in determining whether there are also important environmental risk factors. Momentum behind the search for environmental risk factors has been generated by concern over rising autism prevalence, but other lines of evidence also exist, including consistently observed phenotypic discordance in monozygotic twins and epidemiologic evidence linking rare xenobiotic exposures to autism. The goal of this Invited Education Symposium is to provide an overview of current thinking from the fields of environmental health science, epidemiology, and genetics as it pertains to investigation of potential environmental risk factors for autism. Presenters will review existing evidence, describe current research approaches, and offer informative examples from their own work. Attendees will leave the session with an improved understanding of the rationale behind research on environmental risk factors for autism, a greater sense of the direction of initiatives underway, and an appreciation of the challenges and opportunities that lie ahead.

1 Session Introduction. C. Newschaffer*, *Drexel University School of Public Health*

2 Epidemiologic Designs for Studying Environmental Factors in Autism. I. Hertz-Picciotto*, *University of California at Davis*

Objective: This presentation introduces the various types of epidemiologic study designs that can and have been used in autism research, what we have learned from them, and where the field is heading. The focus is on investigation of environmental factors and the underlying theme is the relevance of neuro-immunomodulatory mechanisms.

Methods: Several designs have been used for epidemiologic research aimed at identification of the environmental determinants of autism. These determinants are either causes or proxies for causes, i.e., factors that contribute to the incidence or severity of autism. The principal designs, their implementation, and their advantages and disadvantages will be discussed, including the ecological study, cohort study and case-control study. Pitfalls in using ecological correlation analyses will be described.

Results: Some retrospective cohort studies have examined existing databases such as medical records or national registries to document both the cases and the exposures of interest. Case-control studies using exposure databases for pesticides or air pollutants have also been employed, as well as population-based specimen banks. Finally, comprehensive case-control studies, such as the CHARGE and SEED studies in which cases are confirmed using standardized instruments, exposure is collected systematically for research purposes, and specimens are obtained for biologic measurements have begun to produce intriguing findings with regard to immune dysregulation and/or pesticides in autism in several studies.

Conclusion: Major weaknesses in much of the existing epidemiologic literature on environmental causes of autism include: reliance on ecological correlation analysis, lack of standardized confirmatory testing of cases, and error-prone exposure assessment methods. Large-scale epidemiologic studies

hold the greatest promise for identification of environmental determinants as well as gene-environment interactions. These prototypic studies are characterized by individual exposure assessment and outcome ascertainment, linked to molecular and other mechanism-oriented methods for analysis of biologic specimens from population-based participants.

3 Importance of a Pathophysiological Foundation To Environmental Research In Autism: On Thimerosal, Vaccines, and More. A. Persico*, *Univ. Campus Bio-Medico*

In recent years, environmental factors have been increasingly perceived as potential contributors to the pathogenesis of autism. On one hand, this has spurred a constructive interest into gene-environment interaction models, yielding a significant amount of experimental and epidemiological data. On the other hand, an oversimplified and at times biased dissemination of these findings has generated misunderstandings, if not even waves of public alarm. For this reason, we emphasize the need for a strong, biologically-based pathophysiological foundation to investigations aimed at elucidating environmental contributions to complex disorders. First, we shall summarize the results of post-mortem brain studies in autism clearly supporting a prenatal origin for this disease. We shall then apply this knowledge to postnatal environmental factors claimed to be involved in autism pathogenesis, focussing on thimerosal and vaccinations. Thimerosal, an ethyl-mercury compound used as a preservative in vaccines, has drawn attention following initial anedoctal reports by some parents linking vaccinations to behavioral regression and to the onset of autism in their child within a matter of days or few weeks. Large retrospective epidemiological studies have excluded that thimerosal may *cause* autism, or provide large-scale contributions to its development. We shall present results suggesting that thimerosal, through its Ca^{2+}-mobilizing effect, could conceivably *precipitate* an abrupt onset in a subset of children who would have anyway developed autistic symptoms, but perhaps more insidiously. Similarly, we shall summarize current data from our group and from others pointing toward analogous roles for vaccine-triggered immune responses, based on current evidence of an ongoing dysreactive autoimmune process in autistic patients. In either case, only evidence-based gene-environment interaction models will be presented, their strengths and limitations will be discussed, and the pathophysiological foundation of candidate environmental pathogens will be elucidated.

4 Relationship of pesticide exposure and pervasive developmental disorder. B. Eskenazi*[1], A. Marks[1], K. Harley[1], K. Kogut[1], C. Johnson[2], A. Bradman[1], N. Holland[1] and D. Barr[3], (1)*University of California Berkeley*, (2)*Private Practice*, (3)*Centers for Disease Control*

"Behavioral teratogens" are chemicals which affect cognitive and behavioral functioning of children due to exposure during fetal or child development. Some have hypoothesized that increases in learning disabilities, attentional deficits, childhood autism and other developmental disorders over the last generation may be due to the use of chemicals in the environment. More than thirty years ago, lead and alcohol were identified as "behavioral teratogens". One other class of chemicals which has been of particular concern is pesticides. Pesticides at high doses are well-known toxins to the nervous system, resulting in numerous poisonings to children and workers every year. Despite animal evidence suggesting neurotoxic effects of lower level exposure to pesticides, few published studies have investigated the neurodevelopmental toxicity of pesticides in humans. We investigated the relation of one important class of pesticides, organophosphates (OP) and the cognitive, motor and behavioral development of children from a low-income Mexican farmworker families in California. These children are participates of the CHAMACOS birth cohort study. We measured metabolites of OP pesticides in urine collected from over 400 mothers twice during pregnancy and from children at the time of their neurodevelopmental assessments. We found that both prenatal and postnatal metabolites were associated with increased odds of maternal report at age two of pervasive developmental disorder. Results were similar when the children were 3.5 years old. Recent evidence suggests that not all individuals are

equially susceptible to effects of pesticide exposure. For example, individuals with certain genotypes (PON1) may be more susceptible to OP pesticide exposure. It has also been hypothesized that these same genotypes may be related to risk for childhood autism. We will examine the inter-relationship of PON1 genotype and related enzyme levels and DAP levels and maternal report of maternal pervasive developmental disorder.

5 Environmental Research on Autism Based on Administrative Data Linkage. E. Roberts*, *California Department of Public Health*

Many of our concerns regarding autism prevalence and epidemiology have arisen from and been addressed through analyses of administrative data, particularly records of social service and educational interventions for children with autism and their families. The linkage of such records to birth certificate files has enabled the estimation of cohort prevalences and provided insight into their temporal trends. The linkage of such records to data describing environmental hazards that may be related to autism can be seen as an extension to this process, yielding information complimentary to clinic-based studies, animal studies, or survey research.

Reliance upon administrative data constrains our ability to verify diagnoses, specify phenotypes, and consider a variety of covariates; it also limits our attention to those environmental hazards for which we have spatially and temporally resolved data. In spite of these limitations, however, advances in Geographic Information Systems (GIS), the spatial and temporal modeling of pollutants, and pharmacokinetics suggest that the validity of data linkages can be expected to increase. With these advances it becomes more likely that environmental epidemiological studies based on data linkage will make contributions to our understanding of autism, particularly in the form of hypothesis generation.

Oral Presentations Program

141 Evoked Response Potentials

141.1 NEURAL CORRELATES OF PERCEPTUAL EXPERTISE IN AUTISM. J. McPartland*[1], C. Bailey[1], R. T. Schultz[2] and A. Klin[1], (1)*Yale Child Study Center*, (2)*Children's Hospital of Philadelphia and the University of Pennsylvania*

Background: Failure to look at people is an early symptom of autism, and individuals with autism exhibit anomalous face recognition, face scanning, and face-related brain activity throughout the lifespan. These deficits have been posited to reflect a lack of expertise resulting from limited social motivation and inattention to faces during development. This hypothesis presupposes an intact capacity for development of perceptual expertise given sufficient attention, interest, and exposure. This notion is difficult to examine because common areas of expertise among individuals with autism are rare. The current study examined brain response to letters of the alphabet as a neurophysiological marker of perceptual expertise.

Objectives: To investigate electrophysiological indices of perceptual expertise for non-social stimuli in individuals with autism.

Methods: High-density event-related potentials (ERPs; 256 channel Geodesic Sensor Net) were recorded from high-functioning adolescents with autism and typically-developing peers matched for age, sex, IQ, and handedness. Participants viewed social and non-social "expert" versus "non-expert" stimuli (human faces versus houses, Roman letters versus pseudoletters). Peak amplitude and latency were extracted for a negative component at 170 milliseconds over lateral posterior scalp (N170).

Results: Typical individuals exhibited enhanced N170 amplitude to both faces (versus houses; right lateralized) and Roman letters (versus pseudoletters; left lateralized), reflecting perceptual expertise for both classes of stimuli. Between-group comparisons indicated atypical ERP response to faces among individuals with autism but comparable response patterns for letters. Analyses in progress will examine correlations among ERP parameters and behavioral measures of letter and face perception.

Conclusions: Results concord with previous studies demonstrating anomalous face-related brain activity in autism. This is the first study to demonstrate intact development of

perceptual expertise for letters in individuals with autism. Results are consistent with the hypothesis that face processing deficits in autism derive from developmental inattention to faces secondary to core impairments in social behavior.

141.2 Children With Autism Show Atypical Early Response to Novel Tactile Stimuli Using Magnetoencephalography (MEG). E. Marco*, K. Khatibi, A. M. Findlay, Z. Zhu, M. Arroyo, S. Vinogradov, H. E. Kirsch, B. Siegel and S. Nagarajan, *University of California, San Francisco*

Background: Children with autism experience sensory processing difficulties which may be at the core of their learning and behavioral deficits. The nature of these deficits, especially in the tactile domain, remains unclear. M50 sensory evoked fields (SEF) collected in response to familiar and novel finger taps reflect the early processing of somatosensory information.
Objectives: This study aims to compare early unimodal cortical processing in children with high functioning autism (AS) and matched healthy controls (HC).
Methods: Responses were recorded for the AS group (N=7, mean age=9.6) and the HC group (N=6, mean age=8.9) using a 275-sensor MEG. The stimuli were pneumatic finger taps (140 ms, ~17 PSI, and ISI 330 ms). Taps to the right index finger (deviant) occurred every 3 -7 taps to the middle finger (standard). The amplitude and latency averages of the M50 were compared between AS and HC for deviant taps, pre-deviant standard taps and post-deviant standard taps.
Results: Reliable parietal M50 was elicited to all tactile stimuli and exhibited a characteristic latency and waveform in the HC group. The HC group demonstrated the expected latency delay and amplitude increase to the deviant stimuli. By contrast, the AS group showed considerable variability in their waveforms, with M50 peak amplitude to deviant stimuli being significantly lower than HC.
Conclusions: Our results suggest an atypical processing of novel tactile information in autism that can be detected as early as the M50 waveform. While this may represent primary sensory cortical dysfunction, we cannot exclude the contribution of disrupted top-down modulation to novel stimuli.

141.3 Audiovisual integration of emotional signals and its interaction with attention in Autism Spectrum Disorder. M. Magnee*[1], B. De Gelder[2], H. Van Engeland[3] and C. Kemner[4], (1)*University Medical Center Utrecht*, (2)*Tilburg University*, (3)*University Medical Center-Utrecht*, (4)*Universiteit Maastricht*

Background: Attentional impairments are among the most consistently reported cognitive deficits in Autism Spectrum Disorders (ASD), and have profound implications for several clinical features of the disorder. Disruptions in the attentional system are particularly explicit in the patient's ability to shift attention between auditory and visual modalities. Several older studies have yielded suggestions that multisensory integration (MSI) is impaired in individuals with ASD. The critical question, however, remains whether anomalous patterns of MSI arise from deficits in specific processes related to integration abilities, or from impairments in attentional capacity.

Objectives: The focus of the present study was on the influence of attention on the integration of emotional visual and auditory information in ASD individuals, using Event-related potentials (ERPs).

Methods: ERPs following emotionally congruent and incongruent face-voice pairs were measured in 23 high-functioning, adult ASD individuals and age- and IQ-matched controls. MSI was studied while attention was directed to both modalities or while participants were either mildly (1D) or heavily (2D) distracted. ERPs to audiovisual stimuli (AV) were compared with the sum of the ERPs to auditory and visual stimuli, measuring low-level MSI. The difference in ERP activity to congruent and incongruent AV stimuli indicated higher-order, or emotion related, MSI.

Results: Low-level MSI was similarly observed in both groups and was shown to be strongest for the fully attended condition. Higher-order MSI was observed most clearly in the fully attended condition, but only for controls. ASD individuals did show higher-order MSI, but

only in the 1D condition. In the 2D condition neither group showed MSI.

Conclusions: ASD individuals are able to process multisensory emotional stimuli on lower as well as higher levels of processing. However, optimal processing occurs while ASD individuals are mildly distracted from the emotion eliciting event. Implications for clinical features of the disorder are discussed.

141.4 Spatial Frequency Processing in 3- and 4-year-olds with Autism Spectrum Disorder (ASD). P. H. J. M. Vlamings* and C. Kemner, *Universiteit Maastricht*

Background: Besides difficulties in social interaction, people with ASD have an atypical visual processing style which is more detail oriented than in typical subjects (Happe and Frith, 2006). This might be explained by abnormal spatial frequency (SF) processing in ASD (Boeschoten et al., 2007). Any input to the visual system consists of luminance variations at various frequencies across space. Low spatial frequencies (LSF) capture large-scale variations (coarse information) whereas high spatial frequencies (HSF) represent small-scale variations (detailed information).

Objectives: In the present study we investigate whether abnormal SF processing is already present in ASD in early childhood and how this is reflected in the brain. We predict faster and/or elevated processing of HSF in ASD.

Methods: Nineteen ASD children (3/4 years) and 21 age matched controls were presented with 90 HSF and 90 LSF gratings, during which EEG was recorded. Diagnosis of ASD was defined as meeting criteria for ASD at the Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview Revised (ADI-R).

Results: Children with ASD showed higher P1 amplitudes for HSF than for LSF, whereas this was not significant in controls. No latency differences between ASD and controls were found for the P1 (positivity at 100 ms) and N2 (negativity at 200 ms) at OZ (electrode above the visual cortex).

Conclusions: In typical adults, amplitude differences between HSF and LSF gratings at the P1 are linked to the involvement of different brain areas for HSF and LSF (Ossenblok & Spekreijse, 1990). The present data suggest that the visual system might be more differentiated and mature at an early age in ASD, as the pattern of larger P1 amplitudes to HSF than LSF gratings is also seen in typical adults.

141.5 Group Differences and Individual Differences in the N170 ERP Component in Autism. C. Hileman*[1], L. C. Newell[2], M. Jaime[1], H. A. Henderson[1] and P. C. Mundy[3], (1)*University of Miami*, (2)*Indiana University of Pennsylvania*, (3)*UC Davis*

Background:

The N170 event related brain potential (ERP) is used as a physiological index to assess face-specific neural processing. Research indicates that the N170 may by atypical in autism.

Objectives:

To examine the N170 in children with high-functioning autism. To examine the relation between the N170 and social behavior and autistic symptomology.

Methods:

27 children with high-functioning autism and 22 children with typical development participated in the study. Participants were fitted with a 128-lead Geodesic sensor net and viewed a slideshow of upright faces, inverted faces, upright vehicles, and inverted vehicles. Six electrodes over the left lateral posterior scalp and over the right lateral posterior scalp were used to identify N170 amplitude and latency.

Results:

There was a significant interaction between diagnostic group and stimulus orientation, $F(1, 45) = 6.46$, $p = 0.15$, and a marginal interaction between diagnostic group and stimulus type, $F(1, 45) = 3.50$, $p = 0.68$, on N170 amplitude. Children with typical development differentiated between stimulus orientation and type to a greater extent than children with autism. There was a main effect

of diagnostic group on N170 latency,$F(1, 45) = 6.16$, $p = 0.17$, such that children with autism had longer N170 latencies than children with typical development. For both groups, there was no relation between N170 and social behavior and autistic symptomology.

Conclusions:

Children with autism seem to approach all stimuli with a steady level of interest and mental processing, while children with typical development almost immediately adjust their level of interest and mental processing to match stimulus meaning. The delayed N170 latency in autism may be caused by cortical underconnectivity. Finally, the lack of a relation between N170 and social behavior and autistic symptomology was surprising, given that face processing has been hypothesized to be a primary deficit in autism.

141.6 MEG Investigations of Neural Synchrony: Speech Sound Processing in Children with Autistic Disorder, their Unaffected Siblings, and Typically Developing Controls. A. L. Isenberg*, M. A. Spence and N. M. Gage, *University of California, Irvine*

Background: Recent research has implicated impaired neural synchrony in autistic disorder (AD) as a key mechanism underlying reduced abilities to integrate sensory information into coherent representations. Speech processing and language acquisition rely critically on the exquisite temporal resolution of the auditory system. In healthy adults, latency of the M100 as detected by MEG, is closely coupled in time (<20ms) in left (LH) and right hemispheres (RH), with LH latency typically peaking slightly later than RH. Although the neural bases remain unknown, it is observed in response to both speech and non-speech sounds. Far less is known about the temporal coupling of M100 in LH and RH in typical development and language disorders, such as autism.

Objectives: To assess neural synchrony in cortical processing of natural speech tokens in children with AD.

Methods: We measured M100 latency in typically developing children (TD, N=9), children with AD (N=15), and their unaffected siblings (SIB, N=8) in response to natural speech tokens: consonant-vowel (CVs) syllables that differ in distinctive features: place of articulation, voice onset time or both. Difference in LH-RH M100 time-to-peak (offset) was examined by computing absolute M100 latency differences and by calculating a laterality index (LI) ([2(L-R)/(L+R)].

Results: TD mean absolute offsets ranged 0-46ms. AD mean absolute offsets ranged 0-98ms. SIB: mean absolute offsets ranged 0-53ms. Greater variability is seen in offsets for AD compared to TD and SIB. SIB have greater offset than TD. TD and SIB LIs were leftward for voiced CVs and rightward for unvoiced. AD LIs were leftward for all conditions.

Conclusions: TD hemisphere asymmetries are greater than adults and may reflect slow-to-mature cortical processes. Greater asymmetries in children with AD provide evidence for poor neural synchrony in cortical processes underlying speech perception. Unaffected siblings show greater hemisphere asymmetries than TD, but smaller than their AD siblings.

141.7 N400 Responses to Final Words during Sentence Reading in Individuals with Autism: A MEG Study. B. Ahtam*, S. Braeutigam and A. Bailey, *University of Oxford*

Background: Individuals with autism are impaired in spontaneously making use of sentence context to decide on the correct pronunciation of words with several meanings; a finding in line with the weak central coherence theory.

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

Methods: 14 individuals with ASD and 14 typically developing adults participated in the study. Participants were matched on age, gender, and IQ. All measurements were taken at the Oxford Neurodevelopmental Magnetoencephalography Centre using a Neuromag-306 VectorView™ system, providing a helmet-shaped array of 102 pairs of gradiometers. Participants read sentences ending either with a homonym (dominant vs.

subordinate meanings) or an unambiguous word. The sentences were followed by a probe word that was semantically related or unrelated to the meaning of the sentence. This study has been approved by the local NHS (UK) Ethics Committee. All participants gave written informed consent before the experiment.

Results: At 100ms, the responses to all three types of final words are very similar in both groups and consistent with the primary visual response. The word response at 150ms is weakest in the subordinate homonym condition in the ASD group. At 450ms latency, a stronger parietal activation of N400-like responses in all three conditions is seen in the ASD group compared to the control group.

Conclusions: These results suggest that the initial stages of word processing in ASD exhibit typical patterns. The strong N4 activity in ASD may indicate unusual word processing above that required by task demands and consistent with current models of anomalous semantic networks in ASD.

141.8 ABNORMAL AUDITORY INFORMATION PROCESSING IN YOUNG CHILDREN WITH AUTISM. F. C. L. Donkers*[1], O. Van der stelt[2], N. Lucena[1], J. E. Lorenzi[1], G. T. Baranek[1] and A. Belger[1], (1)*University of North Carolina at Chapel Hill*, (2)*Otto-von-Guericke University*

Background: Atypical responses to sensory stimuli, particularly in the auditory modality, have often been observed clinically as associated features in many children and adults with autism (Gilberg and Coleman, 2000; Waterhouse et al., 1996). Behavioral responses to auditory stimuli range from completely ignoring sounds to acoustic hypersensitivity. Although impaired auditory processing in children with autism is prominent and likely compromises the development of cognitive functions, particularly speech and language, the unusual sensitivity to sounds in these children has been sparsely investigated.

Objectives: To analyze scalp-recorded event-related brain potentials (ERPs) to index the sensory, perceptual, and cognitive processing of auditory information in children with autism.

Methods: Children (ages 4-8) who met research criteria for autism were compared with normally developing children. ERPs were collected using a "passive-ignore" auditory paradigm in which the children are watching a cartoon at a low volume setting and are presented with rapid sequences of auditory stimuli, consisting of infrequent deviant tones, unique environmental sounds and frequent standard tones. This paradigm allowed us to investigate: (1) the P1, which is associated with initial sensory detection; (2) the 'mismatch negativity' (MMN), which is associated with pre-attentive sensory discrimination; and (3) the P3a, which is associated with orienting and attention-dependent cognitive discrimination.

Results: Preliminary analyses on 16 children suggest group differences are primarily found in the P1 and MMN and to a lesser degree in the P3a.

Conclusions: Children with autism exhibit abnormalities in early processing of sounds as well as in pre-attentive discrimination of sounds but not in orienting and attention-dependent discrimination of sounds. Future study plans include the recruitment of 35 children with autism, 20 developmentally delayed controls and 30 normally developing controls in order to further characterize the relationships between EEG/ERP abnormalities and various measures including, IQ, autism symptom severity, and sensory response patterns.

Oral Presentations Program

142 Cognition 2

142.1 Can Executive Failure Explain the Social Symptoms of Autism?. S. White*[1], E. Hill[2] and U. Frith[1], (1)*University College London*, (2)*Goldsmiths, University of London*

Background: While both mentalising and executive impairments have received support as causal theories of autism and these impairments appear to be related in autism, it is still unclear why they are associated and how they relate to the social impairments seen in autism.

Objectives: To explore the relationship between mentalising and executive impairments and their causal roles in the social symptoms of autism.

Methods: 57 children with ASD were compared to 27 normally-developing 7-12 year olds on a battery of tasks assessing verbal and non-verbal intelligence, mentalising abilities and executive dysfunction. The children also took part in direct and indirect measures of their everyday behavioural symptoms.

Results: Group differences were found on all mentalising and some executive tasks; approximately half of the children with ASD showed severe impairment in mentalising and a third in executive function. As expected, mentalising and verbal ability were highly associated within both groups, while mentalising and executive function were related only in the autism group. An additional surprising association between executive function and verbal ability was present in the autism group but this could not account for the relationship between mentalising and executive function. There was a tendency for children to display: mentalising and executive impairment, just mentalising impairment, or neither. The behavioural data indicated associations only between mentalising and social skills.

Conclusions: This pattern of results may indicate that executive failure is primary to mentalising difficulties. However, an alternative explanation could be that poor executive *task performance* might emerge from poor mentalising ability, which would also lead to impaired social skill. Indeed, an analysis of the errors made in the executive tasks revealed an unusual pattern of idiosyncratic or egocentric performance and suggested that impaired performance on executive *tasks* may result from difficulties forming an implicit understanding of the experimenter's expectations for the task.

142.2 Perception of Physical and Social Contingencies in Infants with Autism. D. Lin*, G. Ramsay, W. Jones and A. Klin, *Yale School of Medicine*

Background: Recent studies examining visual fixation in infants with autism spectrum disorders (ASD) revealed that their viewing patterns appeared to be driven by physical contingencies present in the stimuli rather than by social contingencies implicit in the scenes. These results suggest the hypothesis that infants with autism may perceive the world around them, and specifically the faces of people, as a collection of physical properties detached from their social context.

Objectives: The goal of the current project is to (1) assess the sensitivity of infants with ASD to audiovisual synchrony, a specific physical contingency, and (2) measure the effect of biasing social context on the perception of audiovisual synchrony in infants with ASD.

Methods: 12-24 month-old infants with ASD, typically-developing (TD) infants, and non-autistic development-delayed (DD) infants were eye-tracked while presented with a series of preferential viewing experiments. The first series of experiments tested baseline sensitivities to audiovisual synchrony. The second series of experiments tested how sensitivities to audiovisual synchrony were altered when biasing social contexts (faces and human speech) were introduced.

Results: Preliminary results show that infants with autism are as sensitive as their peers to the perception of audiovisual synchrony. However, audiovisual synchrony detection in infants with autism is less influenced by accompanying social context: while the introduction of biasing social context altered the preferential viewing patterns of TD and DD controls, the change in contextual information did not alter the viewing patterns of the infants with ASD.

Conclusions: The present study suggests that, although infants with autism are capable of integrating auditory and visual information when perceiving physical contingencies, their ability to perceive social contingencies may be impaired. Closer examination of the neurobiological mechanisms underlying perception of audiovisual synchrony may further efforts at early diagnosis and treatment of autism.

142.3 Reduced top-down modulation in autism: The role of prior knowledge in the

visual perception of fragmented pictures. E. Loth*[1] and F. Happé[2], (1)*University of Cambridge*, (2)*Institute of Psychiatry, Kings College London*

Background:

It has been suggested that the cognitive profile of Autism Spectrum Conditions (ASC) involves reduced top-down processes; abnormalities in using prior knowledge and past experience in modulating cognitive processes (Frith, 2003). In previous studies we showed diminished use of prior knowledge in modulating attention, memory, and aspects of face perception in high-functioning individuals with ASC. Here we investigated the effect of prior knowledge on the visual perception of fragmented pictures (faces, objects). Past research has shown that in typical development, this process is achieved by an interaction between face/ object-specific processes and higher-level processes of attention, memory, and mental imagery (Dolan et al., 1997).

Objectives:

We tested the alternative hypotheses that in people with ASC, perceptual learning may be overall reduced, or, given known abnormalities in face processing, that perceptual learning may be specifically reduced for faces.

Methods:

Participants were shown fragmented images of faces and objects before and after they were shown the corresponding black-and-white image. When first seen, the fragments look like random blobs but after having seen the real photographs, TD viewers can easily recognize the blobs as, for example, a face. Using eye-tracking technology, we also studied differences in visual fixations on the face/ object versus background between the pre- and post-learning phases. Twelve individuals with high-functioning ASC and 12 TD individuals, matched in terms of age and ability levels, took part in this study.

Results: Both groups recognized significantly more faces and objects after having seen the corresponding image. However, in the ASD group, the perceptual learning effect was significantly reduced only for the face stimuli.

Conclusions: Our data suggest reduced influence of prior experience on visual perception of social stimuli. We discuss our findings in the context of the hypothesis of reduced top-down modulations and implications for potential abnormalities at the neuro-functional level.

142.4 Failure On Task-Switching Performance In ASD Depends On Working Memory And Not Attentional Shifting. B. López*[1] and G. Stoet[2], (1)*University of the West of England*, (2)*University of Leeds*

Background: People with autism suffer from impaired executive functions. There are various executive functions (e.g., mental flexibility and inhibitory control) but all are not equally affected in autism, possibly because these different functions are implemented in different brain circuits. More research is necessary to characterize which executive functions are affected most, which are intact, and, possibly, which are superior.

Objectives: We aim to refine our understanding of executive impairments in children with autism. We used the task-switching paradigm, which offers a good assessment of executive functions, in particular of the skill to switch attention between tasks, and the skill to inhibit irrelevant information.

Methods: Two versions of a task-switching paradigm were used. The first version administered was a standard cued task-switching paradigm. The second version used was an easier version which does not rely strongly on working memory.

Results: The ASD group performed poorly in the standard task-switching paradigm, with several children working at chance level. However, in the low-memory load version of the task, they performed more accurately than typically developed adults (TDA), and relative switch costs were smaller (marginally significant: p=.51). Further, in the low-memory version, inhibition of irrelevant

stimulus information was similar in both groups.

Conclusions: Children with ASD have intact skills of rapidly switching task between rules and inhibiting irrelevant stimulus features, as long as this switching does not require the use of working memory. As soon as it does, the children fail. This indicates that problems with working memory may help to explain, at least shifting difficulty in autism, if not other various executive deficits. At the same time, the finding of better performance than TD adults in the low-memory condition suggests that the task-switching paradigm is useful for studying the savant skills observed in about 10% of children with autism.

142.5 Altered face scanning and impaired recognition of biological motion in 2-year-olds with autism. A. Klin*[1] and W. Jones[2], (1)*Yale Child Study Center*, (2)*Yale School of Medicine*

Background: Preferential attention to the eyes of others and the ability to perceive motion tied to a biological context are early emerging and highly conserved social behaviors. Here we build on findings on two older cohorts to study these basic mechanisms of socialization in toddlers with ASD.

Objectives: To quantify preferential attention to the eyes of others (first study) and processing of biological motion (second study) at what is presently the earliest point of diagnosis.

Methods: Participants were toddlers with ASD well matched on nonverbal mental age to typically developing toddlers, and on verbal mental age to non-autistic developmentally delayed toddlers. We presented them with 10 videos showing a female actor playing the role of caregiver (first study), and with 5 sets of point-light social animations each presented in right-side up and inverted forms side by side in a half-screen format (second study). Visual fixation patterns and preferential viewing were measured by eye-tracking.

Results: First study: Looking at the eyes of others was significantly decreased ($p<.001$) while looking at mouths was increased ($p<.1$) in toddlers with ASD relative to controls. Less fixation on eyes predicted greater social disability ($r= -.669$, $p<.1$). Second study: Toddlers with ASD lacked preferential sensitivity to upright point-light animations relative to both control groups ($p<.0001$). Further, 90% of the viewing behavior of toddlers with ASD could be accounted for in terms of their acute sensitivity to normally unprocessed audiovisual synchronies between point-light movements and the speech sounds of the accompanying audio.

Conclusions:

The combined results suggest that toddlers with ASD view social action as a composite of physical (not social) contingencies since the mouth region of the face contains maximal episodes of purely physical contingencies: the synchronous occurrences of mouth movements and speech sounds. Implications for subsequent neuroplastic specialization of the social brain are discussed.

142.6 Impaired Disengagement and its Relationship to Temperament in Infants at High Risk for ASD. S. E. Bryson*[1], N. Garon[2], J. Brian[3], I. M. Smith[1], T. McCormick[2], W. Roberts[4], P. Szatmari[5] and L. Zwaigenbaum[6], (1)*Dalhousie University*, (2)*IWK Health Centre*, (3)*Hospital for Sick Children, and Bloorview Kids Rehab*, (4)*University of Toronto*, (5)*Offord Centre for Child Studies, McMaster University*, (6)*University of Alberta*

Background: Young children with ASD have difficulty disengaging visual attention from one of two competing stimuli (Landry & Bryson, 2004), but little is known about the early emergence or underlying mechanisms of this impairment.

Objectives: To determine whether impaired disengagement distinguishes ASD in high-risk infants, and whether this impairment is associated with the Behavioural Approach dimension of temperament (Rothbart & Bates, 1998).

Methods: Participants were recruited from our prospective study of high-risk infants with an older sibling with ASD, and low-risk controls with no family history of ASD. Infants were assessed on a visual orienting paradigm at 6 and 12 months of age, and their parents completed the Infant Behavor Quesionnaire at

12 months. An independent diagnositc assessment for ASD was conducted at 36 months of age, yielding 3 groups: ASD sibs (n=14), non-ASD sibs (n=43) and controls (n=44).

Results: A repeated measures ANOVA conducted on reaction times (RTs) to disengage and shift attention revealed a significant Group X Attention Condition X Side interaction, $F(2, 98)=3.77$, $p<.3$. At 12 (vs. 6) months, infants who were subsequently diagnosed with ASD were distinguished from non-ASD sibs and controls by significantly longer disengage RTs on the left than on the right side of space. No significant left-right RT differences were found for either the non-ASD sibs or controls. Left-right asymmetries in disengaging visual attention were significantly related to low Behavioural Approach in both the ASD sibs ($r=.49$, $p=.6$) and non-ASD sibs ($r=.41$, $p=.003$).

Conclusions: Our finding that asymmetries in disengaging attention distinguish ASD at 12 but not 6 months implicates dysfunction of frontal or executive control of attention (Johnson, 1996). This asymmetry, and its relationship to low Behavioural Approach, is consistent with evidence of right cortical asymmetry in a subgroup with ASD (Mundly et al., 2007; Sutton et al., 2005).

142.7 Impaired Face Recognition in Parents and Siblings of Children with ASD: a Differential Sex Effect. D. H. Skuse, G. Salter and A. Seigal*, *Institute of Child Health*

Background: The heterogeneity of the phenotype suggests that autism has a multigenic aetiology. Our understanding of the complex multigenic aetiology of autistic spectrum disorders (ASD) may be increased by family studies of the broader autism phenotype, measured at the level of heritable endophenotypic variation in specific cognitive skills.
Objectives: Our objective was to identify heritable markers of genetic susceptibility among families containing a single child with an ASD. We aimed to use standardized measures of cognitive function in the social domain, which had been developed from studies of the general population and which would be applicable to both children and adults. Our focus was on potential X-linked genes that confer vulnerability to males.
Methods: All participants were tested on a standardized task of face recognition memory. Case families (82 autistic probands, 179 parents, and 67 siblings) were closely matched to population controls, and to a second comparison group of women with X-monosomy (Turner syndrome) which is associated with autistic behaviours. Families with an autistic child and X-monosomic females were assessed for autistic traits by self-report. The second comparison group comprised 151 adult females with X-monosomy, of similar verbal IQ to control females. Results: Autistic probands, their mothers and brothers showed a significant deficit in face recognition memory, compared to controls. In X-monosomic females face recognition memory was much poorer than in population control females.
Conclusions:This is the first study to find evidence for an autism-related endophenotype that is present in mothers, their male autistic offspring and brothers of those offspring, but which is less evident in fathers and absent in female siblings. We present preliminary evidence pointing to inheritance of a genetic risk for face-recognition memory that is X-linked.

142.8 Are ADHD Traits Dissociable From the Autistic Profile? Links Between Cognition and Behaviour. C. Ames*[1] and S. White[2], (1)*Social, Genetic and Developmental Psychiatry Centre*, (2)*University College London*

Background: Autism and ADHD appear to show a degree of behavioural, cognitive and genetic overlap. It is not clear whether these are co-occurring disorders or whether they share some neural and cognitive features which lead to similarities in behavioural profiles.

Objectives:To identify the presence of ADHD related behaviours in a sample of children with ASD, and their relationship with the ASD triad of impairments symptoms and related cognitive impairments.

Methods: A semi-structured interview (3Di) elicited parental reports of ASD and ADHD symptoms. Children (n = 53) completed a

comprehensive battery of cognitive assessment.

Results: 90% of children were reported to display significant levels of hyperactivity, impulsivity or inattention. Only one child showed above threshold levels of each ADHD component.

ADHD traits were significantly related to the ASD triad. Social interaction correlated with both hyperactivity and impulsivity. Communication correlated with inattention, hyperactivity and impulsivity. Repetitive behaviours correlated with impulsivity.

Previous research into inhibitory control deficits has produced inconsistent results, and indeed, inhibitory control in this study did not correlate with any component of the ASD triad of impairments. However, a measure of inhibitory control was found to be related to hyperactivity. In contrast, while there was a relationship between autistic symptomatology and theory of mind ability there was no such relationship with behaviours related to ADHD.

Conclusions: Parents reported significant levels of ADHD related behaviours in this group of children with ASD. These behaviours co-occurred with increasing severity of ASD. However, the relationship between cognition and behaviour varies between these traits of ASD and ADHD, suggesting that ASD and ADHD have a degree of shared cognitive underpinning.

Poster Presentations Program

143 Services Posters 2

1 143.1 IMPACT OF AUTISM INTERVENTION INSTRUCTION ON TEACHER PRACTICE. L. H. Sullivan*[1], A. Mastergeorge[1], K. Jennifer[1] and P. Schetter[2], (1)*University of California, Davis*, (2)*Autism and Behavior Training Associates*

Background: Classroom-based autism intervention programs are not commonly examined for fidelity of implementation. It is important to consider the impact these programs have on both classroom practice and student outcomes.
Objectives: This study examines an intervention program comprised of specific strategies and current research for teachers working with students with autism spectrum disorders (ASD). Data from self-competency ratings and knowledge of ASD were utilized to determine the effectiveness of the intervention. In-depth interviews were conducted with participants to understand how interventions are applied in classroom environments. Interviews examined the successes and challenges that arose during implementation of the ASD teaching principles in the classroom.
Methods: 162 teachers from five cohorts participated in the study. All participants had completed an intensive autism training course which covered best practices in ASD interventions, data collection techniques, understanding current research in the field, and applied behavioral analysis strategies. Data was collected in four areas (pre and post intervention): test scores, self-competency and knowledge ratings, demographic data, and interviews.
Results: Analyses indicate significant increases in competency and knowledge following the training program. ANOVA analyses showed significant trends in years of experience teachers had working with ASD students as well as the types and number of strategies implemented in the classroom. Interviews revealed that increased knowledge of current research on ASD influenced the quality of interactions with students, parents and other educators. Prevalent challenges emerged in the areas of time, resources, levels of support, and data collection. In addition, themes for challenges and successes of classroom implementation were delineated.
Conclusions: Classroom intervention training has important implications for teachers of students with ASD. Increases in knowledge and competency in autism appears to augment teacher preparation in academic and social support areas, and contributes overall to the developmental and academic outcomes of ASD students.

2 143.2 Research to Real World: Effective Dissemination of Evidence-Based Practice to Community Programs for Children with Autism

Spectrum Disorders. S. Dufek*[1], L. Schreibman[1] and A. Stahmer[2], (1)*University of California, San Diego*, (2)*Rady Children's Hospital*

Background:
Parents of children with autism and community Autism Service Providers (ASPs) are faced with difficult decisions about which interventions to include in early intervention programs and how those interventions should be implemented (Anderson & Romanczyk, 1999; Guralnick, 1998; Ramey & Ramey, 1998; Schreibman, 2005). Unfortunately, the field of autism suffers from a lack of effective dissemination of evidence-based practices (EBPs), a common malady experienced by other fields related to treatment of medical and psychological disorders (Matson et al., 1996).
Objectives:
Utilize data from other fields to provide recommendations for effective dissemination of EBPs into the autism practice community.
Methods:
This presentation reviews data from various fields (i.e., medicine, education, substance abuse, general child and adult mental health) and develops recommendations to address lack of EBP dissemination in autism.
Results:
Three main components of EBP dissemination discussed in the literature are: 1) knowledge transfer, 2) implementation, and 3) compliance. These techniques are not currently utilized effectively by autism treatment researchers (Barwick et al, 2005; Stahmer et al., 2005; Ruef et al., 1995). The literature review uncovered many innovative techniques from other fields that may be adapted to develop effective dissemination strategies for autism researchers, program administrators, policy makers, and ASPs. Specific strategies will be examined and adaptations recommended.
Conclusions:
Dissemination of EBP for children with autism has been identified by the NIH as a critical area of focus. Without successful dissemination of EBP into the autism practice community, researchers and ASPs are not likely to help the children to whom their efforts are targeted. In order to be disseminated effectively, EBPs have to be acceptable, useful, and also travel accurately from one autism stakeholder group to another. Examination of the components related to effective dissemination of EBP can inform stakeholders about how, when, and what techniques should be utilized.

3 143.3 Access to substance abuse treatment among adults with and without autism. E. M. Slayter*, *Salem State College*

Background: Little is known about substance abuse (SA) among people with diagnoses of autism – a population that has experienced increasing levels of community inclusion over the past forty years – a freedom which has facilitated access to alcohol and drugs and the potential for developing SA disorders.
Objectives: Given documented barriers to accessing SA treatment among many populations with disabilities, this study expands knowledge of SA treatment utilization patterns among people with autism.
Methods: This study utilizes standardized performance measures designed by a team of clinicians and health services researchers to measure SA treatment utilization (operationalized as treatment initiation and engagement). Utilization rates are examined retrospectively for people with and without diagnoses of autism (operationalized through the use of the ICD-9-CM diagnostic code 299, childhood psychosis disorder) among the population of low-income people with Medicaid coverage in the United States in 1999. Beneficiaries with autism (N=664) are compared with a random sample of their counterparts without autism (N=700) in logistic regression modeling guided by Ronald Andersen's sociobehavioral model of healthcare utilization. This model assesses the impact of autism on SA treatment utilization while controlling for predisposing characteristics, enabling resources and need factors.
Results: 25.8 percent of people with autism initiated SA treatment while only 45.2 percent engaged in SA treatment. Multivariate logistic regression modeling suggests that while people with autism were equally likely to access SA treatment as compared to people without autism, they were less likely to engage in SA treatment (adjusted odds ratio=0.53***). People with autism and co-

occurring diagnoses of schizophrenia were less likely to initiate SA treatment than were their counterparts (OR=0.51**).
Conclusions: Clinical practice implications relate to needed improvements in behavioral health care for people with autism through cross-system collaboration and the use of integrated treatment approaches.

4 143.4 Comparison of the Original and Revised ADOS Algorithms in a Children's Community Mental Health Clinic. C. Roncadin*[1], S. Berry[1], W. Roberts[2], J. Brian[2] and L. Zwaigenbaum[3], (1)*Peel Children's Centre*, (2)*Hospital for Sick Children*, (3)*University of Alberta*

Background: As the incidence of ASDs has increased, so have referrals for diagnostic assessment in our children's community mental health clinic. Beginning in 2006, children with suspected ASD have been assessed using the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000), which has been scored using the original and revised (Gotham et al., 2006) algorithms.

Objectives: In a community-based clinic, to examine how the original and revised ADOS algorithms compare in the classification of children relative to contemporaneous clinical diagnoses, and to compare the new ADOS module divisions.

Methods: Since 2006, ten consecutive referrals for suspected ASD were seen for diagnostic assessment. Diagnosis was based on clinical best judgement by an experienced clinician using DSM-IV criteria, a structured diagnostic interview, and the ADOS. Clinical diagnosis was independent of ADOS scores. Children ranged in age from 3 to 10 years (nonverbal IQ > 70, with at least single words).

Results: There was 60% agreement between clinical diagnosis (ASD vs. Non-ASD) and the original algorithm, but it increased to 90% with the revised algorithm. Sensitivity was 63% for the original algorithm, whereas it was 100% for the revised algorithm. Specificity was 67% for both algorithms. Further comparison of the revised algorithm to clinical diagnosis (Autism vs. ASD vs. Non-ASD) revealed 100% congruence for Module 1–Some Words, Module 2–Younger, and Module 3, but only 50% for Module 2–Older. The noncongruent cases included one child with ASD whose high RRB score put him into the Autism range, and another child with ADHD, ODD, and LD who had sub-threshold ADI-R scores despite being in the Autism range on the ADOS.

Conclusions: These preliminary data suggest that the revised ADOS algorithm may show better agreement than the original algorithm with contemporaneous clinical diagnosis in our community-based clinic.

5 143.5 Identification of Children with Autism Spectrum Disorders (ASDs) by the Ages and Stages Questionnaires (ASQ). R. Nickel*[1], K. Murphy[2], K. Grant[1] and J. Squires[2], (1)*Child Development and Rehabilitation Center, Oregon Health & Science University*, (2)*University of Oregon*

Background: Several targeted screens for autism have been developed for use by primary care providers (PCPs), and American Academy of Pediatrics' guidelines recommend use of a targeted screen at 18 months. PCPs, however, do not use developmental screens regularly in their practices, have little familiarity with autism screens, and are unlikely to add a second formal screening test to well child visits.

Objectives: Determine the accuracy of a general developmental screen, the ASQ, in identifying children with ASD in a referral sample.

Methods: Ongoing chart review of children 1-5 years of age who received a diagnosis of an ASD based on comprehensive evaluation including developmental assessment, ADOS and structured autism interview. The Ages & Stages Questionnaire (ASQ), a parent-completed developmental screen, was completed by parents just prior to the autism or child development clinic appointment. The ASQ, a series of questionnaires for children 4-60 months of age, contains questions on adaptive, communication, gross motor, fine motor and personal-social skills.

Results: 48 children had an ASD diagnosis and ASQ data, 13.5 to 51 months of age. 83% of children had autism, 17% other ASD, and 90% DQ <70. All of the children failed one or more areas on the ASQ; 95.8% failed the communication section; 87.5% personal-social and 83.3% problem solving. A typical pattern on the ASQ for young children with ASD appeared to be delays in all skill areas except for passes in gross and/or fine motor skills.

Conclusions: This study reports preliminary data that a developmental screen, the ASQ, has high sensitivity in the identification of children with ASD. Limitations of this study are the referral sample, small sample size, few high-functioning children with ASD and few children ≤ 2 years of age.

6 143.6 Symptom diversity, level, and frequency in children with autism spectrum disorder as predictors of maternal well-being. N. Ekas* and T. L. Whitman, *University of Notre Dame*

Background: Previous studies have reported that autism-related symptomatology can impact maternal stress, depression, affect, and well-being. However, these factors have not been investigated together in the same study to determine the best predictor of maternal outcomes.

Objectives: To investigate the role of autism symptom diversity, level, and frequency as predictors of maternal functioning, including stress, depression, general affect, and well-being.

Methods: Participants consisted of 123 mothers with a child with autism spectrum disorder. Mothers completed the following questionnaires: Parenting Stress Index (PSI), Center for Epidemiological Studies – Depression Scale (CES-D), Psychological Well-Being (Environmental Mastery, Purpose in Life, and Personal Growth scales), Positive and Negative Affect Scales (PANAS), Satisfaction with Life (SWL), Childhood Autism Rating Scale (CARS), and Autism Severity Index (ASI).

Results: Together, symptom diversity, level, and frequency significantly predict maternal stress, depression, life satisfaction, environmental mastery, and negative affect. Hierarchical regression analyses were conducted to determine which aspect of symptomatology was a better predictor of maternal outcomes. Preliminary results show that symptom frequency significantly predicted maternal stress (R2 change=15.7%, B=.898, $p < .001$), depression (R2 change=3.5%, B=.214, $p = .5$), environmental mastery (R2 change=5.3%, B=-.248, $p < .5$), life satisfaction (R2 change=5.6%, B=-.186, $p < .5$), and negative affect (R2 change=8.4%, B=.216, $p < .001$) controlling for symptom level and diversity.

Conclusions: Findings confirm that autism symptom severity predicts stress, depression, negative affect, and well-being among mothers of children with autism spectrum disorder. However, it is the frequency of symptoms as opposed to the number or level of symptoms that is a better, as well as unique, predictor of maternal outcomes. These findings suggest that interventions need to focus on not only symptom type and intensity, but also frequency of symptom occurrence when developing interventions to promote successful family outcomes.

7 143.7 Identity and disability-understanding of children who have a sibling with Autism. S. Takura*, *Nagoya University*

Background: Children who have a sibling with disability tend to have lower self esteem or adjustment problems. The purpose of this study was to reveal an effect on the program for children who have a sibling with Autism. The program was focused on their understanding of themselves and sibling's disability.

Objectives: The participants were 6-13 years old (8 boys and 11 girls). Their siblings were diagnosed with Autism and belong to the Asperger and the LD society.

Methods: Childrenspent 5 days on Himaka island of Japan in August, 2007. The program was composed with self-understanding, disability understanding program and marine education, such as swimming, crab fishing and so on. Their behaviors in the activities and

sentences of daily questionnaire were evaluated by a coordinator and 5 staff of the program.

Results: After the program, they could notice their strong points and weak points as well as those of sibling's. Also they could understand common characteristics among each sibling with Autism and verbally express their anxiety and anger when they had spent with their siblings. Moreover, some could recognize sibling's uniqueness and differences from other participant's relations as strength. Also marine education promotes communication between children and effectively works as pleasure.

Conclusions:The program encouraged participant's understanding of themselves and sibling's characteristics. Using marine education, it provided more chances to communicate with children in similar situations. It made it easier for them to openly talk about their feelings and discuss the answers when they get into quarrels with their kin. However, we could not reveal consistent effects of this program. It is important to follow children in regular meetings and sophisticate the program which can provide result at various settings.

8 143.8 An Evaluation of a Resource Book for Parents of Children Newly Diagnosed with Autism Spectrum Disorder. J. Mulligan*, D. B. Nicholas, L. Steel and R. MacCulloch, *The Hospital for Sick Children*

Background: For parents of a child with Autism Spectrum Disorder (ASD), the uncertainty surrounding diagnosis combined with the emotional distress related to coping with their child's symptoms can make diagnosis a uniquely stressful experience for parents.

Objectives: This study sought to evaluate a newly published information book for parents of children diagnosed with ASD. The book, entitled, *"Autism Spectrum Disorder: Information for Parents",* was developed in 2003 at The Hospital for Sick Children, Child Development Centre (CDC).
Methods: This study involved (1) a review of the educational book by parents and autism service providers and (2) participation in a 2 hour focus group session. A purposive sample of 13 participants were invited to review the parent information book and participate in one of three follow-up focus group discussions where they were asked their opinions about the content, usefulness and accessibility of the booklet.
Results: The feedback from these focus groups suggests that parents and autism service providers are currently in need of a concise yet comprehensive psycho-educational resource at the time of diagnosis. Feedback found the booklet to be useful, accessible and - most importantly for parents - warm, friendly and hopeful in tone. In addition, parents expressed a substantial need for more guidance and information regarding resources for their child than they are currently receiving.
Conclusions: Interventions tailored to the specific needs of parents during the diagnostic process are lacking. Based on the findings of these focus groups, the application of a concise and hopeful psycho-educational resource at the time of diagnosis such as this booklet should be considered a useful and helpful intervention.

9 143.9 Rising autism trends in an Indian inpatient population- a pilot study. M. Prabhuswamy*[1], R. Jairam[2], S. Srinath[1], S. Girimaji[1] and S. Seshadri[1], (1)*National Institute of Mental Health and Neuro Sciences (NIMHANS)*, (2)*Gna Ka Lun, Campbelltown Hospital*

Background: Global literature suggests concerns in rising trends of autism spectrum disorders (ASD).

Objectives: This study aims at comparing the diagnostic profiles of inpatients in an Indian tertiary child and adolescent psychiatric unit over three decades.

Methods: Data from the inpatient Child and Adolescent psychiatry (CAP) unit at the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India were used for descriptive analyses of the diagnosed psychiatric disorders during the years 1987, 1996 and 2002. Changes over

time in rates of diagnosis of ASD, attention deficit hyperactivity disorder (ADHD), and other disorders were examined and compared.

Results: During the years 1987, 1996 and 2002 there were 160, 143 and 309 new admissions respectively. The most common diagnoses were ASD, ADHD, dissociative disorder, bipolar disorder, psychoses and depressive disorders. The diagnosis rates of ASD had increased by eight-fold and that of ADHD had doubled.

Conclusions: Over the decades the biggest change has been the increase in the number of children admitted with ASD and ADHD. The reasons for the same could be a true increase in the prevalence of these disorders, increased community awareness and/ or a change in the admission policy and referral pattern of the CAP unit.

10 143.10 How do families face the disclosure of an autism diagnosis? A pilot survey among families of children with autism spectrum disorder. T. Miyachi*[1], M. Kamiya[2], Y. Yoshihashi[1] and M. Tsujii[1], (1)*Osaka-Hamamatsu Joint Center for Child Mental Development*, (2)*Osaka-hamamatsu Joint Center for Child Mental Development*

Background: Most families of a child with autism spectrum disorder (ASD) have difficulty accepting the diagnosis when they are first faced with it. Although acceptance is inherently taken for granted among the professionals, studies in the West have reported that some families must undergo an extended process toward acceptance, which in turn is regarded as having a negative impact on the prognosis of the child. This is also the case in Japan, where practitioners encounter many families who refuse to accept the diagnosis and thus raise their ASD child without the necessary information on the disorder.

Objectives: As a pilot survey, the present study determined 1) when the families were first notified of the child having a diagnosis of ASD; 2) what the families were told at that time; 3) who, other than the parents (e.g. the child, the siblings), were notified; 4) whether the families accepted the diagnosis; and 5) whether the disclosure had any impact on the child's development.

Methods: We enrolled 100 parents who are members of a non-profit organization for families having a child with ASD. They were willing to fill out a self-report questionnaire on the disclosure of the diagnosis and their acceptance of it.

Results: We found that most parents having a child with ASD had difficulties accepting the diagnosis. Furthermore, they tended to conceal the information from relatives and close friends until they had finally accepted the diagnosis.

Conclusions: The results underscore the importance of an interactive process between families and practitioners to help the parents accept the disorder.

11 143.11 Shifting Roles: The Lived Experience of Mothers of Children with Autism. D. B. Nicholas*, *The Hospital for Sick Children*

Background: The needs and clinical manifestations of autism shift substantially over the course of childhood, adolescence, and young adulthood. In caring for their child with autism, mothers often play key and diverse caregiving roles.
Objectives: In addressing the experiences of mothers in providing this care and in understanding the provision and impact of family care over time, this preliminary qualitative review examined the experiences of mothers of children with autism, as well as family-based impacts of care over time.
Methods: As part of a larger study, focus groups were conducted with (1) parents of children with autism and (2) autism service providers. In total, 2 focus groups with parents were conducted, and 1 focus group with service providers in autism care. Focus groups identified issues and challenges faced by families in which a child has autism.
Results: The three focus groups comprised a total of 13 participants: 9 mothers of a child with autism and four service providers. One family had 2 children with autism. Findings included a range of experiences and challenges, over time, that face families in

which a child has autism. Emergent themes demonstrated: (1) extraordinary maternal involvement in care, (2) negative impacts of autism on family functioning; (3) emotional strain experienced by family members, (4) impediments to obtaining resources, and (5) continual shifts in autism-based experiences and needs over time.

Conclusions: Given the shifting nature of autism in the life of the developing child as well as mothers' key role in caregiving, greater knowledge about maternal and family experiences and shifts are integral in potentially improving developmentally-based needs assessment, treatment planning, support strategies, and resource allocation. The study has important implications for understanding and ultimately enhancing maternal and family experience, which has a direct link to the care and outcomes of children with autism.

12 143.12 PERCEIVED NEGATIVE IMPACT OVER TIME IN AN AFRICAN AMERICAN AND CAUCASIAN SAMPLE. T. Carr*[1], S. L. Bishop[2], D. K. Anderson[1] and C. Lord[1], (1)*University of Michigan Autism and Communication Disorders Center*, (2)*Waisman Center, University of Wisconsin-Madison*

Background: Research has examined the difficulties faced by mothers caring for a child with Autism Spectrum Disorder (ASD), but there has been less focus on examining such factors across diverse cultural backgrounds.

Objectives: To examine the stability and predictors of perceived negative impact over a five year period in a sample of African American and Caucasian mothers caring for a child with ASD.

Methods: Data were collected as part of the Early Diagnosis Study, a longitudinal study of children with ASD. Mothers of participants were asked to complete a number of questionnaires including the Child and Adolescent Impact Assessment interview, the Aberrant Behavior Checklist, and the Vineland Adaptive Behavior Scales-II. A linear mixed model analysis was employed to examine the stability of perceived negative impact over time (as assessed by the CAIA) and to examine significant predictors of perceived negative impact over the five-year period.

Results: Data are collected on 125 children with ASD at two time points (Time 1, mean age= 9.3 years; Time 2, mean age = 14.1 years) and their families. 33 of the families are African American and 92 are Caucasian. Preliminary analyses indicate that perceived negative impact increased significantly over time, with African American mothers reporting significantly lower levels than Caucasian mothers at both times. In addition to time and racial category, child behavior problems and social support received were significant predictors of perceived negative impact.

Conclusions: The present research suggests differences in the experiences of African American and Caucasian families of children with ASD. Future research will examine the contribution of cultural variables to the perception of perceived negative impact.

13 143.13 Community Interventions for Autism 1998-2003: Did We Meet the Guidelines?. L. M. Elder*, A. M. Estes, G. Dawson and J. Munson, *University of Washington*

Background: The National Research Council (NRC; 2001) recommends 20-45 hours a week of multidisplinary intervention beginning before the age of three to treat autism. It is important to evaluate how closely interventions received in the community match recommended guidelines.

Objectives: Describe interventions received by children with autism enrolled in a longitudinal study in terms of number of hours and types of interventions received. Investigate factors predicting the hours of intervention received. Evaluate whether interventions match NRC guidelines.

Methods: Seventy-five participants with an Autism Spectrum Disorder (ASD) were assessed as part of a longitudinal study. Participants received diagnostic assessments at ages 3-4 and age 6. Month-by month information on behavioral interventions was collected every 6 months.

Results: Participants received an average of six hours per month of intervention at age 2, 14.8 hours at age 3, and 24.98 hours per month at age 6, below recommended guidelines. At age 3 the types of interventions received were: 96% preschool or kindergarten, 93% speech therapy, 65% occupational or physical therapy (OT/PT), 41% Applied Behavioral Analysis (ABA), 1.3% individual psychological therapy, and 0% social skills training. By age 6 the percent enrolled in each type of intervention was: 100% preschool or kindergarten, 85% speech therapy, 65% OT/PT, 41% ABA, 10% individual psychological therapy, and 10% social skills training. Increased symptom scores on the ADOS at age 3-4 were associated with increased hours of intervention from age 3-6 ($\beta = .29$, $p = .4$) over and above initial Mullen DQ. Sex and initial DSM-IV diagnosis were not significant predictors of hours received.

Conclusions: In accordance with NRC guidelines, participants received multidisciplinary interventions and all participants had started one intervention by age 3. However, the average hours received fell short of NRC guidelines. Implications of the findings in terms of optimal early intervention will be discussed.

14 143.14 The relationship of religiosity, stress, depression, affect, and well-being in mothers of children with autism spectrum disorder. T. L. Whitman and N. Ekas*, *University of Notre Dame*

Background: Studies have found that social support can act as a moderator of the relationship between autism symptom severity and maternal outcomes. However, limited studies have investigated religiosity as a possible moderator of these relationships.

Objectives:To investigate the direct relationship between religiosity and maternal outcomes. A second purpose is to explore the role of religiosity as a moderator of the relationship between autism symptom severity and maternal outcomes.

Methods:Participants consisted of 123 mothers with a child with autism spectrum disorder. Mothers completed the following questionnaires: Parenting Stress Index (PSI), Center for Epidemiological Studies – Depression Scale (CES-D), Psychological Well-Being (Environmental Mastery, Purpose in Life, and Personal Growth scales), Positive and Negative Affect Scales (PANAS), Satisfaction with Life (SWL), Childhood Autism Rating Scale (CARS), and Multidimensional Measurement of Religiousness/Spirituality.

Results:Autism symptom severity significantly predicted maternal stress, depression, life satisfaction, negative affect, and purpose in life. Religiosity significantly predicted all maternal outcomes. Hierarchical regression analyses were conducted to determine which aspect of religiosity was a better predictor of maternal outcomes. Preliminary results show that frequency of religious involvement significantly predicted maternal stress. Religious beliefs significantly predicted maternal depression. Finally, spirituality significantly predicted positive affect, life satisfaction, environmental mastery, and purpose in life. Further analyses will be conducted to determine the role of religiosity as a moderator of the relationship between symptom severity and maternal outcomes.

Conclusions:Findings confirm that autism symptom severity and religiosity significantly predicted maternal outcomes. These preliminary results suggest that there is a complex relationship between these variables. Specifically, spirituality appears to be associated with positive outcomes such as life satisfaction, whereas religious beliefs and frequency are associated with negative outcomes such as stress and depression. These findings suggest that incorporating spirituality into daily living may be beneficial for families.

15 143.15 Development of the Controllability of Behavior Questionnaire to assess parent beliefs about their HFA child's ability to control symptomatic and comorbid behaviors. N. Zahka*[1], A. Inge[1], C. Schwartz[1], D. Coman[1], N. Kojkowski[1], C. Hileman[1], L. Mohapatra[1], H. Henderson[1] and P. C. Mundy[2], (1)*University of Miami*, (2)*UC Davis*

Background: Recent bio-behavioral data from our laboratory suggest that processes associated with self-regulation and motivation may be vital to understanding individual differences among HFA children.

Objectives:The goal of this study was to extend our research through the development and validation of a parent-report questionnaire measuring the ability of HFA children to control their autism-related social symptoms and/or their comorbid internalizing and externalizing symptoms.

Methods:Parents completed the SCQ, ASSQ, BASC, and the newly developed Controllability of Behavior Questionnaire (CBQ). The two primary CBQ measures were the Autism Symptom Control (ASC) index and the Comorbidity Symptom Control (CSC) index. Children completed the BASC.

Results:Data were collected on 27 children (3 females) diagnosed with autism spectrum disorders. The results indicated that higher parent ratings of autism symptom control were related to their reports of lower SCQ symptom presentation (SCQ Total, $F = 6.863$, $p < .5$), but not to their BASC ratings of comorbidity. Conversely, parent ratings of higher control of comorbid symptoms were marginally related to their lower BASC ratings of Externalizing Disorders ($F = 3.794$, $p < .10$) and attention problems ($F = 2.971$, $p < .10$). In addition, higher parent rating of autism symptom control was associated with more optimal child self rating on the BASC locus of control scale ($F = 5.446$, $p < .5$).

Conclusions:The validity of the divergent scales of the CBQ was supported by findings that parent reports of ASC was specifically related to their SCQ ratings and parent report of CSC was specifically related to their BASC ratings. Evidence of construct validity was provided by the associations observed between parent report of ASC and children's self-report of the degree to which they experienced control over life events on the BASC Locus of Control scale. Thus, initial data suggest the CBQ may be a useful new measure in research on self-regulation of children affected by HFA.

16 143.16 USING "SCALABLE" MODELS TO IMPROVE ACCESS TO AUTISM SERVICES: SUCCESSES AND CHALLENGES. D. S. Murray*[1], P. Manning-Courtney[2] and C. Luzader[3], (1)*Cincinnati Children's Hospital /University of Cincinnati*, (2)*Cincinnati Children's Hospital/University of Cincinnati*, (3)*Cincinnati Children's Hospital Medical Center*

Background: Autism diagnostic and treatment providers are under increasing pressure to provide effective and timely services to a rapidly growing number of children with ASD. Intervention models are largely unchanged, despite the dramatic increase in demand. Without significant systems change, providers will not be able to meet the growing demand for services.
Objectives: Improve access to autism treatment at a hospital-based, multidisciplinary diagnostic and treatment program using health improvement science.
Methods: Numbers of children undergoing treatment at The Kelly O'Leary Center for Autism Spectrum Disorders (TKOC) were tracked monthly, with a goal of increasing the total number of children accessing treatment services at TKOC by 25% per year utilizing the same FTE staffing. Treatment programs were re-designed to be more "scalable," thus allowing for increased access to children not previously able to receive treatment.
Results: Numbers of children who accessed treatment services at TKOC increased from 178 to 483 for the period from June 2005-Dec 2007. In addition, by applying the concept of scalable models to medical treatment, we were able to add an additional 700 medical follow up visits per year. Secondary benefits included a reduction in no show/cancellation rates (15% Dec 07 from 23% June 05). Additional benefits and challenges will be discussed.
Conclusions: Access to treatment services can be improved through health improvement science techniques. The on-going process improvement work at TKOC continues to provide important learnings to educate providers to more effectively implement "scalable" intervention models. The increased need for autism treatment programs not only

demands research in outcomes of scalable models, but also demands more extensive research in health improvement sciences to investigate the system changes necessary to allow more children with ASD to access much needed services.

17 143.17 Puberty and Relationships 101: A Guide to Growing Up for High Functioning Adolescent Males with Autism Spectrum Disorders. M. Roth and S. Nichols*, *NSLIJ Health System*

Background: Sexuality education for males with high functioning autism spectrum disorders (ASDs) is critical, yet it has not received the attention in the literature that is warranted. These adolescents face unique issues regarding sexuality due to the nature of the disorder. To date there has not been an empirical attempt to address these issues with a group-based educational approach developed specifically for this population. Development and evaluation of a psycho-educational curriculum will enable professionals to best understand how to teach this population about their developing sexuality.

Objectives: To design and evaluate the effectiveness of a psycho-educational curriculum designed to: (a) increase adolescents' and parents' comfort levels discussing sexuality (b) help adolescents and parents achieve two goals predetermined before group (c) decrease parental concerns and increase acceptance of their son's sexuality (d) increase adolescents' understanding of their developing sexuality (e) decrease adolescents' stress levels for issues regarding growing up

Methods: Curriculum development was based on current literature on sexuality development in ASDs and the authors' clinical outcome data. Seven adolescent males and their parents were recruited; adolescents attended eight group sessions. Measures included adolescent self-report, parent-report and parent self-report during pre-group and post-group. Parents and adolescents created two goals each for the adolescent to achieve by the end of the group sessions.

Results: Data analysis is currently ongoing. Preliminary results demonstrate parents' comfort levels discussing their son's developing sexuality increased as well the adolescents' comfort level discussing sexuality. Adolescents' desire to be part of the group increased. Additionally parents and adolescents progressed toward their goals.

Conclusions: Findings from this first sexuality group are promising for addressing the concerns of both the adolescents and parents about the adolescents' emerging sexuality. Continued implementation and evaluation of the group curriculum will make clear the effectiveness of the curriculum and what revisions are needed.

18 143.18 Accuracy Of Family Doctors As Compared To Medical Specialists In Predicting The Presence Of An Autism Spectrum Disorder In Children And Youth. K. Kalynchuk*[1], V. Dua[2] and S. Wellington[2], (1)*Sunny Hill Health Centre part of British Columbia's Children's Hospital*, (2)*University of British Columbia*

Background: Provincial Standards and Guidelines for assessment of an Autism Spectrum Disorder (ASD) introduced in 2002 required that barriers to obtaining diagnostic assessment be reduced. In B.C., as elsewhere, it was reported that requiring a child to see a community pediatrician (or specialist) to obtain a referral for an ASD assessment led to unacceptable delays in identification. As a result, when the British Columbia Autism Assessment Network (BCAAN) was established referrals were accepted from primary care physicians (PCP's) as well as specialist physicians (pediatricians and child psychiatrists). There have been questions about whether this practice would lead to inappropriate referrals.

Objectives: The purpose of this study is to evaluate if PCP's are as accurate in identifying children at risk for an ASD as child specialists.

Methods: All children and youth (C&Y) referred to BCAAN between 2003 and 2007 were included (n=2026; age range=1-18; mean age=7.34). Referral sources for all subjects

and diagnostic conclusions (ASD vs. Not ASD) were tabulated on all subjects.

Results: There was no significant difference between PCP's (51.5% positive, n=392) and specialists (58.3%, n=1634) with regard to accuracy in predicting the presence of an ASD.

Child Psychiatrists (52.1%, n=288) and pediatricians (59.7%, n=1346) also do not differ significantly in predicting the presence of an ASD. C&Y under 6 and over 6 do not differ statistically.

Conclusions: PCPs and specialist physicians are equally likely to identify the presence of an autism spectrum disorder in children and youth. As well, no significant differences exist between child psychiatrists and pediatricians. These data support a policy of minimizing barriers to specific ASD diagnostic assessments including allowing PCPs to directly refer.

19 143.19 British Columbia Autism Assessment Network: A New Service Delivery Model. S. Wellington*[1], K. Kalynchuk[2] and V. Dua[1], (1)*University of British Columbia*, (2)*Sunny Hill Health Centre part of B.C. Children's Hospital*

Background: The British Columbia Autism Assessment Network (BCAAN) was established in 2002. The network includes a service delivery model which enables regional and provincial planning, coordination, standardization and evaluation of clinical assessments and diagnostic services for children and youth in B.C. 0 to 19 referred for assessment of a possible Autism Spectrum Disorder (ASD).

Objectives: The purpose of the study is to evaluate if BCAAN succeeded in its efforts to reduce wait times and increase the number of assessments in the province.

Methods: A provincial web accessible database was developed in 2003 to collect data on wait times, new referrals and the number of completed assessments in B.C. Standardized data definitions were developed to ensure data quality.

Results: 2003-04
New referrals (0-19): 732
Completed assessments: 449
Average wait time (weeks): 54-89 weeks
2004-2005
New referrals (0-19): 1516
Completed assessments: 449
Average wait time (weeks): 23.5 weeks
2005-2006
New referrals (0-19): 1768
Completed assessments: 1315
Average wait time (weeks): 20.7 weeks
2006-2007
New referrals (0-19): 1724
Completed assessments: 1109
Average wait time (weeks): 20.4 weeks
Conclusions: Prior to 2002, wait times generally ranged from 9 to 36 months and less than 400 non standardized assessments per annum were completed.
Since the BC Autism Assessment Network was established in the fall of 2002 referrals have been decentralized, wait times have been reduced to 20.5 weeks or 4 to 5 months for all ages and 1100 or more standardized assessments are completed annually. The BCAAN service delivery model succeeded in its core mandate to reduce wait times and increase the number of assessments in B.C.

20 143.20 Design of Interactive Visual Scheduling Systems. S. J. Kaufman*, D. J. Patterson and G. R. Hayes, *University of California, Irvine*

Background:

Visual schedules are effective tools for supporting children with autism in understanding, structuring, and predicting activities. However, visual schedules can be difficult and time-consuming for caregivers to employ effectively, because caregivers must ensure the visual aids match volatile schedules. Technology-enhanced visual schedules have the capabilities to ease both the use of these aids and the data collection of activities in classrooms.

Objectives:

Understand how visual schedules are currently used and how they new technologies can allow for collaboration amongst teachers and

parents through these schedules. Design and develop technology augmented visual schedules.

Methods:

With 20 caregivers of children with autism, including parents, teachers, and experts, we completed interviews and multiple brainstorming and participatory design exercises. We observed classrooms that currently use visual schedules. Based on these observations and design exercises, we created a large interactive touch-screen visual schedule system for use in a classroom setting. In addition to acting as a visual schedule, this system logs input from caregivers alongside data collected automatically from sensors.

Results:

Using the technology-augmented visual schedules, teachers can quickly and easily update the schedules in their classrooms, reducing the confusion when the schedules do not match reality. School staff can analyze the data from this system to test hypotheses about behavior and learning goals in comparison to sensed and manually entered activity data. Data in digital format aids caregivers in preparation of reports.

Conclusions:

Interactive and collaborative visual schedule systems have the potential to improve the lives of students with autism, both in the classrooms and at homes. Our inquiry into these settings afforded the design and development of one such system, improving efficiency, utility, and enjoyment from visual schedules in classrooms.

Poster Presentations Program

144 Brain Imaging Posters 2

21 144.1 Spectral and Temporal Auditory Processing in Autism: An fMRI Study. F. Samson*[1], T. A. Zeffiro[2], I. Soulieres[3], P. Ahad[4], A. Mendrek[5] and L. Mottron[6], (1)*University of Montréal / Hôpital Rivière-des-Prairies*, (2)*Neural Systems Group, Massachussetts General Hospital*, (3)*Massachusetts General Hospital/ Harvard Medical School*, (4)*McGill University*, (5)*University of Montreal*, (6)*Hopital Rivière des Prairies*

Background: Atypical perceptual processing is one of the mechanisms underlying the superior and inferior abilities of autistic individuals (Mottron et al., 2006). In vision, a performance dissociation in low-level perceptual capabilities led to the formulation of the complexity hypothesis (Bertone et al., 2005), predicting that autistics' sensory processing efficiency is inversely related to the level of neural resources required, with elementary perceptual task performance higher and complex task performance lower. In the auditory modality, evidence of enhanced simple and diminished complex information processing (Samson et al., 2006), support extending the complexity hypothesis to audition.

Objectives: To investigate the regional functional specialization of the neural responses to sounds varying in spectral and temporal complexity and to test if atypical allocation of neural resources in autism extends to audition.

Methods: Using a 3T MRI system and echo-planar imaging, we studied autistics and controls, matched on FSIQ, sex and age, while they listened to auditory stimuli that varied parametrically in spectral (two harmonic modulation levels) or temporal (four frequency modulation levels) complexity. Participants were asked to detect the presence or absence of the modulations. We used ANOVA to identify group, task and group by task interaction effects.

Results: We observed between-group differences in sensitivity to temporal complexity in bilateral non-primary auditory areas, with a stronger linear effect of increasing frequency modulation in controls. In contrast, we did not observe between-group differential sensitivity to spectral complexity, as assessed by harmonic stimulus content.

Conclusions: Consistent with predictions of the complexity hypothesis, increasing temporal

complexity results in stronger modulation of non-primary auditory areas in controls than in autistics. In contrast, harmonic modulation does not. These results suggest that the complexity hypothesis holds for temporal, but not spectral, domains of auditory perception in autistics.

22 144.2 Diffusion tensor imaging in autism and Asperger Syndrome: evidence for impairment of long range white matter integrity. W. Groen*[1], M. Zwiers[2], R. J. Van der Gaag[1] and J. Buitelaar[3], (1)*University Medical Center St Radboud*, (2)*FC Donders Centre for Cognitive Neuroscience*, (3)*Radboud University Nijmegen Medical Centre*

Background: Recently, many studies concerning neural connectivity in autism have been published, leading to hypotheses that entail impaired neural information integration and long distance disconnection. However, little is known about the structural integrity of the white matter tracts that are involved in neural connectivity.

Objectives: To investigate the structural integrity of white matter tracts in autism and Asperger Syndrome. Methods: Diffusion tensor imaging was performed on 12-18-year old participants with high functioning autism, Asperger Syndrome and typically developing children matched for age, IQ, handedness, head circumference, and gender. Scans included the cerebrum and cerebellum and fractional anisotropy and mean diffusivity measures were analyzed in a voxel based morphology manner.

Results: Participants with autism had lower fractional anisotropy in long distance white matter tracts including inferior and superior fronto-occipitial fasciculus and the inferior and superior longitudinal fasciculus bilaterally as well as the cerebello-pontine tract bilaterally. Fractional anisotropy in Asperger Syndrome was intermediate between that of participants with autism and controls, but non-significant.

Conclusions: The findings suggest that there is a generalized reduction of structural integrity of long distance white matter tracts in autism that connect the frontal cortex to other systems. The reductions may contribute to the behavioral pattern observed in autism. The preliminary fractional anisotropy results in the Asperger group suggest that although the same neurobiological causes may underlie autism and Asperger syndrome, the severity and distribution of affected cortical areas differ.

23 144.3 Neural Substrates of Simple and Complex Emotion Recognition in Autism: An fMRI study. J. Goldberg*, K. A. Doyle, P. Szatmari and G. B. Hall, *McMaster University*

Background: While some individuals with autism can succeed with simple emotion recognition, they show deficits with more complex displays of emotion (Baron Cohen, 1997). Therefore, a functional imaging study of simple and complex emotions provides the means to examine a graded response in individuals with autism. Objectives: To investigate functional brain activity during the recognition of simple and complex emotions in high-functioning adult males with autism. Methods: 12 high functioning males with autism and 12 matched controls gave informed consent and participated in the study. Stimuli were presented in a 3T MRI scanner via an overhead visor, with responses made using a hand-held response pad. Functional BOLD imaging was done using an echo-planar imaging sequence with TR/TE=2700/35 msec. We generated a battery of simple and complex emotional stimuli and a block design was used to randomly present 5 simple and 5 complex blocks of emotion matching trials. Each block consisted of 7 matching trials and was followed by a fixation period of 18900 msec. Brain Voyager software was used to identify regions of activation during each task and then subjected to a second-level random effects to identify group effects (Woods, 1996). Results: Individuals with autism showed greater activation in posterior and medial temporo-occipital regions and less robust activation of the fusiform gyrus to emotion face stimuli than controls. Additionally, while individuals with autism activated some regions associated with emotion processing (insula) during both simple and complex emotion recognition, controls showed heightened activation of

emotion related regions as emotion recognition demands increased. Lastly, individuals with autism appear to use associative memory to support increased processing demands during complex emotion recognition. Conclusions: As compared to controls, individuals with autism engage different brain regions for simple and complex emotion recognition, and are increasingly distinguishable as emotion recognition demands increase.

24 144.4 MEG study of Cortical Coherence in Autism. T. Kenet*[1], E. Orekhova[2], N. Shetty[1], A. K. Lee[1], M. Vangel[1], M. R. Herbert[1] and D. Manoach[1], (1)*Massachusetts General Hospital / Harvard Medical School*, (2)*Institute of Neuroscience and Physiology, Sahlgrenska Academy, Gothenburg University, and Massachusetts General Hospital, Boston*

Background: Recently, a significant body of evidence has accumulated in support of the cortical hypo-connectivity hypothesis of autism; the hypothesis states that individuals with autism have weaker than normal long range cortical functional connectivity, which may contribute to the cognitive abnormalities underlying autism. The majority of the studies investigating this thesis are fMRI based. While those studies have enriched the field significantly, they are limited by the low temporal resolution of fMRI, which prohibits fine temporal resolution analysis of functional connectivity.

Objectives: Our goal was to further our understanding of the nature of hypo-connectivity in autism, and specifically its correlation with (1) specific frequency bands, (2) task demands, and (3) distance between the cortical regions.

Methods: We studied 8 high functioning adults with autism and 8 age and gender matched healthy controls (6 of 8 were also verbal IQ matched) using whole head Magnetoencephalography (MEG). We looked at three conditions – fixation with i) no immediate associated task ('fixation'), and in preparation for ii) a saccade or iii) an antisaccade task. For each subject and condition, we analyzed 64 seconds of concatenated data for coherence in the delta, theta and alpha frequency bands.

Results: Significant coherence reduction in autism was observed during 'fixation' and antisaccade preparation ($p<0.2$), but not during prosaccade preparation, in the delta band. A tendency for coherence reduction was also found in theta band during antisaccade preparation ($p<.7$), and in the alpha band ($p<.7$) during 'fixation'. The observed differences tended to be more pronounced for longer distances, ensuring this is not a volume conductance effect. The regions driving the differences were mostly posterior (mainly occipital).

Conclusions: These observations support the hypothesis of weaker long-range cortical functional connectivity in autism. Our thus far preliminary findings indicate that weaker functional connectivity seems to be band, task, and region dependent.

25 144.5 The Early Social Brain – fMRI of Auditory Emotional Processing in Infants. A. B. Thomson*, D. A. Sauter, A. Simmons, M. J. Brammer, F. Happé and D. G. Murphy, *Institute of Psychiatry, Kings College London*

Background: Social communication relies on the ability to interpret non-verbal social signals, but little is known about the early development of the neurocognitive systems underlying this ability. Studies in adults have found that nonverbal emotional stimuli - including observation of emotional facial expressions and passive listening to emotional nonverbal vocalisations - engage premotor regions of cerebral cortex (Carr et al. 2003; Warren et al. 2006), suggesting a link between perception and production of social signals. It has been proposed that this link may be a key component of the empathic response (Agnew et al. 2007). However, it is not known whether such an emotional "mirror" system exists in early infancy.

Objectives: This study aimed to investigate the early development of neural systems involved in the processing of non-verbal human emotional vocal signals, such as laughter and sighing, using functional magnetic resonance imaging.

Methods: Typically developing infants aged between 2 and 5 months were scanned using a fMRI passive listening task. They were played positive and negative nonverbal vocalisations, as well as neutral vocalisations and control sounds. Following pre-processing, fMRI volumes were mapped to an infant brain template.

Results: Preliminary group analyses suggest that frontal premotor, superior temporal and anterior cingulate areas are active in response to positively valenced vocalisations. Negatively valenced vocalisations activate cortical areas including posterior cingulate and superior temporal gyrus.

Conclusions: These results demonstrate that infant brain function is modulated by emotional sound, and in similar brain regions to adults. These include limbic structures, cortical 'motor preparatory' areas, and regions including mirror neurons. We plan further investigations into how infants who are at risk of neurodevelopmental disorders differ from neurotypical controls.

26 144.6 Can the EQ and SQ-R Be Used to Predict Structural Differences in Cognitive Styles?. S. A. Sadek*[1], B. Chakrabarti[1], M. V. Lombardo[1], G. Pasco[1], S. J. Wheelwright[1], E. Bullmore[2], J. Suckling[2], D. G. Murphy[3], A. Bailey[4], S. Baron-Cohen[1] and T. MRC AIMS Consortium[5], (1)*Autism Research Centre, University of Cambridge*, (2)*Brain Mapping Unit, University of Cambridge*, (3)*Institute of Psychiatry, Kings College London*, (4)*University of Oxford*, (5)*University of Cambridge; Institute of Psychiatry, King's College London; University of Oxford*

Background: The empathizing-systemizing (E-S) theory (Baron-Cohen, 2002) was proposed to explain both psychological sex differences and the cognitive style associated with autism spectrum conditions (ASC). Empathizing (E) is the drive to identify an agent's emotions and mental states, and is stronger in females. Systemizing (S) is the drive to analyse or construct any system, and is stronger in males. They can be quantitatively assessed using two self report questionnaires; the Empathizing Quotient (EQ; Baron-Cohen and Wheelwright, 2004) and the Systemizing Quotient – Revised (SQ-R; Wheelwright et al, 2006). These can be used to determine three main cognitive styles in individuals; (1) E-type: empathizing is at a higher level than systemizing, (2) B-Type (balanced): systemizing and empathizing skills are at an equal level, and (3) S-type: systemizing is at a higher level than empathizing. Autism corresponds to the last of these cognitive styles (Wheelwright et al, 2006), but it is yet to be determined how these three cognitive styles correspond to structural differences in the brain.Objectives: To test for structural differences in the brain that correlate to these three cognitive styles.

Methods: 45 typical male volunteers (age and IQ matched; 15 in each of the three cognitive styles), were scanned in a GE 3T machine, using an SPGR sequence. Voxel based morphometry was used to compare local grey matter volumes.

Results: Parametric analyses at the whole-brain level were conducted using SPM5. Additionally, volumetric comparisons were made of the Inferior Frontal Gyrus (previously associated with EQ; Chakrabarti et al, 2006), and the dorsolateral prefrontal cortex (previously associated with SQ; Billington et al, 2007) between the three brain-types.

Conclusions: Studies of typical individual differences in cognitive style at a neurological level can help us in understanding brain development in autism, which is characterized as an extreme of a dimension of typical individual differences.

27 144.7 ATYPICAL WHITE MATTER MICROSTRUCTURE IN AUTISM AND ASPERGER'S SYNDROME. E. B. Barbeau*[1], T. A. Zeffiro[2], I. Soulieres[3], G. Strangman[2], A. Mendrek[4] and L. Mottron[5], (1)*University of Montreal / Riviere-des-Prairies Hospital*, (2)*Neural Systems Group, Massachussetts General Hospital*, (3)*Massachusetts General Hospital/ Harvard Medical School*, (4)*University of Montreal*, (5)*Université de Montréal*

Background: Growing evidence supports the idea that integration among functionally specialized brain regions is atypical in autistics, variously described as reduced long-range interactions, enhanced intraregional interactions or increased functional independence among cortical regions. However, it is not known whether these hypothesized differences in effective connectivity are associated with, or possibly result from, atypical anatomical connectivity. In addition, while reduced fractional anisotropy (FA) has been demonstrated in the corpus callosum and temporal white matter, it is not known if these effects are confined solely to autistics, or are also characteristic of Asperger's syndrome.

Objectives: We used diffusion tensor imaging (DTI) to estimate regional white matter microstructural properties in autistic and Asperger participants.

Methods: Our sample included 21 autistic, 18 Asperger and 21 typical participants, matched on IQ, age (range 14-35), sex and manual preference. Using a 3T MRI system, we collected seventy-five 2mm axial slices, covering the entire cerebrum and cerebellum. For each slice, ten reference (b=0) and sixty diffusion-weighted (b=700) images with unique non-collinear diffusion encoding were obtained. The diffusion tensor and derivative parametric values including fractional anisotropy were estimated for each 2mm voxel. After transformation to a common anatomical space, FA image values were used as measures in a one-way ANOVA.

Results: Linear contrasts revealed a large cluster of voxels encompassing the corpus callosum and adjacent white matter, in which the FA values were linearly decreasing among the comparison, Asperger and autistic groups. Reductions in cerebellar white matter FA were also seen in the autistic group.

Conclusions: We observed supratentorial alterations in white matter microstructure in both the Asperger and autistic groups, consistent with the assertion that differences in anatomical connectivity may be responsible for altered patterns of intra- and inter-hemispheric effective connectivity in autism and Asperger's syndrome.

28 144.8 An imaging study of Theory of Mind: How is the 'network' affected in ASD?. S. J. Carrington*, M. Rushworth and A. Bailey, *University of Oxford*

Background: Theory of Mind (ToM) is a complex cognitive function underlying social interaction and reasoning. Several distinct brain regions have been implicated in ToM, including the medial prefrontal cortex, superior temporal regions and the temporoparietal junction. The interaction between these regions is likely to be critical for intact ToM, effectively forming a network of interconnected regions similar to the 'social brain' (Brothers, 1990). Impaired ToM is a core deficit in autism spectrum disorder (ASD), a neurodevelopmental disorder associated with aberrant connectivity. Furthermore, reduced functional and structural connectivity has been reported in individuals with ASD between regions typically associated with ToM (Barnea-Goraly et al., 2004; Castelli et al., 2002).

Objectives: To establish whether there is a ToM 'network' in typically developing (TD) individuals, and to determine how the purported network is affected in ASD.

Methods: Data from five males with ASD and five TD males will be reported. ToM will be assessed using a comic strip paradigm based on the task devised by Sarfati et al. (1997). DTI data will be acquired and tract-based spatial statistics conducted to assess white matter (WM) integrity. Finally, probabilistic tractography will be initiated from seed masks placed within WM tracts running between cortical regions associated with ToM in controls.

Results: The behavioural, functional imaging and diffusion data from 5 adult males with ASD and 5 TD adult males will be presented.

Conclusions: It is anticipated that individuals with ASD will exhibit different patterns of ToM-related activity compared with TD controls. Furthermore, it is predicted that individuals with ASD will exhibit decreased WM integrity over the whole brain, and regionally in WM regions connections areas associated with ToM in TD individuals. Such findings would support

the theory that aberrant connectivity may partially underlie the cognitive profile of ASD.

29 144.9 LEARNING TO DETECT LIES IN AUTISM. S. E. Schipul*[1], D. L. Williams[2], T. A. Keller[1], R. K. Kana[3], N. J. Minshew[4] and M. A. Just[1], (1)*Center for Cognitive Brain Imaging, Carnegie Mellon University*, (2)*Duquesne University*, (3)*University of Alabama, Birmingham; Carnegie Mellon University*, (4)*University of Pittsburgh School of Medicine*

Background: A key feature of autism is the inability to mentalize, or attribute mental states to others. Mentalizing is necessary to understand the meanings and intentions of others. Frith states (1989), "the mentalizing mechanism enables the [typically developing] child to learn surprisingly fast about… deception." Because of their impairments in mentalizing, individuals with autism may be more susceptible to being deceived.

Objectives: This fMRI study investigated the neural activity of high functioning individuals with autism and neurotypical individuals while they tried to detect lies in computer animated videos.

Methods: 15 high-functioning individuals with autism and 15 age and IQ matched controls viewed pairs of computer animated avatars uttering a sentence. The task was to choose the video out of each pair in which the avatar was lying. Lying was implemented through several auditory and visual clues previously found to be associated with lying (DePaulo et al., 2003). The experiment consisted of a pretest, a training session with feedback, and a posttest.

Results: Both before and after training, the autism group had greater activation than the control group during the lie discrimination task. With training, the autism group showed a significantly smaller increase in inter-region synchronization of activation than the control group. Throughout the experiment the behavioral performance was comparable between the two groups.

Conclusions: The greater activation in the autism group throughout the experiment suggests that they recruited more neural resources, while showing the same behavioral performance as the control group. The smaller increase in synchronization of activation with training for the autism group suggests that they less efficiently automatized the lie discrimination task than did the controls.

30 144.10 Magnetic Resonance Spectroscopy and Metabolomics of the Autistic Brain. L. Karstens[1], A. Sierra[2], I. Pelczer[1] and M. Maletic-Savatic*[2], (1)*Princeton University*, (2)*Stony Brook University*

Background: The ability to diagnose and predict the course of autism is a pressing goal in clinical medicine. However, the specific biomarkers of the disease are unknown, and the diagnosis relies on clinical and neuropsychological criteria. It is now evident that the genetic background is not sufficient to produce a specific autistic phenotype, and that other, epigenetic factors play a significant role in development of the disease. On the cellular level, the intersection of the genetic background and the environmental, or, in broader terms, epigenetic factors is reflected by the cell biochemistry. Herein, we propose to investigate a complex biochemical fingerprint of the autistic brain which might provide crucial insights into the mechanisms that contribute to the development of autism.
Objectives: The main goal of this study is to investigate the metabolomic profiles of the brain tissue in autism, using proton magnetic resonance spectroscopy (^{1}H-MRS).
Methods: ^{1}H-MRS spectra of the hippocampus/amygdala and cerebellum of subjects with Asperger Syndrome (AS) and Pervasive Developmental Disorder Not Otherwise Specified (PDD/NOS) were obtained using a 1.5T MRI scanner. Subjects were selected based on their ADOS evaluations and were not on medications.
Results: The ^{1}H-MRS data were processed using multivariate analysis. We have observed substantial differences in the profiles of the two subject groups, as well as when compared to healthy controls. Both AS and PDD/NOS subjects clustered together and away from each other, while control group clustered in the middle. Further analysis of the metabolites that contribute to this difference is under way.

Conclusions: Our data indicate that there is a metabolic difference in the brains of AS and PDD/NOS subjects. These are the first data that provide the insight into the functional status of the autistic brain using ^{1}H-MRS Metabolomics, which might lead to the development of diagnostic biomarkers for clinical use in autism.

31 144.11 Abnormal Functional Connectivity During Baseline Relates to Social Symptom Severity In Autism Spectrum Disorders. J. A. Lee*[1], S. J. Peltier[1], S. J. Weng[1], C. Fulton[1], S. Risi[1], C. Lord[2] and C. S. Monk[1], (1)*University of Michigan*, (2)*University of Michigan Autism and Communication Disorders Center*

Background: Abnormalities in functional connectivity, or synchronicity of time courses in neural networks, has been implicated in Autism Spectrum Disorders (ASD). ASD individuals display underconnectivity during the resting state in the default mode network, which is activated when not doing a specific task. As default mode has been associated with social-emotional and introspective concepts, including theory of mind, this has implications for understanding the social-emotional deficits of ASD. However, no study has yet directly related degree of default mode connectivity to symptom severity in ASD. Moreover, no study has examined connectivity of amygdala, also involved in social-emotional processing, during baseline in ASD individuals.

Objectives: This study examines connectivity in socially relevant parts of the brain, default mode network and amygdala, in relation to ASD symptoms. Social symptom severity is hypothesized to be related to underconnectivity within default mode network and abnormal connectivity of amygdala to frontal cortex. Additionally, ASD individuals are expected to have altered connectivity of amygdala with frontal cortex compared to normal controls.

Methods: 12 adults with ASD and 12 matched controls were instructed to "let your mind wander" while looking at a fixation cross for 10 minutes during fMRI acquisition.

Results: Preliminary analyses indicate both groups show default mode connectivity, but without significant between-group differences. Additionally, amygdala connectivity with left middle frontal gyrus (lMFG) was significantly higher in ASD participants compared to controls. Although ASD and control participants showed positive connectivity, the ASD group had a much larger degree of synchrony between amygdala and lMFG. Analyses correlating symptom severity to connectivity in default mode and amygdala-lMFG networks are underway.

Conclusions: Preliminary evidence suggests ASD individuals exhibit abnormal coupling between emotional and social centers of the brain, which may relate to social-emotional symptoms. This approach revealed altered interactions among structures in the absence of a driving task.

32 144.12 Lateralisation of Perisylvian Pathways with Age in Asperger's Syndrome – a Cross-sectional DTI Study. L. Pugliese*, A. B. Thomson, E. Daly, M. Catani and D. G. Murphy, *Institute of Psychiatry, Kings College London*

Background: Abnormalities in cortical long-range connectivity and white matter enlargement during brain maturation may underlie some of the deficits observed in autism spectrum disorders (Herbert et al. 2004). In particular children with autism and language impairment have reversed asymmetry in frontal language-related cortex (De Fosse et al. 2004). The arcuate fasciculus connects perisylvian fronto-parietal-temporal areas, which have been demonstrated to be involved in theory of mind, language and social cognition. This perisylvian network is also thought to overlap with the mirror neuron system (Frith & Frith 2006).

Objectives: To investigate age-related changes in the lateralization pattern of perisylvian pathways in people with Asperger's syndrome using diffusion tensor imaging tractography.

Methods: We recruited 83 subjects: 61 healthy controls and 22 subjects with Asperger's Syndrome diagnosed according to the ICD-10 criteria. The 22 subjects with Asperger's Syndrome (mean age 24.3±13.2) and 61 age-

and gender-matched controls (mean age 26.3±10.6) were investigated with DT-MRI tractography. Tract-specific measurements of number of streamlines (SL) were acquired in both hemispheres for the arcuate fasiculus and for each of its segments. A lateralization index was calculated for each segment by counting the number of streamlines in both hemispheres (LI = difference between left and right hemispheres / average number of streamlines in each hemisphere).

Results: Correlation of lateralisation index with age between groups differed significantly for the posterior indirect pathway: it was symmetrical at all ages for people with Asperger's syndrome but controls developed rightward lateralisation with increasing age. No significant differences were found for the anterior and the long segment.

Conclusions: The indirect pathway of the arcuate fasciculus shows abnormal development with age in people with Asperger's syndrome. This suggests that abnormalities in white matter development may be a key feature of autism spectrum disorders and may explain impairments in language and communication.

33 144.13 Neurofunctional correlates of everyday life relevant social cognition in adults with autism spectrum conditions. I. Wolf*, I. Dziobek, J. Kirchner, C. Yang, S. Schneider and H. Heekeren, *Max-Planck-Institute for Human Development*

Background:

There is a lack of neuroimaging studies investigating the neuronal mechanisms of Theory of Mind (ToM) processes under close to real-life conditions in individuals with autism spectrum conditions (ASC). We have previously developed a more naturalistic, video-based measure of ToM, the "Movie for the Assessement of Social Cognition" (MASC) that requires participants to infer mental states of movie characters.

Objectives:

To develop an fMRI adaptation of the MASC and to compare brain activation of adults with ASC and matched controls during this naturalistic social cognition task.

Methods:

In this study, 14 high-functioning adults with ASC and 14 controls matched for age, gender, and IQ underwent fMRI scanning. Participants watched 11 consecutive scenes of the MASC 3 times under 1.) a ToM, 2.) a physical inference (PI), and 3.) a free viewing (FV) condition. Under the ToM and PI conditions, questions concerning the actors' mental states and concerning physical entities of the scene, respectively, were asked. During the FV condition, participants were asked to watch the scenes without specific task instructions.

Results:

A conjunction analysis of the contrast ToM and PI showed that under more naturalistic conditions both the ASC and the control group activated a previously identified ToM network encompassing the temporal pole, superior temporal sulcus and medial prefrontal cortex bilaterally. During the FV condition the ASC group showed a greater increase in fMRI signal in the amygdala than the control group. Notably amygdala activation was negatively correlated with emotion regulation (measured with Emotional experience scales; SEE) in both groups ($r = -0.46$, $p = 0.5$).

Conclusions:

Under conditions close to everyday life demands, individuals with ASC show greater activation of the amygdala than normal controls, which might be a correlate of emotion regulation in naturalistic social settings and which might lend further support to an amygdala theory of autism.

34 144.14 Functional neuroimaging of set shifting in children with Autism Spectrum Disorder (ASD). K. M. Mak-Fan*[1], D. Morris[2], W. Roberts[1] and M. J. Taylor[2], (1)*University of Toronto*, (2)*Hospital for Sick Children*

Background: Accumulating research on structural abnormalities strongly implicates the involvement of the frontal lobes in autism spectrum disorders (ASD). The current study

will focus on differences in frontal activity in children with ASD as elicited by a set-shifting task, an executive function considered to be primarily mediated by the dorsolateral prefrontal cortex.

Objectives: To examine the neural activation in frontal cortex during a set-shifting task in a group of typically developing (TD) children and a group of children with ASD.

Methods: Participants are typically developing children and high-functioning children with ASD, between the ages of 7 and 12 years. Using colourful, child-friendly stimuli, the task requires participants to make a series of choices between bidimensional compound stimuli, based on a given rule. Periodically, the rule shifts; these shifts are either intradimensional or extradimensional. Neural activity is measured at the time of shift using functional Magnetic Resonance Imaging (fMRI). The ability to shift set/dimension is also measured behaviourally using the Cambridge Intradimensional Extradimensional Shift task, and general executive function using the Test of Everyday Attention for Children (TEAch).

Results: Based on results with a group of 13 young adults, it was hypothesized that the set-shifting task would elicit activation in the prefrontal cortex in the TD group, with intradimensional shifts activating more dorsolateral regions, a pattern that may become more focal with age; and these developmental trends would be abnormal or altered in the ASD group. It was also hypothesized that the pattern and extent of functional activity would be correlated with performance on behavioural measures of set shifting and executive function.

Conclusions: If differences are found in the pattern of neural activation in the children with ASD during the shifts, this lends weight to the theory that frontal dysfunction, and consequently executive dysfunction, may be contributing to symptoms of ASD.

35 144.15 Motion perception in autistic disorders: a functional MRI study. C. M. Freitag*, M. Häberlen, C. Kleser and C. Krick, *Saarland University Hospital*

Background: Individuals with Autistic Disorder (AD) show impairments in social interaction and communication, and stereotyped interests and repetitive behaviour. Difficulties processing biological motion have been described previously and might be related to impaired imitation abilities in AD.

Objectives: To assess neuronal activation during the perception of biological motion in AD and control individuals, to compare reaction times during processing biological motion information, to assess correlation with phenotypic data.

Methods: Neuronal activation during the perception of biological motion was compared in 15 individuals with AD and 15 age, IQ, and sex matched controls. Correlation analyses with neuronal activation pattern and performance in a computer based reaction task were calculated for a measure of social interaction, ADI-R subscales, imitation and gross motor abilities.

Results: Different neuronal activation patterns as well as slower reaction time to perceive biological motion were observed in AD compared to control individuals. Imitation abilities strongly correlated with neuronal activation in the inferior parietal lobule.

Conclusions: This study is the first fMRI study on biological motion perception in AD, showing decreased neural activation and specific correlation patterns with activation in brain regions and networks which previously have been found to be affected in AD.

36 144.16 Neural Connectivity in Autism: A Systematic Review of the Neuroimaging Data. W. M. Rafelson*[1], J. McCleery[1], E. Hubbard[2] and C. Nelson[1], (1)*Harvard Medical School*, (2)*INSERM*

Background:

Over the past several years investigators have uncovered evidence for abnormalities in functional and structural brain connectivity in individuals with autism. From this work several models have been proposed to characterize these abnormalities, including 1) general under-connectivity, 2) local over-

connectivity with long-distance under-connectivity, and 3) abnormal connectivity in those systems that underlie social processing but intact connectivity in systems that do not underlie social processing.

Objectives:

Systematically review the literature that directly examines structural and functional connectivity in individuals with autism in an effort to evaluate the major theories that have been proposed to account for abnormal neural connectivity in autism.

Methods:

PubMed, Medline, and PsycInfo were searched online and key journals were searched manually for articles on neural connectivity in autism. Seventy-seven articles were identified. Eighteen articles involved direct comparisons of functional or structural connectivity (via DTI, fMRI, or fcMRI) between individuals with autism and controls, and were systematically reviewed.

Results:

Thirteen studies provided direct support for long-distance under-connectivity in autism, whereas three studies provided evidence inconsistent with long-distance under-connectivity. Three studies provided direct support for local over-connectivity, whereas six studies did not support local over-connectivity (3-null, 3-underconnectivity). Six studies provided direct support for the social impairment model of connectivity, whereas nine studies provided evidence inconsistent with the social impairment model.

Conclusions:

Of the theories examined, the long-distance under-connectivity model currently has the strongest support. To date, there is little support for a consistent pattern of local over-connectivity in autism. Finally, the data strongly suggest that abnormalities of connectivity are not limited to the neural systems that underlie social processing. The implications of these findings will be addressed in the context of research on other disorders associated with abnormalities in neural connectivity (e.g., schizophrenia, dyslexia), as well as methodological challenges associated with examining neural connectivity in disordered populations.

37 144.17 Noradrenergic Modulation of Effective Connectivity in Autism Spectrum Disorder. A. Narayanan*[1], C. White[1], S. Saklayen[1], A. Abduljalil[1], P. Schmalbrock[1] and D. Q. Beversdorf[2], (1)*The Ohio State University*, (2)*University of Missouri*

Background: Previous experiments have demonstrated decreased functional connectivity in subjects diagnosed with ASD when compared to controls, during language tasks. Therefore, drugs that affect functional connectivity may be beneficial in ASD. Stress causes a decrease in the Semantic Network Flexibility (SNF), and the noradrenergic system is upregulated in stress. In addition, the SNF impairment is reversed by administration of centrally mediated noradrenergic antagonists. Propranolol (β-blocker) has also shown benefit in language and social behavior in ASD.

Objectives: We proposed to find whether administration of propranolol in ASD increases functional connectivity observed during language tasks.

Methods: Subjects with ASD and age and IQ-matched controls without neurodevepmental diagnoses were scanned using a Philips 3T Signa scanner, and a 8-channel head coil with the following parameters: TR = 3s; Flip Angle = 90; 3.75x3.75 in-plane resolution; 64x64 matrix reconstructed to 128x128; 35 axial slices; 5mm slice thickness. Subjects were instructed to respond to the meaning (semantic) or the pronunciation (phonological) of a word related to a cue word in two block-design tasks. Data was preprocessed and analyzed using SPM5.

Results: Preliminary results replicate reports that individuals with ASD have a lesser functional connectivity when compared to controls. In addition, administration of propranolol has revealed a significant increase in the functional connectivity between selected brain regions.

Conclusions: These results reveal an increased functional connectivity upon administration of propranolol in ASD. This may suggests an anatomical substrate of the effects of noradrenergic agents during tasks involving a network search within the brain.

38 144.18 The Neural Circuitry of Social Reward in Autism Spectrum Disorders. S. J. Weng*[1], J. A. Lee[1], H. M. C. Louro[1], H. Zucker[1], C. Fulton[1], S. Risi[2], C. Lord[2] and C. S. Monk[1], (1)*University of Michigan, Ann Arbor*, (2)*University of Michigan Autism and Communication Disorders Center*

Background: Research has consistently shown that individuals with Autism Spectrum Disorders (ASD) attend less to social stimuli and engage less in social interactions relative to typically developing (TD) individuals. It has been proposed that reduced motivation towards social situations may relate in part to a disturbed neural circuit of social reward. This study seeks to link the gap between reward-related brain regions, namely the ventral striatum and the social deficits observed in ASD.

Objectives: Using a functional MRI (fMRI) task with a jittering paradigm which allows better separation of BOLD signal, we are evaluating differences in brain function between ASD and TD youths. We hypothesize that ASD youth will show less activation in the striatum, relative to TD youth when viewing positively-valenced faces. More severe symptoms in the social domain will relate to reduced striatal activation.

Methods: During fMRI acquisition, participants view faces (happy, neutral, fearful and sad) presented for 250 ms. Participants respond by making gender identification judgments to each face, thereby ensuring that they are attending to the social stimuli. Following the fMRI, subjects complete a computer-based behavioral task to obtain an index of the approach-worthiness of the social stimuli. Social functioning scores as measured by the ADOS, ADI and SRS are included as covariates in the analysis. Youths (aged 13-18 years) are recruited through the University of Michigan Autism and Communications Disorders Center and the community. ASD youth are diagnosed with the ADOS and ADI-R.

Results: Preliminary results show differences in striatal activation to emotional faces in ASD individuals compared to TD individuals. Analyses will focus on group differences in the striatum and related brain regions associated with reward circuitry.

Conclusions: By examining group differences to brief presentation of faces, it will be possible to better characterize the neural basis of social deficits in ASD.

39 144.19 Analysis of the Basal Ganglia Morphometry in Autism Using Large Deformation Diffeomorphic Metric Mapping (LDDMM). D. Crocetti[1], A. Qui[2], M. C. Adler[1], M. I. Miller[2] and S. H. Mostofsky*[1], (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins University*

Background: Studies have shown that autism is associated with abnormalities suggestive of basal ganglia dysfunction, including repetitive and stereotyped patterns of behavior and consistent findings of abnormalities in motor examination. Neuroimaging investigations of basal ganglia structures have thus far been limited to examination of whole volume analysis and are prone to missing localized abnormalities. Large deformation diffeomorphic metric mapping (LDDMM), a powerful computational tool used for detailed analysis of the morphology (e.g., shape, thickness) of cortical/subcortical brain regions, may provide better understanding of differences in basal ganglia structures.

Objectives: To apply LDDMM to detailed analysis of basal ganglia structure in children with autism.

Methods: The structures of the basal ganglia (caudate, nucleus accumbens, putamen, globus pallidus) were manually delineated in 23 (5 females) children with autism and 23 (5 females) unaffected controls, ages 8-12 years. LDDMM was then used to map and assess differences in shape across each structure. To test significance, we performed a principal components expansion on the vector displacement fields of the subjects, extracted a small number of components using a scree

plot, then performed a standard permutation test of the significance of the group differences using these coefficients.

Results: The findings revealed the anterior portion of the right putamen to be significantly contracted in children with autism compared to controls; in contrast the posterior portion was significantly expanded.

Conclusions: The findings suggest abnormalities in the structure of the putamen, which has been linked to "sensorimotor" and "associative" (visuo-motor) functioning, and have demonstrated how a detailed analysis of shape can provide greater insight into the structural abnormalities associated with autism. These methods can also be applied to examination of brain-behavioral correlations and may prove to be more valuable in identifying neuroanatomic biomarkers of autism.

40 144.20 NEURAL CORRELATES OF GREATER DUALTASKING COSTS IN AUTISM: AN fMRI STUDY OF TWO UNRELATED TASKS. S. R. Damarla*[1], T. A. Keller[2], R. K. Kana[3], D. L. Williams[4], C. Prat[1], N. J. Minshew[5] and M. A. Just[1], (1)*Carnegie Mellon University*, (2)*Center for Cognitive Brain Imaging, Carnegie Mellon University*, (3)*University of Alabama, Birmingham; Carnegie Mellon University*, (4)*Duquesne University*, (5)*University of Pittsburgh School of Medicine*

Background: People with high functioning autism (HFA) are impaired on most high-level cognitive tasks, but demonstrate intact/enhanced visuospatial performance. Concurrent performance of two tasks may require even more resources than doing a single high-level task. Previous studies have shown a greater dualtasking decrement in performance in autism (Garcia-Villamisar & Della Sala, 2002), however none have investigated the neural underpinnings of the psychological processes underlying these costs in autism.

Objectives: The goal of the current study was to investigate the neural correlates of greater dualtasking costs in autism than controls (performance was worse on both the tasks) from the perspective of two theoretical accounts: cortical underconnectivity (Just et al., 2004, 2007) and cortical capacity constraints (Just et al., 2001, 2007).

Methods: We used a combination of methodological tools: behavioral, fMRI, functional connectivity, and corpus callosum morphometry. Thirteen participants with HFA and 13 controls (age-, IQ-, and gender-matched) were scanned while performing a visuospatial task, an auditory sentence comprehension task, and both concurrently.

Results: The autism group demonstrated less cortical synchronization than controls between executive and language networks on the dual task. Also, the autism group reached their cortical capacity limit sooner by demonstrating A) Greater underadditivity than controls (the activation in the dual task was less than the sum of the activations in two single tasks), and B) Less new activation (regions that showed activation in the dual but not in the single tasks) than the control group. In addition, the corpus callosum (CC) was smaller in the autism group. Finally, a correlation between CC size and functional connectivity of language and executive networks was found in the autism group, but not in controls.

Conclusions: Reduced cortical connectivity and less availability of cortical resources may underlie greater impairment observed in dualtasking in autism.

41 144.21 Activation of the Fusiform Face Area in Response to Implicit Social Semantic Attributions. M. South*[1], D. Grupe[2] and R. T. Schultz[3], (1)*Brigham Young University*, (2)*Yale University*, (3)*Children's Hospital of Philadelphia and the University of Pennsylvania*

Background:
Converging lines of evidence suggest that the fusiform face area (FFA) may be part of the core pathobiology in autism spectrum disorders (ASD). One criticism of fMRI studies of this region is that the existing evidence is confined to face perception. We have hypothesized that the fusiform may be

involved in semantic representations of people, not just perceptual representations of faces.
Objectives:
We sought to determine if the fusiform might automatically activate to implicit representations of people, independent of a perceptual representation of a face.
Methods:
Over five hours of training, 22 typical adults learned to associate unique grayscale "Blobs" with sets of semantic terms that described either social ("friendly, jealous, gentle") or physical characteristics ("grainy, hollow, damp"). Participants then completed an fMRI task, which involved deciding whether two Blobs on the screen were visually identical, without reference to the learned semantic descriptors.
Results:
Random effects region-of-interest analyses showed significantly greater activity in the left FFA in response to social, relative to physical Blobs ($t(22)=3.78$, $p<.005$). Social Blobs also activated regions of the motive circuit involving globus pallidus, amygdala, and cingulate cortex, suggesting that the socially-relevant associations were ingrained and rewarding for visual processing tasks.
Conclusions:
Automatic activation of the fusiform gyrus to abstract visual objects associated with social semantic attributes provides evidence that this part of the ventral visual pathway may be instrumental in linking percepts with cognitive representations. Atypical function in this region could be instrumental in bringing about the primary signs and symptoms of autism. The FFA seems to be involved in person recognition and understanding, independent of its role in perceptual analyses of the face. We suggest that the FFA really might be better referred to as the fusiform person area, to expand its role beyond elementary perceptual processes to semantic representations and social knowledge.

42 144.22 Self Responses Along Cingulate Cortex Reveal Quantitative Neural Phenotype For High Functioning Autism. P. Chiu*[1], A. Kayali[1], K. Kishida[1], D. Tomlin[1], L. Klinger[2], M. Klinger[2] and R. Montague[1], (1)*Baylor College of Medicine*, (2)*University of Alabama*

Background: Typical social interaction requires the ability to recognize one's role in an interpersonal exchange. In particular, attributing behavioral outcomes correctly to oneself or to other agents is essential for productive social interaction.

Objectives: The capacity to attribute social outcomes to the appropriate agents may be missing or perturbed in individuals with autism. We approach this issue in high-functioning males with autism spectrum disorder (ASD) using functional magnetic resonance imaging (fMRI).

Methods: First, using a visual imagery task, we extract a basis set for responses along the cingulate cortex of control subjects that reveals an agent-specific eigenvector (self eigenmode) associated with imagining oneself executing a specific motor act. Second, we show that the same self eigenmode arises in controls during one's own decision (the self phase) in an interpersonal exchange game (iterated trust game). Third, we assessed hemodynamic activations as high-functioning adolescents with autism engaged in the iterated trust game with a social partner.

Results: Using the iterated trust game, we show that ASD males exhibit a severely diminished self eigenmode when playing the game with a human partner. This diminished response covaries parametrically with their behaviorally assessed symptom severity suggesting its value as an objective endophenotype.

Conclusions: The perturbed neural response in autism, evoked within an active interpersonal exchange, provides a quantitative neural phenotype that may identify new subtypes of autism and further be used to seek covariates in genetic databases.

43 144.23 AGE-RELATED CHANGES IN CORPUS CALLOSUM MICROSTUCTURE. M. DuBray*[1], A. Alexander[2], J. E. Lee[2], M. Lazar[3], A. Froehlich[1], N. Lange[4], E. Bigler[5] and J. Lainhart[1], (1)*University of Utah*, (2)*University of Wisconsin*, (3)*New York University School of Medicine*, (4)*Laboratory for Statistical*

Neuroimaging McLean Hospital, (5)*Brigham Young University*

Background: The developmental neuropathology of white matter maturation in the autism brain is unknown. Abnormalities in functional connectivity suggest that white matter pathways may differ in autism. Structural MRI studies of autism suggest aberrant age-related changes.

Objectives: The data were collected as part of an ongoing longitudinal MRI study on brain development in autism. In this analysis, we use cross-sectional data from Time 1 to investigate age-related differences in corpus callosum neurodevelopment.

Methods: High-resolution DTI images obtained from a 3T MRI scanner were analyzed on 74 individuals with autism and 41 control subjects. Individuals were broken down into 4 age bins: young children age 3-6, older children age 7-11, adolescents age 12-17, and young adults 18+. Volume and microstructure (fractional anisotropy, mean diffusivity, and axial and radial diffusivity) were compared for the total corpus callosum and subregions.

Results: Significant group by age interaction effects were found in the total and subregional corpus callosum measures of fractional anisotropy (FA) and radial diffusivity (Dr). These effects were driven by an increase in FA and decrease in Dr with age in controls that was *absent* in autism. A comparison within the autism group surprisingly showed elevated FA in young children compared to older children and adults.

Conclusions: Our cross-sectional findings suggest abnormal age-related white matter developmental trajectories in the corpus callosum in autism. These results suggest early abnormal "maturation" followed by abnormal CC development. The findings indicate white matter pathology in a major interhemispheric communication pathway in autism.

44 144.24 NEURAL CORRELATES OF COHERENT AND BIOLOGICAL MOTION PERCEPTION DEFICITS IN AUTISM. K. Koldewyn*[1], D. Whitney[1] and S. M. Rivera[2], (1)*Center for Mind and Brain, UC Davis*, (2)*M.I.N.D. Institute, UC Davis*

Background: Quick, accurate biological motion perception is fundamental to our understanding of a dynamically shifting visual social world. Recent evidence has suggested that people with autism may show a selective deficit in visual motion processing, including deficits in biological motion perception. Such deficits in processing movement (particularly the movement of people) could significantly contribute to the difficulties in social cognition evident in autism.

Objectives: To investigate the neural correlates of potential coherent and biological motion processing deficits in adolescents with autism.

Methods: Coherent motion, biological motion and coherent form perception thresholds were measured psychophysically using the method of constant stimuli. Neural response to visual motion was measured during fMRI while participants viewed coherent and biological motion displays. Coherent motion perception was measured with random-dot displays where coherence was varied through a standard "random-walk" manipulation. Biological motion displays were point-light depictions of a person walking embedded in moving dot displays whose coherence was varied. Global form perception stimuli were static glass patterns whose coherence was varied based on the percentage of dots aligned along a global form.

Results: As a group, those with autism showed both higher coherent and biological motion thresholds while matching control group performance on the coherent form task. During fMRI scanning, the autism group showed reduced MT+, STS and parietal area activation while showing similar levels of activation in V1. Additionally, activation in MT+ and STS in control individuals steadily increased with increasing directional motion or biological motion coherence. No consistent relationship between psychophysical and neural responses was evident in data from individuals in the autism group.

Conclusions: These results provide evidence for a selective impairment in psychophysical and neural processing of visual motion in individuals with autism and highlight the possibility that deficits in visual processing may significantly contribute to the autism phenotype.

45 144.25 fMRI evidence of reduced emotional face processing automaticity in autism spectrum disorders. N. M. Kleinhans*, T. R. Richards, C. Johnson, J. Greenson, G. Dawson and E. H. Aylward, *University of Washington*

Background: Recent evidence suggests that a rapid, automatic face-detection system is supported by subcortical structures including the amygdala, pulvinar, and superior colliculus. Early emerging abnormalities in these structures may be related to reduced social orienting in children with autism, and subsequently, to aberrant development of cortical circuits involved in face processing.

Objectives: To investigate functional abnormalities in the subcortical face processing system in adults with autism spectrum disorders (ASD).

Methods: Twenty-eight individuals with ASD and 25 controls group-matched on age, IQ, and behavioral performance were included in the fMRI study. The ASD group met diagnostic criteria on the ADI-R, ADOS-G, and DSM-IV. Stimuli were 78 photos of adults with a fearful facial expression and 78 perceptual masks created by scrambling the images. Supraliminal (23 ms) presentations of masked fearful faces were compared to scrambled-image-only blocks using FSL. Participants were instructed to press a button when pseudo-randomly presented fixation crosses appeared to ensure attention to the stimuli.

Results: Both the ASD and control groups showed significant activation in bilateral fusiform gyri and inferior occipital lobes. The control group exhibited additional significant clusters in the right amygdala, right pulvinar, and bilateral superior colliculi. In the direct group comparison, the controls showed significantly greater activation in the left amygdala, right fusiform gyrus, right pulvinar, bilateral superior colliculi, and right orbital frontal lobe. No brain region showed significantly greater activation in the ASD group compared to the controls.

Conclusions: Basic face identification mechanisms appear to be intact in the ASD. However, individuals with ASD failed to engage the subcortical brain regions involved in automatic emotional face processing, suggesting a core mechanism for impaired socioemotional processing in ASD. Further, reduced right fusiform activation in the ASD group may be related to a failure of subcortical circuits to appropriately modulate cortical brain regions in ASD.

Poster Presentations Program

145 Social Function Posters 2

46 145.1 A Pilot Study of Social Cognition Training for Adults with High-Functioning Autism. T. D. Perry*[1], L. M. Turner Brown[2], G. Dichter[2], D. L. Roberts[1], J. W. Bodfish[3] and D. L. Penn[1], (1)*University of North Carolina at Chapel Hill*, (2)*University of North Carolina*, (3)*University of North Carolina - Chapel Hill*

Background: Difficulty with social interaction is universal in autism spectrum disorders and often constitutes the most debilitating feature of these conditions. Impaired social cognition (i.e., perceiving the emotions and intentions of others) makes it difficult to establish friendships and form positive social relationships, and is particularly incapacitating for adults with autism who must navigate the world unaided by parents.

Objectives: The goal of this study was to examine the feasibility of a group-based cognitive behavioral intervention to improve social-cognitive functioning in adults with high-functioning autism (HFA).

Methods: We modified the treatment manual of a previously validated form of group-based intervention, Social Cognition and Interaction Training (SCIT), for optimal use with HFA adults. We then conducted a pilot study to compare SCIT for autism (N=6) to treatment as usual (TAU) (N=4).

Results: High levels of attendance and overwhelmingly positive satisfaction reports supported the feasibility of SCIT with this population Participants in SCIT showed larger improvements in theory of mind skills and emotion identification skills when compared with individuals in the TAU condition.

Conclusions: Findings indicate SCIT is an intervention program with promise for use with adults who have HFA. More research is needed to clarify the role of SCIT in improving social functioning for individuals with HFA beyond research settings.

47 145.2 Promoting social play skills in children with autism using video modeling. C. K. Nikopoulos*[1] and M. Keenan[2], (1)*Brunel University*, (2)*University of Ulster*

Background: Peer relations serve many important functions in children's development. In autism, however, reciprocity of social exchange is missing and this has a devastating effect on the skill of relating. Recently video modeling has been regarded as an effective procedure that may offer some help.

Objectives: The overall aim of this presentation is to demonstrate scientific evidence for video modeling as a valuable technique for promoting social play skills in children with autism. Critical components of this procedure will be highlighted through a brief exploration of three experimental studies. Some data from these studies have already been published in peer-reviewed journals and a book.

Methods: In total, 13 children with autism participated and experimental control was demonstrated using either a multiple-baseline across subjects or a multiple-treatment designs. Study 1 investigated the general notion of promoting social play skills in children with autism. Study 2 assessed the effectiveness of video modeling in establishing generalized responding of these target behaviors. Study 3 examined how many sequences of behavior could be included in individual video clips in terms that effective activity schedules would be constructed using video clips instead of booklets of pictures. Particular aspects of the intervention were systematically analyzed in each study to determine the effective components of video modeling, independently of the behavioral characteristics of the children and in the absence of any experimenter-implemented prompts.

Results: Collectively, results revealed that video modeling can enhance social play skills; establish generalized responding; and build a sequence of social play behaviors. Data also showed that all competing behaviors like disruptive or self-stimulatory reduced substantially as soon as social play skills occurred; behavior gains generalized across stimuli, settings, and peers and maintained after 1-, 2-, or 3-month follow-up periods.

Conclusions: Video modeling can become a time-efficient and powerful educational tool for individuals with autism.

48 145.3 General and specific indicators of social cognition: the role of joint attention skills for children with ASD. L. J. Bornholt*, *Watervale Systems*

Background: The project was designed to target the particular social-cognitive qualities that are useful in education for children who have mild ASD Autism Spectrum Disorders.

Objectives: were to show (a) the specific rather than general social-cognitive developmental delays of ASD; and (b) that the specific joint attention skills are responsive to brief training.

Methods: Part 1 was a correlational study of general and specific social and cognitive indicators. Part 2 was an experiment to show whether joint attention improves for children with ASD.

Participants (N = 68) were children aged 5.0 to 12.6 years (mean 8.9, SD 2.0). The sample included children with mild ASD (N = 12) aged 6.3 to 12.6 years (mean age = 9.1, SD = 2.1).

Results: Specific indicators of children's theory of mind and executive functioning were sensitive and specific to ASD. In contrast, general cognitive functioning was not

necessarily low for children with ASD. Self concepts of cognitive, physical and social activities were also similar (except a stronger sense of individuality for children with ASD). As expected, the experiment improved joint attention, specifically proto-declarative not proto-imperative indicators. (The brief intervention did not target Theory of Mind and executive functioning.)

Conclusions: Findings show some of the specific rather than general social-cognitive indicators that support learning for children with mild ASD. These joint attention skills are amenable to change in brief focused one-to-one sessions. The useful tools used in this project also suggest how we may discover in further long-term studies the roles of children's sense of individuality and joint attention skills as precursors to theory of mind.

49 145.4 From classic Asperger Syndrome to schizoid Asperger Syndrome. P. Gorczyca* and A. Kapinos-Gorczyca, *Medical University of Silesia*

Background: Autistic syndrome, especially Asperger syndrome (AS), often differs from schizoid personality in childhood. Several attempts have been made to compare these diagnostic concepts (Tantam, 1988; Nagy, Szatmari, 1986).These diagnostic categories were differentiated in terms of the level and pervasiveness of social disability (more severe in AS).
Objectives: We have proposed to connect these two diagnostic categories into one, but with or without schizotypical symptoms.
Methods: We have examined and classified close to a hundred patients with primary diagnosis of Asperger syndrome by using DSM IV TR and Gillberg criteria.
Results: We have obtained roughly a 50/50 proportion between AS with and without schizotypical symptoms. The patients with AS and schizotypical symptoms were found to have better results in psychotherapy and did not have to take neuroleptics in contrast to children with classic AS.
Conclusions: We think that in the one illness we may have observed two kinds of AS: classic and with schizotypical factors, but also with a less intensivity of the core symptoms of AS. But if these schizotypical (more introversive) symptoms lead to the better prognosis, we may label it as the spectrum of Asperger Syndrome--from AS to Introversion.

50 145.5 FEAR OF NEGATIVE CLOSE VERSUS PUBLIC SOCIAL JUDGEMENT IN MOTHERS OF CHILDREN WITH AUTISM SPECTRUM DISORDERS. A. Rombough*[1], K. Hurd[1], C. Pederson[2], T. Elfers[1], J. Yager[1] and G. Iarocci[1], (1)*Simon Fraser University*, (2)*Kwantlen University College*

Background: Mothers of children with autism report anxiety when taking their child out in public because they fear negative social judgment (e.g. Koegel, 1992). Recent findings from our lab suggest that maternal Fear of Negative Social Judgement (FNSJ) is a significant predictor of parenting stress for mothers of children with autism.

Objectives: The current study attempts to define the construct of FNSJ by examining the correlates of Fear of Close Social Judgment (FCSJ) versus Fear of Public Judgment (FPJ) and their relations to parenting stress. FCSJ refers to a mother's concern that her close family and friends do not accept her child with autism. FPJ refers to a mother's fear that her child is not accepted by the public.

Methods: 68 mothers of children with autism spectrum disorders (mean age of 9 years) completed phone interviews. Participants completed 5 scales: the Parenting Stress Index Short-Form (PSI), Scales of Independent Behaviour-Revised Adaptive Behaviour Scale, Autism Behaviour Checklist, the Social Support Questionnaire and a revision of the Family Impact Questionnaire (designed to assess parent efficacy and fear of social judgment).

Results: Although both FCSJ and FPJ were significantly correlated with parenting stress, FCSJ was more highly correlated with maternal distress on the PSI (r = .70, p <.00) than FPJ (r = .46, p < .00). Mothers with a larger family support network reported less FCSJ (r = -.329, p <.00). The quantity of "autism-like" behaviours (e.g., echolalia, "flapping") displayed by their child was significantly correlated with maternal FPJ (r = .60, p < .00) but not FCSJ.

Conclusions: It is informative to conceptualize FNSJ as being comprised of FPJ and FCSJ given that separate factors are related to these more specific constructs. Future studies should explore whether high FCSJ is more detrimental to maternal mental health than elevated FPJ.

51 145.6 A Longitudinal Investigation of Behavioral Abnormalities in Autism. J. M. Phillips* and A. Y. Hardan, *Stanford University*

Background: Autism is described as a chronic condition with most individuals suffering from this disorder demonstrating changes over time in the core symptom deficits and in associated behaviors. Studies suggest that many children with autism show improvements in social interaction and reduction in repetitive behaviors, but a limited number of investigations have focused on the course of emotional and behavioral trajectories.
Objectives: This investigation was conducted to examine the development of emotional and behavioral functioning in school-age children with autism and to compare them with healthy normal controls.
Methods: Research data including the Child Behavior Checklist (CBCL) were collected from 13 boys with autism and 14 age- and gender-matched controls at baseline and at follow-up. The mean age of participants was 10.6 ± 1.4 years at baseline with an average 28.5 months interval to follow-up. The mean Full Scale IQ in the autism group was 90.8 ± 19.2, and 112.3 ± 12.9 in the control group.
Results: As expected, children with autism demonstrated clinically significant elevations (i.e. T scores ≥ 70) in several behavioral domains including Social Problems, Thought Problems, and Attention Problems at baseline and at follow-up. In contrast, no scores were elevated in the control sample at any time. Interestingly, changes in behavioral symptoms were observed between baseline and follow-up in children with autism, with these children showing significant reduction over time in overall Social Problems (p = .3); Rule Breaking Behavior (p = .26); Aggression (p = .13); Externalizing Behaviors (p = .002); and Total Problem Behaviors (p = .4).
Conclusions: School-age children with autism demonstrate social and behavioral deficits above those seen in their typical age-mates. However, the above findings suggest that as these children mature, they demonstrate significant improvements in social and behavioral functioning, including reductions in social deficits and problem behaviors.

52 145.7 NOVEL WEARABLE APPARATUS FOR QUANTIFYING AND RELIABLY MEASURING SOCIAL-EMOTIONAL EXPRESSION RECOGNITION IN NATURAL FACE-TO-FACE INTERACTION. A. Teeters[1], R. El Kaliouby*[1], M. Goodwin[2], M. Shandell[1] and R. W. Picard[1], (1)*Massachusetts Institute of Technology*, (2)*The Groden Center, Inc.*

Background: Many individuals on the autism spectrum have difficulties interpreting nonverbal cues such as facial expressions in real-time social interactions. There are currently no tools that measure social-emotional expression and understanding in natural face-to-face conversation.

Objectives: Our long-term aim is to develop technology interventions that help people on the autism spectrum to read facial-head gestures in real-time natural social interactions. To evaluate the efficacy of these technologies, an accurate baseline of recognition ability is needed, including testing dynamic expression recognition in familiar people and strangers.

Methods: We set up dyadic conversations including autistic-typical and typical-typical pairs, where each participant wore a tiny video camera to record facial and head movements. We collected over 100 videos of these natural

conversations, and then segmented them based on expressive content. Ten typically developing adults, who scored well on the Eyes Test, independently labeled the expressions in the videos and rated them for difficulty. We then formulated a test using video clips with the highest inter-rater reliability. The videos were balanced for difficulty and for six generalization conditions (self, peer, familiar adult, stranger, unknown actor from Mind Reading DVD).

Results: We achieved high inter-rater reliability in the expressive categories of *smiling, happy, thinking, unsure,* and *interested*. Samples from these categories were used in a preliminary assessment of 8 typical people and 5 individuals aged 18-20 with a diagnosis of high-functioning autism. Scores varied greatly among the participants on the spectrum, some of whom scored just above random while some approached the abilities of well-scoring neurotypicals. Self vs. other, familiar vs. stranger and other results will be presented.

Conclusions: Our technology and method for evaluating expression recognition accuracy on self, peers, and strangers *in situ* could have several applications to future social skills training in persons on the autism spectrum.

53 145.8 A New Predictor of Stress in Mothers of Children with Autism. K. Hurd*[1], C. Pedersen[2], J. Yager[1], A. Rombough[1] and G. Iarocci[1], (1)*Simon Fraser University*, (2)*Kwantlen University*

Background: Mothers of children with autism (CWA) often demonstrate clinically significant stress levels and high rates of depression (Tomanik et al., 2004; Abbeduto et all, 2004). Factors associated with maternal stress include parenting efficacy, social support and negative child behaviors. Mothers of CWA participate less in social activities, have smaller support networks, and reportedly fear that the public will not understand their child (Seltzer et al., 2001; Koegel et al., 1992). Thus, it appears fear of negative social judgment (FNSJ) may also contribute to elevated maternal stress levels. FNSJ may have further influences on child development by altering his/her social environment and community-learning opportunities (Bronfenbrenner, 1998; Iarocci et al., 2006).
Objectives: The current study investigates the addition of FNSJ (negative judgment by social network members and unknown people in public situations) as a possible predictor of maternal stress.
Methods: 68 mothers of CWA participated in a one-hour phone interview in which the Parenting Stress Index, Scales of Independent Behavior-R, Autism Behavior Checklist, the Social Support Questionnaire and the Family Impact Questionnaire (revised to assess parent efficacy and fear of social judgment) were administered.
Results: A simple regression analysis was used to examine FNSJ as a predictor of maternal stress levels. Overall, results indicated that the addition of FNSJ to the traditional predictors of maternal stress significantly predicted maternal stress levels (r^2 = .49, p < .001). FNSJ was found to be a greater predictor of maternal stress than either the child's adaptive behavior or maternal social network satisfaction.
Conclusions: The current study reveals that FNSJ, a previously un-examined construct, is a significant new and unique predictor of maternal stress. The assessment of FNSJ may help to identify mothers of CWA at high risk for adverse mental health outcomes and may have implications for programs/interventions aimed at supporting family functioning.

54 145.9 DEVELOPMENT OF A NEW TOOLKIT ENABLING WEARABLE WIRELESS AUTONOMIC NERVOUS SYSTEM COMMUNICATION FOR PERSONS ON THE AUTISM SPECTRUM. R. W. Picard*[1], M. Goodwin[2], R. Fletcher[1], H. Eydgahi[1], C. Williams[1], A. Marecki[1], C. H. J. Lee[1], R. Morris[1], K. Kim[1], S. Mota[1] and R. El Kaliouby[1], (1)*Massachusetts Institute of Technology*, (2)*The Groden Center, Inc.*

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, perspiration, discharge of urine, shifting of attention, signaling of anticipation and

salience, biasing of memory, and more. The autism literature includes many measures of ANS activity, showing, for example, that both skin conductance and heart rate responses in children and adults on the spectrum are generally increased or decreased compared to non-autistic controls. However, these studies have been limited to short intervals of measurement in research laboratories because the sensors are cumbersome, wired to medical devices, subject to motion artifacts, or prohibitively expensive.

Objectives: To develop low-cost tools enabling comfortable, wireless, ultra-dense accurate measurement and communication of in-situ ANS data for people on the autism spectrum while they go about natural activities.

Methods: We are constructing a wrist-worn wireless device that includes skin conductance, motion, and heart-rate sensing. We tested the skin conductance portion in four individuals with high-functioning autism while they engaged in a conversation with familiar teachers in a school and with one non-verbal 6-year-old diagnosed with autism for several days and nights of typical activity. We are evaluating comfort, ease of use, motion artifacts, and validity of data.

Results: All the participants tolerated wearing the device. We observed minimal motion artifacts. Concomitant analyses of skin conductance and conversational topic preferences revealed sensitivity to changes in arousability. Data capture from the non-verbal child showed skin conductance patterns during rocking, flapping, seizures, and sleep. We will present this data graphically with annotations, together with a live demonstration of the new technology.

Conclusions: We have the first working pieces of a low-cost, comfortable toolkit that will enable autism researchers and people on the spectrum to begin to characterize and communicate continuous ANS activity in natural environments.

55 145.10 Comparison of production of facial expressions by children with and without Autism. A. Biswas*[1], P. Mitchell[2] and O. Pascalis[1], (1)*University of Sheffield*, (2)*University of Nottingham*

Background: Facial expression production represents a vital part of non-verbal communication in everyday life which improves during development (Herba and Phillips, 2004). When presented on pictures, happy expressions are recognised at the age of two, sad and anger at four to five whereas fear, surprise and disgust are recognised only around the age of 10 (Gross and Baliff, 1991).

One of the cardinal features of Autism is atypical face processing, meaning complete disinterest in faces (Klin et al., 1999) and lack of facial expressions (ICD 10 and ADI-R).

Objectives: our aim was to compare facial expression production and understanding, in children with Autism (mean age of 12.1 and mean IQ of 96.3) and their matched controls.

Methods: Participants were filmed in the following situations: a-Baseline task - participants were asked to copy facial movements that are required to produce the 6 basic facial expressions to determine if the voluntary movement were possible. b-Participants were then asked to produce expressions on demand without any audio or visual cue. c-Lastly, twelve short stories were presented and participants were asked to label, then to produce each emotion felt by the main character.

Results: Two raters scored all videos. Chi-square tests showed that baseline tasks were performed well above chance level with no significant group differences. For production of facial expressions both with and without context and for emotion labelling tasks split-plot ANOVAs were performed. Both groups were equally good at producing happy, fear and anger but the autistic participants were significantly worse for disgust, surprise and sad. If labelling helps the overall production's performance in typical population it failed to do so in children with Autism with the exception of happiness.

Conclusions: Complex emotion production improved in typically developing children

within appropriate context but failed to do so in children with Autism.

56 145.11 Social responsiveness associated with psychopathology: a community-based study. S. Unal*[1], C. Dedeoglu[1], B. Taskin[1] and M. Y. Yazgan[2], (1)*Guzel gunler saglik hizmetleri*, (2)*Marmara Universitesi Tip Fakultesi*

Background:

While pervasive developmental disorders can present with symptoms commonly found in mood and anxiety disorders, children with varying degrees of impairment in social responsiveness may also display high on scales of psychopathology.

Objectives:

Impairment of social responsivity, a core feature of autism, at varying degrees may be associated with psychopathology other than autism itself. Clinical scores on the Social Responsiveness Scale (SRS) were proposed to provide a quantitative description ("socially impaired") of this core feature. We compared the children with clinical and nonclinical scores on SRS in a community sample, on parent ratings of psychopathology, to investigate the association between social responsiveness and psychopathology.

Methods:

The sample included 3892 students (age=10.6 ± 2.3 years; 53% males), 479 of who had been administered the same protocol two years before the current re-administration (age= 9.9,± 1.4 years; 51.1% males). Parents were asked to complete The Child Behavior Checklist (CBCL) and the Social Responsiveness Scales (SRS)

Results:

In the logistic regression analysis, CBCL attention (Wald score χ^2=5.5 p<.5), aggression (χ^2=9.1 p<.1) and anxiety (χ^2=12.7 p<.1) scores were significantly associated with having SRS scores in the 'socially impaired range'. The socially impaired group had higher t scores on sub measures of CBCL (total t(280)=17.47, p=.000, anxiety t(262)=13.90, p=.000, aggression t(299)=11.8, p=.000; attention t(259)=14.65, p=.000) when compared to the group with nonclinical SRS scores.

Conclusions:

Social impairment on SRS may be associated with symptoms of mood, anxiety and aggression in a community based sample, suggesting that the impairment in social responsivity, which is a key feature of autism, may also be linked to regulatory disturbances even in the absence the manifest symptoms of autism. These symptoms should be sought during the evaluation for autism to increase the detection rate of those treatable symptoms.

57 145.12 Validating a Japanese version of the Ritvo Autism and Asperger's Diagnostic Scale: a pilot study. K. Matsumoto*[1], K. J. Tsuchiya[1], E. R. Ritvo[2] and M. Tsujii[3], (1)*Hamamatsu University School of Medicine*, (2)*UCLA School of Medicine*, (3)*Osaka-hamamatsu Joint Center for Child Mental Development*

Background:

Currently it is estimated that approximately two in 1,000 people worldwide have Autism, about six per 1,000 for ASD, such as Asperger's Disorder (AD) however, this number is increasing (Baird et al., 2006). On the other hand, unfortunately the number of child psychiatrists in Japan is extremely limited and even then, those available may not have enough experiences to make a precise diagnosis. Moreover, assessing medical and long-time developmental history of adults is time-consuming, and the information may not be reliable enough, because the diagnostic process with an interview heavily relies on subjects' and families' memories. Screening tests for ASD such as The Autism-Spectrum Quotient Japanese version (AQ-J) and PDD-Autism Society Japan Rating Scales (PARS) are currently being used, but they still need a psychiatrist to make the final diagnosis. These limitations resulted in only a few studies have done on adults with these disorders in Japan; a problem faced with research is how to make

a reliable diagnosis without taking time in various clinical settings.

Objectives:

Before now we did not have any paper and pencil diagnostic tools for people with ASD however, Ritvo et al., (2007) developed a new diagnostic scale to distinguish people with and without ASD. This scale, the Ritvo Autism and Asperger's Diagnostic Scale (RAADS) is an 80 item scale to assist clinicians diagnosing ASD in adults. RAADS is based on ICD-10 and DSM-IV therefore, making it a reliable scale to determine specifically people with Autism and Asperger's Disorder according to the total scores. We translated the original RAADS into Japanese to test the validity of this scale.

Methods:

This pilot study included 33 normal adults as well as those with ASD (data is still obtaining). Statistical analyses of sensitivity and specificity will be presented.

Results:

available at the conference.

Conclusions:

available at the conference.

58 145.13 Attachment Behaviors in Young Children with Autism Spectrum Disorders: An Examination of Factors Associated with Separation and Reunion. R. L. Grzadzinski*[1], A. G. Spencer[1], R. Luyster[2] and C. Lord[1], (1)*University of Michigan Autism and Communication Disorders Center*, (2)*Autism Consortium*

Background:Previous studies have emphasized the need for additional research on attachment behaviors of toddlers with Autism Spectrum Disorders with their mothers and fathers.

Objectives:To identify how diagnosis, parental gender, and cognitive skills are related to toddler's responses in a modified Strange Situation Paradigm (SSP) with mothers and fathers.

Methods:Data were collected as part of an ongoing longitudinal study of children with ASD. Participants were referrals from four different regional state-funded sites (TEACCH Centers) in North Carolina and an autism center in Chicago. Participants were administered the PL-ADOS which included a modified SSP to elicit attachment behaviors of the children. Using diagnosis at age 9, 300 children were characterized as on the autism spectrum, 63 children as having non-spectrum developmental delays, and 56 children as typically developing. 390 children participated in a modified SSP with mothers and 125 children participated with fathers.

Results:*Separation:* Using generalized linear modeling, overall results indicate that neither diagnosis nor mental age were significant predictors of child response during separation to their mother or their father. However, children with ASD had significantly different responses toward mothers than fathers, *(*x^2=19.81, df=1, p<.001), which was not observed in typical or non-spectrum children. *Reunion:* Using generalized linear modeling, results indicated a significant effect of diagnosis for reunions with mothers, (x^2=14.705, df=2, p<.1). Children with ASD, unlike typical and non-spectrum children, had significantly different responses to their mothers than to their fathers, (x^2=6.84, df=1, p<.5). Moreover, mental age was significant in predicting reunion responses toward mothers [t(276)=5.10, p<.001] and toward fathers [t(62)=4.5, p<.001] in children with autism spectrum disorders.

Conclusions:These results build on previous studies supporting the importance of reunion behaviors in differentiating ASD from developmentally delayed and typical children, and also suggest that observations of social behavior with fathers may also be useful.

59 145.14 Symptom dimension in ASD. A study based on ADI-R and ADOS-G factor analyses. R. Igliozzi*, B. Parrini, R. Tancredi, A. Battaglia, C. Pecini and F. Muratori, *I.R.C.C.S. Stella Maris*

Background:

Many studies on ADI-R algorithm items pointed out a two-factor structure composed of a socio-communicative and a stereotyped behaviours factor, whereas factor analysis of the ADOS-G identified only the socio-communicative factor (Robertson, 1999; Lord, 1999, 2000; Constantino, 2004). Besides, recent findings suggest that the restricted, repetitive behaviour area may contribute to diagnostic stability (Lord, 2006). These findings suggest that the current ADI-R and ADOS-G structures need to be revised so that they can reflect more accurately the relationships between sub-scales and create algorithms composed of items that best differentiate between clinical diagnoses.

Objectives:

to individuate the factors underlining autistic symptoms as identified through ADI-R and ADOS-G in a sample of carefully diagnosed individuals with ASD.

Methods:

ADI-R and ADOS-G were administered to 70 ASD referred for diagnosis to a second level hospital. Participants included 56 individuals with Autism (mean age: 8.5years; sd: 3.5years; mean total IQ: 68,6; sd: 26,3) and 14 with PDD-NOS (mean age: 9.5years; sd: 3years; mean total IQ: 69,4; sd: 26,3). All subjects met the DSM-IV clinical criteria for the two diagnoses. Exploratory factor analyses were conducted on ADI-R and ADOS-G.

Results:

ADI-R shows two main factors grouping most of socio-communicative (22% of accounted variance) and restricted, repetitive sub-scales (19% of accounted variance). ADOS-G shows one main factor (% of accounted variance ranges from 18% to 38%) relating to socio-communicative area.

Conclusions:

This study confirms the studies of Robertson (1999) and Constantino (2004) and suggests that two factors underline two different functional systems in carefully diagnosed individuals with ASD. This study can help to organise the ADI and ADOS items into a new algorithm and could contribute to reorient future research in genetic of ASD.

60 145.15 CHANGES IN VARIOUS CLINICAL MEASURES IN PATIENTS WITH ASPERGER DISORDER AND PDD-NOS. EFFECTS OF A GROUP TREATMENT

O. F. *. L. S. ;. V. M. ;. P. O. ;. C. R. ;. C. Ojados*, *Clínic Hospital (Barcelona)*

Background:Pervasive Developmental Disorders (PDD) are characterized by delays in the development of multiple basic functions, especially in language and communication deficits and lack of social relationships. Cognitive deficits embrace stiffness, short number of interests, motor stereotypical behaviour and lack of mental theory. Asperger patients have higher verbal performance, however, their language, including their non-verbal communication, is unfit in a multitude of social situations.

Objectives:The training in social skills, abilities of effective communication, and empathy, among others, are shown as important parts of psychology treatment to patients with this disorder.

Methods:In our study, parents of eight children (8 to 10 years of age) who were diagnosed with Asperger disorder or PDD-NOS completed a series of questionnaires (Childhood Asperger Syndrome Test CAST, Australian Scale for Asperger Disorder, and Vineland developmental scales) and answered the Autism Diagnostic Interview ADI-R. Children attend social and emotional skill groups during 9 month period (October to June), one every 15 days. The contents in the group are dynamically trained, with role-playing and tasks to do in their natural context (home and school). The themes learned are: recognition of feelings, self-control, problem solving, communication skills (assertiveness, improved eye contact...), self-esteem...

Results:A global scores improvement in the questionnaires (to be assessed on March 2008) is expected only after the patients have completed most of the group sessions. We especially hypothesize that in ADIR-R, language and communication performance, social and play development, and aggressive

behaviour will improve significantly in comparison to the answers obtained at the beginning of the course.

Conclusions:Attending to the questionnaires, in the Australian scale, improvements in scores (under a 2 in more items than in the pretest) are hypothesized as well as in the social-emotional and communication scales, in the Vineland and in the CAST test, it is expected that the overall scores decrease.

61 145.16 Mother-Child Interactions Predict One-Year Changes in Autism Symptoms and Co-occurring Problems in Toddlers with an Autism Spectrum Disorder. S. A. Grossman*[1], A. S. Carter[2] and K. Wachtel[2], (1)*Boston University*, (2)*University of Massachusetts Boston*

Background: Maternal behaviors including synchrony, responsiveness, and directiveness predict language and social-emotional gains in typically and developmentally delayed children. There is also some preliminary evidence that they predict similar gains in toddlers with autism spectrum disorders (ASD).

Objectives: Examine the relation between a mother's parenting behavior with her toddler with ASD and changes in the toddler's ASD-related symptoms and problem behaviors one year later.

Methods: Ninety-nine mothers and their toddlers between 18 and 33 months with an ASD diagnosis participated a longitudinal research study. Developmental level was assessed using the Mullen Scales of Early Learning, autism symptoms were assessed using the Autism Diagnostic Observation Schedule (ADOS), and problem behaviors were assessed by parent report on the Infant-Toddler Social and Emotional Assessment (ITSEA). Mother-child interactions were rated on dimensions of parenting and dyadic engagement using the Parent-Child Interaction Rating Scale (PCIRS) from a 7 minute mother-child play episode in Year 1 (Y1). Factor analysis yielded 3 composite variables: Sensitive Engagement (Cronbach's Alpha = .81), Disengaged (Chronbach's Alpha = .73), and Cognitive Engagement (Chronbach's Alpha = .81). Mothers and children completed the same assessments 1 year later, however only Y1 PCIRS was used in this analysis.

Results: Mean child age was 28 months, range = 18–33 months, and 75 % were male. Analyses indicated that, when controlling for the child's age and developmental level at Y1, Disengaged parenting was significantly associated with increases in communication problems (ΔR^2=.33) and social difficulty symptoms (ΔR^2=.46) on the ADOS. For children with higher developmental scores in Y1, Disengaged parenting was also associated with greater gains in dysregulation (ΔR^2=.36) and internalizing symptoms (ΔR^2=.64).

Conclusions: Findings emphasize the importance of parenting behaviors for optimal social-communication and emotional development in toddlers with ASD, and thus have important implications for clinical practice.
Sponsor: NIMH
General Clinical Research Center

62 145.17 Assessment of social competence by preschool teachers in children with the Autism Spectrum Disorder. J. Kodric*, P. Lesnik Musek, D. Gosar and M. Macedoni-Luksic, *University Medical Centre Ljubljana, Division of Paediatrics, Department of Neurology*

Background: Impaired social interaction and communication are beside a restricted repertoire of activities and behaviours the core features of Autism Spectrum Disorder (ASD). As these feature manifests themselves by the age of three they may greatly hamper the child's inclusion into preschool institution and may require special educational interventions.

Objectives: The aim of the study was to assess the behavioural characteristics of children with ASD by preschool teachers by using the Slovenian adaptation of the Social Competence and Behavioral Evaluation (LaFreniere, Dumas, Zupancic, Gril & Kavcic, 2001).

Methods: Our study included 33 children between the ages 31 and 80 months of age (*M*=54 months) who were given the diagnosis of ASD based on DSM-IV criteria. The teachers observed and rated the children's social

adaptation and functioning within the preschool classroom.

Results: The group of children with ASD received lower general competence scores (t=9.77, p<.001) on the SBCE, as well as lower scores on the externalizing problems (t=2.63, p<.13) and internalizing problems summary scales (t=7.56, p<.001). Teachers noted the greatest difficulties on the social competence summary scale (t=12.88, p<.001), with 79% of children scoring in the clinical range. Teacher's ratings on basic scales also revelled children with ASD included in the study had specific difficulties in emotional regulation, peer- and adult-relationships. They were rated as more anxious (t=9.17, p<.001), isolated (t=12.36, p<.001) and egotistical (t=9.84, p<.001).

Conclusions: The results indicate that the group of Slovenian preschool children with ASD included in our study shows a different pattern of behavioural features than the normative sample. The observed behavioural difficulties may be a starting point to help teachers plan the individualized intervention program in the preschool setting.

63 145.18 BEHAVIORAL OBSERVATIONS OF CHILDREN'S RESPONSES TO OTHERS' DISTRESS PREDICT TEACHER RATINGS OF SOCIAL ABILITIES. A. C. Kemp*[1], M. Siller[1], T. Hutman[2], P. Chan[1] and M. Sigman[2], (1)*Hunter College/ City University of New York*, (2)*UCLA*

Background: Children with autism spend less time gazing at an adult showing distress than matched controls of typically developing children or those with global developmental delays (Sigman et al., 1992). Individuals with autism also show a broad range of social deficits, observable both at home and at school.

Objectives: The current study aims to investigate the relation between children's response to others' distress and parent/teacher reports of a broad range of social behaviors.

Methods: The sample included 63 individuals with autism aged 33-82 months (M=57.2 months). To evaluate responses to distress displayed by others, children participated in an observational procedure in which an examiner pretended to hit her thumb with a toy hammer and cried audibly for 30 seconds. Duration of child gaze orientation to parent, examiner, and toy was coded from videotape using The Observer (NOLDUS). Two independent observers established inter-observer reliability (ICC≥.88 for all measures). To evaluate a range of social abilities, children's parents and a familiar teacher were asked to complete one subscale of the PDD Behavior Inventory (PDDBI; Cohen, Schmidt-Lackner, Romanczyk & Sudhalter, 2003). The PDDBI subscale covers a range of social approach behaviors including positive affect, empathy, social imaginative play, and social interaction behaviors. Children were also administered the Mullen Scales of Early Learning (MSEL).

Results: A significant correlation was found between the time children spent gazing at the parent/examiner during the distress paradigm and teacher reports of children's social behavior (PDDBI), r=.35 (P<.1). This relationship remained significant, even when verbal/nonverbal functioning (MSEL) and chronological age were statistically controlled. No significant correlation was found between parent ratings of children's social abilities (Parent PDDBI scores) and our measure of children's responses to others' distress.

Conclusions: This research suggests that children's early responses to emotions displayed by others may play an important role in children's social development.

64 145.19 Action Prediction in Individuals with Autism Spectrum Disorder. V. Lee*, E. Kelley and J. R. Flanagan, *Queen's University*

Background:

Individuals with ASD have difficulties interpreting the goals of others. Previous studies with neurotypical adults have found that they exhibit proactive rather than reactive eye movements when observing goal-directed actions. In this context, the participants' eye movements predicted the goals of another's

actions, rather than simply tracking their movements.

Objectives:

Using eye-tracking technology, this study investigates the prediction of other's goals in individuals with ASD. We will examine whether adults with ASD engage in reactive or proactive eye movements while watching both themselves and others perform simple goal-directed movements (i.e. stacking blocks).

Methods:

Participants consist of 30 adults- 15 with ASD and 15 neurotypical controls. Eye gaze from each participant are recorded using a video-based ETL 500 pupil/ corneal eye-tracking system. Additionally, the position of the participant's thumb is recorded using FASTRAK miniature electromagnetic sensors attached to the nail in order to calibrate eye movements. Eye movements are measured to determine whether the participants predict the actions of their own movements ("action" condition) and those of others ("action observation" condition), or simply track those movements (reactive gaze).

Results:

We are still in the process of data collection. Data will be analyzed to determine if there is a significant difference between amounts of predictive gaze during both "action" and "action observation" tasks between the two groups.

Conclusions:

If adults with ASD exhibit reactive rather than proactive eye movements during "action observation" task, we would hypothesize that the difficulties individuals with ASD have in social understanding may be derived from a very low-level inability to understand goal-directed movement. If adults with ASD exhibit proactive eye movements during the "action observation task", this would suggest that their pervasive social difficulties derive from a deficit in a higher-level cognitive ability rather than simple goal perception.

65 145.20 The Autism-Spectrum Quotient and its relationships with Emotional Intelligence and the Broader Autism Phenotype Questionnaire. M. Stewart*[1], A. Fugard[2], L. Downey[3], C. Stough[3] and E. Austin[2], (1)*Heriot-Watt University*, (2)*University of Edinburgh*, (3)*Swinburne University*

Background: The Broader Phenotype of ASD is coming under increasing scrutiny. Relatives of individuals on the autism spectrum show milder traits, which are qualitatively similar to the features of disorder. Two self-report measures assess the broader phenotype, where individuals of normal intelligence can be assessed for autistic traits; the Autism-Spectrum Quotient (Baron-Cohen et al., 2001); and the Broader Autism Phenotype Questionnaire (BAPQ; Hurley et al., 2006).

Objectives:

Although studies have assessed, for instance, the utility of the AQ as a screening tool (Woodbury-Smith et al. 2005; Kurita et al. 2005) and its ability to predict performance on social cognition tests (Baron-Cohen et al., 2001; Bayliss & Tipper, 2005), there is still relatively little known about how scores on the AQ relate to other measures. This study aims to test the relationships of the AQ with the BAPQ and Emotional Intelligence (Swinburne University Emotional Intelligence Test; SUEIT, Palmer & Stough, 2001).

Methods:

Participants were recruited from universities in Edinburgh. Participants completed the AQ and either; the SUEIT (n=536; 303 males and 230 females); or the BAPQ (n=184; 67 males and 117 females).

Results:

Total AQ and SUEIT scores were negatively correlated. In general AQ and SUEIT subcomponents were also negatively correlated. AQ and BAPQ total scores were highly correlated and there were large positive correlations amongst most subcomponents. In both cases Attention to Detail subscale was, however, uncorrelated with any SUEIT or BAPQ component.

Conclusions:

Recent studies have shown a 3 factor structure for the AQ of social skills, details/patterns and communication/mind reading (Austin, 2005; Hurst, Mitchell, Kimbrel, Kwapil, & Nelson-Gray, 2007). This study finds that the Attention to Detail subscale is unrelated to emotional processing and to the BAPQ. The exact nature of the broader autism phenotype and which measure most accurately assesses it requires further study.

66 145.21 Gender Differences in Autistic Spectrum Disorders. R. Chilvers*[1], W. Mandy[1], A. Seigal[1], G. Salter[1], U. Chowdhury[2] and D. H. Skuse[1], (1)*Institute of Child Health*, (2)*Dunstable Health Centre*

Background: Autism spectrum disorders (ASDs) are more common in males than females. The gender-ratio increases (up to 10:1 or more) with greater intellectual ability. Males may be generally more vulnerable to genetic risk of ASD. Alternatively, our current conceptualization of autism could be biased toward recognising the male phenotype, leading to underdiagnosis in females. To date, attempts to differentiate the female ASD phenotype have yielded inconsistent results, which may be due to the use of small samples and an excess of intellectually low-functioning participants.

Objectives:

We aimed to test, in a large clinically ascertained sample with normal range intelligence, the consistency of the phenotypic profile of males and females diagnosed with autistic spectrum disorders. Our main objective was to derive precise quantitative measures of impairment. To this end we identified similarities and differences, by gender, using detailed phenotyping based upon a range of standardized measures of behaviour.

Methods:

Data from parental report, questionnaires and observational measures were analysed for a total sample of 493 boys and 100 girls. A smaller age and IQ matched sample of cases (25 boys and 25 girls) was examined in greater detail, to identify more subtle characteristics, in terms of both qualitative and quantitative features, of conventionally ascribed autistic behaviour.

Results:

There were no differences in terms of social or language deficits, in terms of quantity or quality, between the sexes. Girls showed significantly fewer stereotyped and repetitive behaviours than boys and, when present, these behaviours differed significantly from the male pattern in several qualitative characteristics. There were no group differences in general intellectual ability. However, a history of epilepsy and disorders of affect was signficantly more common amongst females with ASD.

Conclusions:

Gender differences in the severity and symptomatic content of repetitive and stereotyped behaviours may lead to a bias against the identification of high-functioning girls with ASD.

67 145.22 Emotion Regulation in Children with and without Autism: The Contribution of Temperament, Executive Function, and Sensory Experiences. L. B. Jahromi*[1] and S. E. Ober-Reynolds[2], (1)*Arizona State University*, (2)*Southwest Autism Research & Resource Center (SARRC)*

Background: Children with autism often show difficulty regulating their emotional reactions and behaviors, as is evidenced by lengthy tantrums and trouble returning to a calm affective state (e.g., Loveland, 2005). Emotion regulation is a critical dimension of typical children's healthy social development and is regarded as an important element of adaptive functioning in social settings for children with ASD. However, there exists limited work to date explaining individual differences in emotion regulation for this population.

Objectives: To investigate emotional competence in children with autism and a

comparison sample of typically-developing children. We will examine expressions of frustration and coping strategies, and whether executive function and sensory experiences explain individual differences in children's emotional competence.

Methods: Participants in the complete study will include 15 children with autism (3 - 6 years) and 15 typically-developing matched children. Measures include a battery of laboratory tasks designed to measure self-regulation and parent questionnaires, including the Child Behavior Questionnaire (CBQ), Sensory Experiences Questionnaire (SEQ), Behavior Rating Inventory of Executive Function-Preschool Version (BRIEF), and Parents' Reports of Children's Coping Reactions.

Results: Preliminary data on nine children with autism indicate variability in the types of coping strategies parents report their children to typically use in stressful social situations. Venting and support-seeking were the most common responses, and instrumental or cognitive restructuring strategies were used least frequently. Children whose sensory experiences were rated by their parents as more hyper-responsive were reported to engage in less attentional focusing, and those rated as more hypo-responsive were reported to have more inhibitory and emotional self-control issues. Further analyses on the complete data set are in progress to assess group differences and to include observed measures of emotional competence from laboratory tasks.

Conclusions: Preliminary findings suggest meaningful individual differences in measures of children's emotion regulation, executive function, and sensory experiences.

68 145.23 VISUAL ATTENTION IN YOUNG CHILDREN WITH AUTISM SPECTRUM DISORDERS. L. B. Swineford, L. Book*, A. M. Wetherby, D. McCoy and A. M. Plumb, *Florida State University*

Background: Few studies have investigated visual attention of children with Autism Spectrum Disorders (ASD) under 24 months of age.
Objectives: The purpose of this prospective, longitudinal study of the FIRST WORDS Project was to describe differences in visual attention in 18-24 month old children with ASD, developmental delay (DD), and typical development (TD).
Methods: Videotapes of *CSBS* (Wetherby & Prizant, 2002) Behavior Samples for 125 children (50 ASD, 50 TD, and 25 DD) were analyzed using the Noldus Observer Pro 5.0 to obtain precise measures of visual attention. Duration measures included the time needed to orient to target objects, attention focused on target objects, and time to shift attention from objects to a person's face. Frequency measures included the number of times that the children looked at objects and people and how many times they shifted their attention from the objects to a person's face.
Results: The visual attention characteristics that distinguished children with ASD were the number of times the children looked at a person's face and the ability to shift attention from a target object to a person's face. The results indicated that children with ASD took significantly more time to shift gaze to a person's face than children with TD. Children with ASD looked at faces and shifted gaze from object to face significantly less often than children with DD and TD.
Conclusions: Building on previous research on social orienting deficits in children with ASD, the results of this investigation indicate that children with ASD at 18 to 24 months have a more difficult time shifting their attention from objects to people. These findings highlight the importance of incorporating a measure of visual attention in the screening and assessment process to improve early identification of ASD.

69 145.24 Empathic Responding and Attachment Security in Young Children At Risk for an Autism Spectrum Disorder. N. M. McDonald*, J. D. Haltigan, K. M. Kelley and D. S. Messinger, *University of Miami*

Background: In typically developing (TD) children attachment security has been associated with the development of empathy, possibly via the development of a theory of mind. However, children with Autism

Spectrum Disorders (ASDs), while demonstrating attachment security at a behavioral level, often have deficits in their theory of mind and empathizing skills. An important question regarding children at risk for ASDs is whether attachment security promotes a developmental climate more favorable for the development of empathy in these children, despite potential difficulties in theory of mind development. Moreover, no studies have explored the development of attachment security or empathy in the infant siblings of children with ASDs (ASD-sibs). Longitudinal research examining the development of attachment security and empathy in samples at risk for ASDs is needed.

Objectives: To investigate the early development of attachment security and empathy in ASD-sibs as compared to TD-sibs.

Methods: 20 TD- and 20 ASD-sibs were measured for attachment security at 15 months and empathic responding at 24 months. Attachment security was assessed using the Strange Situation procedure. Empathic responding was measured from children's responses to parental distress during a free play session.

Results: Initial classification of a subset of our sample has revealed secure and resistant organized attachment strategies as well as evidence of attachment disorganization. A preliminary review of our empathy protocol suggested a wide range of empathic responses. Exploration of whether attachment security differentially influences the empathic responding abilities of the TD- and ASD-sib groups will be conducted using hierarchical regression procedures.

Conclusions: Investigation of infant attachment security and the development of empathy in children at risk for ASDs is important to better understand the singular and combined roles of these constructs in the early social and emotional development of ASD-sibs.

70 145.25 High Functioning Autism: The Relationships among Social Skill Execution, Symptom Expression, and Feelings States. M. Levine*[1], R. J. Calvanio[2], C. O'Callaghan[3] and H. Fishbein[4], (1)*SymTrend, Inc.*, (2)*Massachusetts General Hospital*, (3)*South End Community Health Center*, (4)*Children's Services Council of Broward County*

Background: Persons with Asperger's Syndrome/High Functioning Autism (AS/HFA) differ considerably in social skills execution, predominant autistic symptoms, and intensity of emotions and other feelings. These individual differences raise questions about the nature of the relationship among social skills, autistic symptoms, and feeling states in this population.

Objectives: To elucidate the interrelationships among social skills execution, symptom expression, and feelings expression and to use this elucidation to inform interventions to improve self-understanding and social functioning.

Methods: Twenty students diagnosed with AS/HFA were studied in autism spectrum-only classrooms. Feelings and social skill were measured on a day-to-day basis by teachers and by students using an electronic diary system (EDS) on handheld computers. Autism symptoms were ascertained from conventional rating scales (GARS, GADS, Conners) completed by the teachers.

Results: Findings indicated that (1) feelings status was highly correlated with social skill execution, both on a group and on an individual basis, (2) feelings status typically influenced social skill more than vice versa, and (3) feelings status modulated the relationship between social skills execution and symptom expression.

Conclusions: These findings imply that social skills intervention programs must incorporate a feelings recognition and management component, particularly when there is a psychiatric co-morbidity. In addition, the pattern of correlations among rating scale symptoms, social skill execution, and feelings level can be used to identify which symptoms present the greater obstacles to more successful social functioning. For example, the correlation pattern obtained suggests that in a classroom setting, symptoms of reduced social

reactivity are most indicative of abnormality, and count for more in the evaluation of social skill compromise than do symptoms of reduced social initiation.

71 145.26 Beliefs and attitudes toward ASD among African American and caucasian American parents. S. Maina*[1], J. Weru[2] and J. Brown[3], (1)*International special education coalition*, (2)*NEURODEVELOPMENTAL TREATMENT AND RESEARCH CENTER*, (3)*MIND INSTITUTE*

Background:Full participation and equality of opportunity are internationally accepted goals for persons with disabilities. However, persons with ASD face many obstacles in trying to gain access to available services and in obtaining assistance to meet their special needs. Some of these barriers are physical, but more often they are attitudinal. Still, some are due to beliefs about the causes of disability which in return give parents help seeking direction.

Objectives:It was hypothesized that beliefs about ASD and causal attribution of ASD will independently predict help seeking behaviors for both groups

Methods:A survey method was used to determine the existing beliefs, attitudes and help seeking behaviors among parents of children with ASD. Participants were parents of children between the ages of 5-14 (40 African Americans and 40 Caucasian Americans).

Results: Supernatural beliefs were held by a significant number of parents. These beliefs are significant if held by parents, because they may interfere with intervention efforts. The most negative misconceptions were rejected by an average of 68% of persons, though a realistic 26% thought that persons with ASD could be a burden sometimes.

Conclusions: As predicted, beliefs and causal attribution of ASD independently predicted help seeking behaviors for both African Americans and Caucasian Americans. Specifically, individuals with less negative beliefs about ASD , attribute causes to psychosocial factors are more likely to report willingness to seek psychological help, while those with negative beliefs about disorders, attribute causes to supernatural factors are more likely to report willingness to seek culturally appropriate help.

72 145.27 Help seeking behaviors and differential utilization of services by parents of children with ASD. J. Weru*[1] and J. Brown[2], (1)*NEURODEVELOPMENTAL TREATMENT AND RESEARCH CENTER*, (2)*MIND INSTITUTE*

Background: While autism has been heavily studied, little is known on the factors influencing help seeking behaviors and thus differential utilization of services by different cultural groups. What we know is that African Americans tend not to seek help but gap remains as to why this is.
Objectives: The research question addressed in this study is whether there are factors that influence help seeking behaviors and thus the differential utilization of services. Further, do these factors differ by culture?
Methods: Help seeking behaviors of 80 parents of individuals with ASD (40 Caucasian Americans 40 African Americans) parents of children with autism between the ages of 5-14 were studied. Help seeking behaviors and service utilization questionnaires were used. Data was analyzed using SPSS.

Results: There were significant differences on help seeking behaviors among the two groups. The direction of the difference indicated that African American parents sought help less despite the fact that their children seemed to be more severe. However, Caucasian American parents from low social economic backgrounds showed similar trend. In fact, 90% of African American children participating in the study were non-verbal. It also took these two African Americans longer to receive an official diagnosis which further delayed services. Conclusions: Although this study is far from conclusive, its findings suggest the existence of both systemic, cultural and individual factors that influence help seeking behaviors of parents of children with ASD. While participants described discussed here represent only an example of African American and Caucasian groups, the impact cannot be ignored especially given the fact that for ASD,

early diagnosis means early intervention and thus improved developmental outcome.

73 145.28 Intentions, Social Development, and Mirror Neurons in Autism. C. Colombi*[1], C. Saron[1], S. Rivera[2] and S. Rogers[3], (1)*UCDavis/M.I.N.D. Institute/Center for Mind and Brain*, (2)*U.C. Davis, Psychology/M.I.N.D*, (3)*UC Davis M.I.N.D. Institute*

Background: A mirror neuron system (MNS) dysfunction has been proposed as the neurobiological substrate responsible of the socio-cognitive impairments in autism. However, some recent behavioral experimental evidence suggests that children with autism are not impaired in all the functions thought to be supported by the MNS, particularly understanding of intentions of actions on objects. Thus, the hypothesis of a general malfunctioning of MNS in people with autism is difficult to reconcile with their ability to understand intentional acts on objects.
Objectives: (1) to confirm that children with autism show no specific impairment in understanding others' intentions on objects; (2) to examine mu wave suppression through EEG recording as an index of MNS activation in children with autism.
Methods: four successful intentional trials and four failed intentionality trials administered to 15 young children with autism and 15 with other developmental disabilities matched on CA and non verbal abilities.
Results: Analysis involved a mixed 2 between group (autism vs. DD) by 2 within group (imitation [e.g. successful intention] vs. intentionality [failed intention]) factorial design. Significant main effect of group ($F=5.35$; $p<.5$) was found in the successful intention condition, but not in the failed intention condition.
Based on these results, we propose to examine mu wave suppression as an index of MNS activity in autism and typical development when children are presented with: 1) transitive movements and 2) intransitive movements. We hypothesize an interaction of task by group in which the autism group will demonstrate abnormal MNS activation only in tasks involving intransitive movements.
Conclusions: Children with autism showed preserved abilities to understand others' intentions on objects. The hypothesis of a malfunctioning MNS in people with autism needs further empirical investigation. At the moment, a generalized impairment of the MNS does not fully explain the behavioral phenotype of autism.

74 145.29 Conversational Turn-taking in Children with Autism: Deconstructing reciprocity into specific turn-taking behavior. M. Arie*, A. Tartaro and J. Cassell, *Northwestern University*

Background: Complex dynamics in peer interactions, e.g. non-systematic turn allocation and quick topic transitions, are difficult for children with autism and hard to target in intervention (Charman & Stone, 2006). Following Merrell's (2001) argument that effective intervention requires assessment, and Charman & Stone's (2006) call to merge naturalistic and eliciting approaches in social interventions, we present an assessment that deconstructs the general concept of "lack of reciprocity" into a structured measure of specific turn-taking behaviors with peers and its application to social skills intervention.

Objectives: To identify specific, measurable turn-taking behaviors for assessment-based intervention.

Methods:Five children with high-functioning autism, ages 7-10, matched with a same-age, typically-developing (TD) peer were asked to tell stories using toys. To pinpoint specific behaviors, we analyzed fourteen aspects of turn-taking that characterize typical conversations (Sacks, Schegloff and Jefferson, 1974). We compared children with autism to their TD partners.

Results: We identified violations more often in children with autism than the TD children affecting the following: (1) speaker change occurrence: *turn was not taken unless asked a direct question*; (2) gaps in transitions: *response follows long pause*; (3) discourse continuity: *no reciprocity to sustain conversation*; (4) turn-constructional units: *rigidity in turn length*; (5) turn allocation: *initiations and responses to peer initiations lacking*. Violation categories varied across

individuals but suggested behavior patterns to structure intervention procedures.

Conclusions: We extend studies of peer interaction by providing specificity needed for assessing and modeling natural interactions. Results are first steps towards developing comprehensive assessment of social reciprocity and contribute to designing technology-based interventions that model natural interactions. *Virtual peers* (computer-animated children) that elicit social interaction and model naturally occurring verbal and nonverbal behaviors may address limitations of social interventions with adults (National Research Council, 2001) or trained peers (Lord & Hopkins, 1986).

75 145.30 PILOT USE OF PDA TECHNOLOGY TO TEACH TEENS WITH ASD & NLD ABOUT FLEXIBILITY, FEELINGS AND SENSORY STATES AT A THERAPEUTIC SUMMER DAY CAMP. D. A. Lucci*[1] and D. S. McLeod[2], (1)*MGH/YouthCare*, (2)*MGH Charlestown*

Background: ASD and NLD individuals demonstrate difficulties in cognitive flexibility, social awareness, emotionality and sensory regulation. They have difficulty identifying how these areas impact their social success.

Objectives:To increase the self-awareness of adolescents diagnosed with ASD and NLD in the following areas: social awareness, feeling states, cognitive flexibility and sensory awareness (engine speed) through the use of a PDA.

Methods: Eleven ASD teens and one NLD teen (males, ages 13 – 17) were enrolled in a 7 week 5 day/week summer program. On multiple occasions per day they and four staff recorded simultaneous data for feeling states, sensory states, cognitive flexibility and group participation.

Results: Correlations were computed to evaluate group differences between staff and teen perception recordings on the above measures. In the emotionality arena moderate levels of agreement on the happiness scale were found between staff and teens. No agreement was found on the anxiety scale. While reviewing the graphic representation of anxiety on staff and teen data, teen awareness and insight improved. Staff perception of teens' level of flexibility correlated with the perception of the teens' positive group participation. But teens' perception of their flexibility did not correlate with their perceived level of positive group participation. Concurrent discussions of the data allowed for an individual teen's perspective of flexibility to be elucidated with positive outcome.

Conclusions: For individuals with ASD and NLD, PDAs for data collection and as a teaching tool are valuable. Graphical representations fostered discussion on perceptions of cognitive flexibility, engine speed and feelings states and their influence on social success. Further research using objective data collection (e.g. heart rate, skin conductance etc.) in addition to self and observer reports should be explored.

Poster Presentations Program

146 Clinical Phenotype Posters 2

76 146.1 ABERRANT SIGNAL TRANSDUCTION AND MEMBRANE ABNORMALITIES IN AUTISM. V. Chauhan* and A. Chauhan, *NYS Institute for Basic Research in Developmental Disabilities*

Background: We have reported previously that the levels of aminoglycerophospholipids are altered in autism. There was a decrease in phosphatidylethanolamine (PE) and an increase in phosphatidylserine (PS) in the erythrocyte membrane of autistic subjects, resulting in decreased molar ratio of PE to PS. We also reported increased membrane rigidity in autism. These studies suggest that membrane lipid metabolism and cellular signaling associated with membrane functions may be altered in autism.

Objectives: To study membrane lipids in lymphoblast membrane from autism, and activities of enzymes involved in signal transduction such as phospholipids hydrolyzing enzyme (phospholipase A_2 -PLA_2), protein phosphorylating enzymes such as protein kinase C (PKC) and protein kinase A (PKA), and Ca^{2+}/Mg^{2+}-ATPase.

Methods: Phospholipid phosphorus was measured in lymphoblasts. Ca^{2+}/Mg^{2+}-ATPase activity was measured in the erythrocyte membrane. Phospholipase A_2 activity was measured in the cytosol of lymphoblasts. PKC and PKA activities were measured in the lymphoblasts using protein kinase non-radioactive assay kits.

Results: PE to PS ratio was decreased in the lymphoblast membrane of autism. PLA_2 activity was increased in the lymphoblasts of autism as compared with controls, suggesting that arachiodonic acid-mediated signal pathways may be altered in autism. We also studied the activities of membrane-associated enzymes that control the cellular signaling. The activity of Ca^{2+} / Mg^{2+}-ATPase was higher in erythrocyte membrane of autism as compared to controls, suggesting that intracellular calcium levels may be altered in autism. We then measured the Ca^{2+}-dependent PKC activity in the lymphoblasts from autism and control subjects. PKC activity was decreased in both cytosolic and membrane fractions in autism as compared to controls. On the other hand, the activity of cAMP-dependent PKA was increased in autistic lymphoblasts as compared to control lymphoblasts.

Conclusions: Autism is associated with membrane phospholipids abnormalities, and alterations in the membrane-associated enzyme activities involved in cellular signaling pathways.

77 146.2 Trends in U.S. Autism Research. J. Singh*, J. Illes, L. Lazzeroni and J. Hallmayer, *Stanford University*

Background: During the last two decades autism has moved from relative obscurity to the center of media attention and public awareness. No other childhood disorder has seen such an increase in fund raising activities and lobbying for federal dollars. The National Institutes of Health, and two advocacy groups, the National Alliance for Autism Research and Cure Autism Now (now Autism Speaks) support the majority of autism research.

Objectives: To examine trends in autism research funded in the U.S. between the years of 1997 and 2006.

Methods: Funding data for autism research were collected from three sources: the U.S. National Institutes of Health (NIH), Cure Autism Now (CAN) and the National Alliance for Autism Research (NAAR). We examined changes over time in the numbers and proportions of projects of specific themes (i.e., "brain and behavior", "genetics", "environment", "treatment", "epidemiology", "diagnosis", and "family and services" and types of research (i.e., "Basic"; "Clinical"; or "Translational") using standard Poisson and logistic regression.

Results: The number of autism research grants funded in the U.S. from 1997 – 2006 significantly increased 15% per year ($p<0.001$). Although the majority of projects were concentrated in basic research (65%) compared to clinical research (15%) and translational research (20%), we observed a significant decrease in the proportion of basic research grants per year and a significant increase in the proportion of translational projects per year ($p<0.5$). The number of translational projects funded by NAAR and CAN increased significantly, whereas the number of clinical projects significantly increased for the NIH ($p<0.001$). The focus of newly funded projects within basic sciences is dominated by brain and behavior, and genetics research, regardless of whether the funding is provided through federal agencies or parent advocacy groups.

Conclusions: This study demonstrates the shifting landscape of autism research from basic science to clinical and translational research.

78 146.3 Trajectories of Cognitive Development in Later-born Siblings of Children with ASD. J. H. Foss-Feig*, C. R. McMahon, P. J. Yoder and W. L. Stone, *Vanderbilt University*

Background: Autism is a highly-heritable neurodevelopmental disorder with sibling recurrence estimated at 4%-10%. The outcomes of later-born siblings of children with

ASD (Sibs-ASD) are heterogeneous, and include autism or PDDNOS, language delays, characteristics of the broader autism phenotype (BAP), and typical development.

Objectives: To identify developmental trajectories in cognitive functioning associated with varying outcomes in Sibs-ASD.

Methods: Cognitive functioning of 35 Sibs-ASD and 30 younger siblings of typically developing children (Sibs-TD) was assessed using t-scores from the four Mullen Scales of Early Learning subscales at two time-points, approximately 18 months apart (T1 mean CA:15 mo; T2 mean CA:34 mo). At T2, Sibs-ASD were classified into 3 outcome groups based on ADOS scores and clinical judgment: ASD, BAP, and no ASD concerns (NC), and compared with Sibs-TD. A mixed-design MANOVA was used to examine changes over time within and between groups.

Results: Results revealed a significant main effect of Group for the Visual Reception (VR) (p=.41), Receptive Language (RL) (p=.007), and Expressive Language (EL) (p=.001) subscales, with the ASD group scoring lower than the BAP, NC, and Sibs-TD groups. The NC group did not differ from Sibs-TD on any subscale. A significant main effect of Time was found for the EL (p=.1) and Fine Motor (FM) (p=.001) subscales, with the former increasing over time and the latter decreasing. A significant Group by Time interaction was found for the FM subscale (p=.37), driven by a decline in FM skills from T1 to T2 in the ASD and BAP groups.

Conclusions: Subgroups of Sibs-ASD with different diagnostic outcomes showed different patterns of trajectories in cognitive development, compared to each other and to Sibs-TD. The decline in Fine Motor t-scores over time in Sibs-ASD subgroups warrants further investigation.

79 146.4 Developmental Trajectories of Social-Communicative Abilities in Younger Siblings of Children with ASD. E. E. Malesa*, J. H. Foss-Feig, C. R. McMahon, T. A. Walden, P. J. Yoder and W. A. Stone, *Vanderbilt University*

Background: Younger siblings of children with ASD (SIBS-ASD) are at elevated risk for ASD or autism- related symptomatology, often described as the Broader Autism Phenotype (BAP). Early deficits in social-communicative abilities such as initiating and responding to joint attention (IJA; RJA), functional play, requesting, and imitation have been found in these children at young ages, though little is known about the development of these abilities over time or how they relate to different diagnostic outcomes.
Objectives: To examine the developmental trajectories of social-communicative abilities associated with differential outcome in SIBS-ASD.
Methods: Forty-five SIBS-ASD and 30 younger siblings of typically developing children (SIBS-TD) participated in this study. Children were seen at three time points (mean CAs: T1: 15.6; T2: 19.5 ; T3: 23.5), and were assessed using an RJA task (see Presmanes et al., 2007) and the Screening Tool for Autism in Two-Year Olds (STAT; Stone et al., 2004) from which measures of IJA, requesting, functional play, and imitation were derived. Outcome groups of SIBS-ASD were ASD, BAP, or no ASD concerns (NC), based on ADOS scores and clinical judgment after 24 months of age. A mixed design ANOVA and MANOVA were used to examine changes over time within and between groups.
Results: Results revealed a significant main effect (ME) of Time for RJA (p=.31), Play (p=.004) and IJA (p=.001), and significant ME of Group for RJA (p<.001), Requesting (p=.006), IJA (p=.005), and Imitation (p=.46). Pairwise group comparisons revealed that the: 1) NC group scored lower than the SIBS-TD on Imitation only; 2) ASD group scored lower than the NC group on RJA, Requesting, and IJA; 3) BAP group's performance was similar to the ASD group on some tasks and similar to the NC and SIBS-TD groups on others.
Conclusions: SIBS-ASD with differential outcomes exhibit varying trajectories of social-communicative skills.

80 146.5 Personality style of fathers of children with autism spectrum disorders and impact on parenting experience. B. H. Freedman*[1], J. Stella Durocher[2], M. Alessandri[2] and S. Valley-Gray[1],

(1)*Nova Southeastern University*, (2)*University of Miami*

Background:

Historically, fathers' parenting experiences have been less studied and findings have varied. Studies have also begun to explore the presence of a broader autism phenotype among family members using measures of ASD symptom presentation. In contrast, our study uses a dimensional approach to measure personality dimensions among fathers of children with ASD using a standardized measure of personality. Variability in such personality characteristics is hypothesized to significantly impact fathers' parenting experiences.

Objectives:

1) Determine whether fathers of children with ASD exhibited significant differences on five personality dimensions as compared to the normative population.

2) Identify whether particular personality traits were correlated with parenting stress, marital satisfaction, and maladaptive coping strategies.

Methods:

Participants included fifty-one fathers of children with ASD between the ages of four and nine years old who were married to and living with the biological mother of the child. Participants received measures of personality (NEO-FFI), parenting stress (PSI), coping (WOC), and marital satisfaction (DAS).

Results:

No significant differences were found on any of the five personality dimensions as compared to the standardization population. A bimodal distribution was found for Extraversion while Conscientiousness trended toward higher scores. Fathers also exhibited significantly higher levels of parenting stress and lower marital satisfaction. Extraversion was significantly negatively correlated with parenting stress and positively correlated with marital satisfaction.

Conclusions:

Contrary to expectations, our sample of fathers of children with ASD was not found to exhibit personality dimensions suggestive of a broader autism phenotype. However, most fathers showed extreme scores (either high or low) on a measure of the desire and capacity to socialize (Extraversion), and trended toward more rigid and goal-oriented characteristics (Conscientiousness). Further, fathers also reported high levels of parenting stress and lower marital satisfaction, with fathers with particular personality characteristics at greater risk for these outcomes.

81 146.6 FEVER IN AUTISM SPECTRUM DISORDERS (ASD): SPONTANEOUS REPORTS.

A. W. Zimmerman*, S. L. Connors and L. K. Curran, *Kennedy Krieger Institute*

Background: Based on parent reports, we recently documented decreased aberrant behaviors (irritability, hyperactivity, stereotypy, inappropriate speech) in 30 children with ASD during fever compared to ASD controls (Pediatrics 2007;120:1386).

Objectives: To present 46 spontaneous reports of functional improvements in ASD and non-ASD children and adults, according to fever, mode of heating and type of illness or disorder, that we received following publication of our study of fever in ASD. These may guide further studies.

Methods: Reports were tabulated after we evaluated and answered them in order to verify their origins and facts if they were unclear.

Results: Reports included 33 with ASD, 13 non-ASD (37 children, 9 adults). A diagnosis of autistic disorder was verified (12), and PDD/NOS or high functioning autism (12). Most with ASD improved with illness or fever (24 children, 5 adults). Without fever, 4 children had improved language, attention or social interaction either in a steam room, hot bath or sauna, or with pain (fracture). Six non-ASD children included one each with a language disorder, complications of prematurity, sensory integration disorder, bipolar disorder, Tourette syndrome and

ADHD. One family reported "improved personality" in 2 neurotypical children. We also received reports of improvements, as well as elimination of positive responses, with ibuprofen therapy. Among 4 non-ASD adults who improved with fever, one each had Lyme disease, cerebral palsy and mental retardation, Alzheimer disease, or strokes secondary to endocarditis.

Conclusions: These unsolicited reports by families expand the range and nature of functional improvements, both during fever and from increasing core temperature in children and adults with ASD as well as non-ASD disorders. The underlying physiological mechanisms are unknown but reports suggest that heating alone may be effective, separate from immune responses, and may result from changes in cell membranes, signaling or synaptic pathways in the CNS.

82 146.7 Language and Intellectual Ability Differentially Moderate Outcome in High Functioning Autism and Asperger Syndrome. D. O. Black*[1], G. L. Wallace[1], L. K. Case[1], J. L. Sokoloff[2], J. Strang[2], J. A. Silvers[1] and L. Kenworthy[2], (1)*NIMH*, (2)*Children's National Medical Center, George Washington University*

Background:

Intellectual ability and language level have been identified as important factors in autism spectrum disorders (ASD). It remains unclear which of these abilities are most important in moderating symptom severity and outcome in ASD and whether the effects of these variables differ in children with high functioning autism (HFA) versus Asperger syndrome. Further refining how these variables impact symptom presentation and functioning may have implications for treatment priorities

Objectives:

Examine: 1) the influence of verbal knowledge (Vocabulary), nonverbal ability (Block Design), and language impairment (sentence memory) on the presentation of autism symptoms and adaptive functioning in ASD and 2) the effect of these variables by diagnostic group (HFA, Asperger, PDD-NOS).

Methods:

Subjects were a clinically referred sample of 86 school age children (mean age: 9.6±2.8 years; 82% male; verbal or nonverbal IQ ≥75) diagnosed with an ASD based on the Autism Diagnostic Interview, Autism Diagnostic Observation Schedule, and clinical impression. Parents of subjects were interviewed using the Vineland Adaptive Behavior Scale (VABS). Data were analyzed using partial correlations, controlling for age.

Results:

For the whole sample, Vocabulary was related to autism communication symptoms (*pr*=-.26), VABS Communication (*pr*=.65) and VABS Daily Living Skills (*pr*=.29). Sentence memory was related to VABS Communication (*pr*=.54) and VABS Daily Living Skills (*pr*=.28). Block Design was only related to VABS Communication (*pr*=.34). No language or nonverbal ability measure was significantly related to autism social symptoms, autism restricted/repetitive behaviors, or VABS Socialization. This pattern of results held for the HFA and PDD-NOS groups, but none of the cognitive or language variables were related to autism symptoms or adaptive functioning within the Asperger syndrome group.

Conclusions:

We find that better cognitive and language abilities support adaptive functioning and reduce the severity of autism communication symptoms among individuals with HFA and PDD-NOS but not those with Asperger syndrome.

83 146.8 Reconceptualizing Autistic Spectrum Disorders as Autistic Learning Disabilities. B. Siegel*, *University of California, San Francisco*

Background:

Autism has become understood as a spectrum of signs and symptoms varying in severity and number across individuals. As autistic spectrum disorders (ASDs) have become more broadly-defined and widely-recognized, there is support for viewing etiologies as heterogeneous—resulting in many 'autisms': These can be characterized in terms of

genotypic, phenotypic, neuroanatomical, and neurochemical differences (e.g., Geschwind, IMFAR, 2007). Concurrently, the need to help ASD-identified individuals has increased exponentially with treatments including pharmacological, behavioral, developmental, and educational approaches. Among clinicians and clinical researchers involved in treatment, there is increasing understanding that this heterogeneity means that treatment is not one-size-fits-all, though there is little agreement on a conceptual framework for aligning symptoms/ profiles/ subtypes with specific treatment approaches.

Objectives:

The approach taken here is that ASDs can be re-conceptualized as related autism-specific learning disabilities (ALDs) and autism-specific learning styles (ALSs).

Methods:

Symptoms of ASDs can be operationally understood, then deconstructed by viewing them as arising from a matrix of specific disabilities cross-tabulated by preserved abilities. Each ALD can be characterized as the product of specific defects in perception, processing, retention or expression of some perceptual, affective or cognitive stimuli. Then, preserved abilities form naturally-arising compensations depending on ALDs, resulting in self-accommodations wherein stronger capacities are deployed when specific neuropathology blocks expression of typical function (Siegel, 2003, 2005, 2007).

Results:

Using this model, targeted clinical treatments can be selected accordingly, and characterized as taught accommodations that optimize efficiency of self-accommodation processes.

Conclusions:

The ALD/ALS model has two important applications: 1) It breaks symptoms of ASDs into what are essentially, readily observed endophenotypes (e.g., low affiliative drive) which should be more useful in characterization of homologues within pedigrees than diagnosis alone, and 2) precisely specifies learning defects so they can be addressed with more targeted intervention strategies (e.g., pivotal response strategies to leverage low affiliative drive).

84 146.9 PILOT STUDY: AN ETIOLOGIC CLASSIFICATION OF PERVASIVE DEVELOPMENTAL DISORDERS. L. Gabis*[1], Y. Kesner-Baruch[1] and J. C. Pomeroy[2], (1)*Tel-Aviv University Sackler School of Medicine*, (2)*Stony Brook University Medical Center*

Background: Pervasive Developmental Disorders (PDD) is etiologically heterogeneous. Objectives: To classify children diagnosed with PDD according to organic diagnoses. Methods: Comparable with epilepsy classification, we separated 436 children diagnosed with PDD into three groups: Symptomatic - a diagnosed organic- neurologic disorder was identified Cryptogenic - an underlying etiology was suspected Idiopathic- without evidence of other neurological disorders Children were recruited from an Israeli (N=351) and American (N=85) databases. Results: American database: Nine children were classified as symptomatic (44%males), 23 cryptogenic (74%males) and 53 idiopathic (81%males). PDD subtype also differed between the groups - 53% idiopathic, 43% cryptogenic and 11% symptomatic meeting full criteria for Autism. Among other findings, there was evidence for higher rates of language delay (89% vs. 66%) and no evidence for regression in the symptomatic group, but similar rates of each between idiopathic and cryptogenic groups (21-34%). Israeli database: Twenty two children were classified as symptomatic (36.3%males), 92 cryptogenic (86.9%males) and 237 idiopathic (79.3%males). After excluding the Rett syndrome (N=8) from the symptomatic group, the percentage of males and females became almost equal (57.1% males). PDD subtype also differed between the groups - 43% idiopathic (44.1% vs 38.7% in males and females respectively), 47.8% cryptogenic (47.5% vs 50% in males and females respectively) and 42.8% symptomatic (37.5% vs 50% in males and females respectively) meeting full criteria for Autism. Among other findings, the entire symptomatic group showed language delay but almost none had evidence for regression. Similar rates of each were seen in both idiopathic and cryptogenic groups (above 90% had language delay, and a fifth showed evidence for regression). Conclusions: In this study, differences in gender, clinical and diagnostic features were found when etiology was used to create subtypes of PDD.

This classification could have heuristic importance in search for an autism gene(s).

85 146.10 PSYCHIATRIC AND AUTISTIC COMORBIDITY IN FRAGILE X SYNDROME ACROSS AGES. Y. Kesner-Baruch*[1], J. Evron[1] and L. Gabis[2], (1)*Sheba Medical Center*, (2)*Tel-Aviv University Sackler School of Medicine*

Background: Fragile X syndrome (FXS) is the most common form, known today, of inherited mental retardation. The syndrome is caused by an unstable expansion of CGG trinucleotide repeat, within the promoter region of the human FMR1 (Fragile X Mental Retardation) gene on the X chromosome. This mutation can change sizes over generations, becoming more unstable, and thus the conditions may occur more frequently or severely in subsequent generations. Children with FXS have a typical psychiatric and behavioral profile. In addition to mental deficit manifested in language, cognitive and motor delay, high prevalence of psychiatric comorbidity, sensory sensitivity and hyper-arousal are also common along lifespan. Moreover, 90% of all children with FXS show some autistic characteristics. About a third of these children meet the criteria for pervasive developmental disorder (PDD), what makes FXS the most common known single gene cause of autism. Objectives: To characterize psychiatric and autistic comorbidities in children and adolescents with fragile X syndrome. Methods: Subjects were recruited from a cohort of families that are part of the Israeli parents' non-profit organization for fragile X syndrome. Results: Initial results (N=18) show a change in psychiatric comorbidity prevalence across ages. While attention deficits, specific and social phobias and dysthymia show great reduction, obsessive-compulsive behaviors, motor and vocal tics remain relatively the same or even increase. In addition, our results show that autistic-like behaviors decrease with age. Conclusions: The typical profile of children with FXS changes with age. Awareness to these characteristics can help understanding and treating the child with FXS.

86 146.11 Sex differences in core autism symptoms in cases with autistic disorder. L. Hjort*[1], E. Parner[1], M. B. Lauritsen[2], M. Jørgensen[3], S. Lemcke[1], S. Toft[3] and P. Thorsen[1], (1)*University of Aarhus*, (2)*Regional Psychiatric Center for Children and Adolescents*, (3)*Århus University Hospital, Regional Psychiatric Center for Children and Adolescents*

Background:

Sex differences in core autism symptoms have not been fully investigated. Boys with autism have been reported to show less pretend play, more inappropriate stereotypic play, and more unusual visual interests than girls with autism. Cognitive ability is hypothesized to influence core autism symptoms.

Objectives:

To study sex differences in core autism symptoms according to DSM-IV diagnostic criteria.

Methods:

All children born in Denmark from 1990-1999 registered with a diagnosis of autistic disorder in The Danish Central Psychiatric Register by February 1, 2001 formed the population. Register diagnoses were validated by DSM-IV diagnostic criteria of autistic disorder using a record review method. Cases with a confirmed diagnosis constituted the study cohort: a total of 469 cases, 92 girls, 377 boys. The DSM-IV lists four items in each of the three autism core areas: impaired social interaction, impaired communication, and restricted/stereotyped behaviour. Compliance with six items or more confirm the diagnosis.

Results:

Males met on average 0.63 (95%CI=0.20-1.6; p=0.004) more items from DSM-IV diagnostic criteria than females. Further, males on average met 0.29 (95%CI=0.7-0.51; p=0.11) more items concerning impaired communication and 0.28 (95%CI=0.7-0.50; p=0.11) more items concerning restricted behaviours than females. A similar trend was seen concerning impaired social interaction.

For autism cases without mental retardation males overall met on average 0.69 (95%CI=-0.6-1.44; p= 0.73) more items than females

and on average 0.66 (95%CI=0.29-1.2; p=0.001) more items concerning restricted behaviours when adjusting for age. Similar trends were seen concerning impaired communication and impaired social interaction. For cases with mental retardation largely the same trend was found.

Conclusions:

In a population-based cohort of validated cases of autistic disorder compliance with DSM-IV diagnostic criteria items differed significantly between sexes: Consistently males met more items than females. Current diagnostic criteria may favour diagnosis of males. More studies are needed on female autistic behaviour.

87 146.12 Language Profiles and Memory Components in Specific Language Impairment and Autism Spectrum Disorders in Relation to the Broader Phenotype. K. Dworzynski*[1], G. Baird[2], V. Slonims[3] and E. Simonoff[4], (1)*Institute of Psychiatry, King's College London*, (2)*Guy's Hospital*, (3)*Guy's and St. Thomas' NHS Trust*, (4)*Institute of Psychiatry*

Background: Phenotypic overlap between autism spectrum disorder (ASD) and specific language impairment (SLI) is currently debated in the literature. One aspect of controversy is related to whether children's phonological short term memory (PhSTM) performance is a possible clinical marker in both SLI and ASD.

Objectives: To assess memory abilities including PhSTM in children with SLI compared to children with SLI and additional significant ASD traits with standardised memory tests designed for clinical use with children. These profiles are then related to their own and their parents' PhSTM.

Methods: 61 children with current SLI but without autistic traits (SLI-) are compared with 31 children with SLI plus additional autistic traits (SLI+) (assessed by the family history questionnaire) as well as 52 unimpaired siblings all aged 5-16.9 years on measures of language, IQ, memory and learning (using the Wide Ranging Assessment of Memory and Learning – WRAML). They came from 75 families. Their parents' nonword repetition data were also analysed.

Results: Both SLI+ and SLI- groups (by definition) showed impairment in receptive and expressive language compared with unimpaired siblings. Group comparisons showed equal impairment in verbal memory for SLI- and SLI+ groups. Visual memory and learning were comparative strengths for both groups. The SLI+ group showed a mixed pattern of impairment in PhSTM. In the SLI+ group, if PhSTM was impaired, verbal memory was also impaired and receptive language impairment greater than in the SLI- group. Parental PhSTM was impaired if their children had poor PhSTM, a finding only in the SLI- group.

Conclusions: Verbal memory skills are significantly impaired in children with SLI regardless of whether or not they have additional autistic traits with SLI+. The significant component of memory appears to be PhSTM. Impairment in parental nonword repetition is correlated with NWR in children with SLI- suggesting familiality.

88 146.13 Social Cognition in the Broader Autism Phenotype. K. B. White*, S. Wallace, J. Parr, M. N. Coutanche, S. Foley, A. Bailey and I. M.G.S.A.C., *University of Oxford*

Background:

Some relatives of children with ASD show milder phenotypes related to autism, known as the broader autism phenotype (BAP). There is an increasing interest in characterising the cognitive profile of the BAP, as affected relatives may use alternative cognitive strategies in comparison with the typically developing population.

Objectives:

Preliminary exploration of social cognition in the Broader Autism Phenotype.

Methods:

To date fifty parents in UK families with multiple incidence of ASD have been assessed on three 'Theory of Mind' tasks: The Reading

the Mind in the Eyes Task (Baron- Cohen et al., 2001), the Social Attribution Task (Klin, 2000) and the Village Task (unpublished). The Village Task is a non-verbal social cartoon during which participants are asked mental state questions. A revised Family History Interview (FHI) designed to assess behaviours associated with the BAP was administered to the participant (FHIS) and an informant (FHII). The interview questions fall into different behavioural domains – communication, repetitive behaviours and social. Scores derived from the social domain were used in this study.

Results:

The Reading the Mind in the Eyes Task positively correlated with verbal IQ, but did not correlate with the FHI social domain. The Village Task positively correlated with IQ and with the FHII social domain. Scores in the Reading the Mind in the Eyes Task and the Village Task were not correlated with each other. Data on the relationship between the Social Attribution Task and the other two social cognition tasks will also be presented.

Conclusions:

This preliminary data suggests that there is an association between the BAP, assessed through an interview measure, and an experimental measure of social cognition. The Reading the Mind in the Eyes task was not associated with the interview assessment of the BAP, but did correlate with verbal IQ.

89 146.14 COMPARISON OF BEHAVIORAL AND SYMPTOMATIC CHARACTERISTICS BETWEEN ASPERGER'S DISORDER AND ATTENTION-DEFICIT /HYPERACTIVITY DISORDER: A SAMPLE OF TAIWANESE CHILDREN. T. N. Tsai*[1], S. R. Lee[2], C. C. Chao[1], Y. Y. Wu[2], Z. Y. Yen[1] and L. Y. Wang[1], (1)*Chang Gung University*, (2)*Chang Gung Memorial Hospital*

Background:Recent researches have reported observed similarities in the behavioral and symptomatic characteristics between children with Asperger's disorder (AD) and those with attention-deficit/hyperactivity disorder (ADHD). Difficulty in making differential diagnosis of AD and ADHD has been encountered by many clinicians. More studies are needed to examine this phenomenon and address the diagnostic issue.

Objectives:This study intends to examine and compare the behavioral and symptomatic characteristics of Taiwanese children with Asperger's disorder and those with attention-deficit/hyperactivity disorder.

Methods:Twenty-nine boys (14 with AD and 15 with ADHD) and their parents and teachers participated in this study. AD and ADHD groups were matched on their age and IQ (Mean age = 9.3 years, Range = 6~15 years; Mean IQ = 102.75, Range = 75~129). Data included (1) parental ratings on Child Behavior Checklist (CBCL)**,** Gilliam Asperger's Disorder Scale (GADS), and Swanson, Nolan, and Pelham, Version 4th(SNAP-4th); (2) teacher's ratings on Teacher Report Form (TRF), GADS, and SNAP-4th; and (3) Children's performance on Conners' Continuous Performance Test-II (CCPT-II) and Children's version of the Reading the Mind in the Eyes Test.

Results:The results showed no significant difference was observed between groups on all the measures, except GADS. On the GADS, compared to ADHD group, AD group received significantly higher parental ratings on symptoms of cognitive patterns (p=.003) and pragmatic skills (p=.26), as well as higher teacher's ratings on cognitive patterns (p=.15).

Conclusions:The results of this study are consistent with previous findings that AD and ADHD children displayed many similar behavioral and symptomatic characteristics. The only measure that differentiated our AD and ADHD samples is the GADS, suggesting the importance of collecting information from parents and teachers regarding AD symptoms in making differential diagnosis of AD and ADHD. Further studies should include a larger sample and more sensitive measures.

90 146.15 Factors Associated With Timing Of Diagnosis In A Large Sample Of Preschool Children With ASD. M. Steiman*[1], R. Simon[1], E. Fombonne[1], L. Zwaigenbaum[2], P. Szatmari[3],

S. Bryson[4], P. Mirenda[5], W. Roberts[6], I. M. Smith[7], T. Vaillancourt[3], J. Volden[2], C. Waddell[8], S. Georgiades[9] and E. Duku[10], (1)*Montreal Children's Hospital*, (2)*University of Alberta*, (3)*Offord Centre for Child Studies, McMaster University*, (4)*Dalhousie University/IWK Health Centre*, (5)*University of British Columbia*, (6)*Hospital for Sick Children*, (7)*Autism Research Centre*, (8)*Simon Fraser University*, (9)*Offord Centre for Child Studies & McMaster University*, (10)*McMaster University*

Background: The availability and efficacy of early intervention programs render early diagnosis of ASD important. However, long intervals still persist between first parental concerns and final diagnostic confirmation of ASD. Objectives: To examine the age range at which young preschoolers with ASD are diagnosed and to identify factors associated with age at diagnosis.
Methods: The sample comes from a multisite longitudinal Canadian study (Pathways in ASD) and consisted of 274 preschoolers (mean age at study entry: 39.2 months; 232 males). For analyses purposes, baseline data on diagnostic and psychometric measures were used.

Results: Mean age at diagnosis was 37.9 months, with no gender differences. Preschoolers with an ADOS score consistent with autistic disorder were diagnosed 3.3 months earlier (p=.25) than those in the ASD range. Children with a Merrill-Palmer–Revised score of 70 or above were diagnosed significantly later (mean age = 42.6 months) than those with scores below 70 (mean age = 36.8 months). Correlations were not significant between age and CBCL Internalizing, Externalizing, or Total scores; RBS-R total score; Parental Stress Index scores; VABS composite scores; or ADI-R Social and Non-verbal scores. Small to moderate correlations were found between SRS Total scores (r=.17), ADI-R Repetitive scores (r=.23), ADOS Play scores (r=-0.53) and 3 ABC subscales (Irritability: r=.18; Hyperactivity: r=.19; Inappropriate Speech: r=.40). Socio-demographic variables (family structure, household income, and mother's education, employment status and ethnicity,) were not related to age at diagnosis. Broadly similar results emerged on analyses conducted on the delay between age at first parental concern and age at diagnosis (mean delay=19 months). Multivariate analyses will evaluate the effect of individual predictors of age and diagnostic delay. Conclusions: Diagnosis occurred after the third birthday, 19 months after parents first concerns. As these delays are compounded by waits for treatment they must be reduced to improve outcomes.

91 146.16 Finite Mixture Modeling of Multidimensional Cognitive Style in Autism. J. Breidbord*, S. Baron-Cohen, S. Wheelwright and B. Chakrabarti, *Cambridge University*

Background: Autism-spectrum conditions are associated with impaired empathising alongside intact or superior systemising/visual search abilities. As a strategy to reduce heterogeneity and thereby improve clinical classification of individuals with autism, the use of endophenotypes will ease identification of autism-susceptibility genes. The present study examines whether measures of empathy (the Reading the Mind in the Eyes ("Eyes") test) and systemising/visual search (the Embedded Figures Test (EFT) and the Mental Rotation Test (MRT)) present valid endophenotypes in their joint underlying structure.

Objectives: To identify good endophenotypic indicators of autism susceptibility via admixture analysis of cognitive-style measures in a large, genetically informative sample.

Methods: The sample comprised adults with a clinical diagnosis of autism (n=232) and typical adults with (n=138) or without (n=808) a child with autism. Mean response times for the Eyes test, EFT, and MRT administered online were subject to multivariate admixture analysis. Models of 1–4 latent components were evaluated using the Bayesian information criterion and posterior predictive checks; posterior probabilities were used to estimate each participant's component membership, which served as a grouping variable in subsequent inferential analysis.

Results: Mixture modeling revealed evidence of ternary structure underlying the joint

normal distribution of these performance data. The major latent component showed typical performance and comprised 70% of the sample. Remaining taxa with discrete shifts in performance contained unaffected parents or adults with autism in significant frequency. Mental rotation was undifferentiated in this model, whilst performance of the Eyes test was the most efficient endophenotypic marker. Further analysis found no artifacts in distributional characteristics or participants' clinical features.

Conclusions: Multivariate admixture analysis suggests that the Eyes test and EFT are candidate autism endophenotypes with broad relevance to research as objective criteria for the classification of individuals with autism.

92 146.17 Mitochondrial abnormalities in lymphoblasts from autism. A. Chauhan*, M. M. Essa, B. Muthaiyah, W. T. Brown and V. Chauhan, *NYS Institute for Basic Research in Developmental Disabilities*

Background: Recent reports indicate role of oxidative stress in autism. Disturbance of energy metabolism has also been suggested in the brain of patients with autism. The free radicals, namely, reactive oxygen species (ROS) and reactive nitrogen species (RNS) are generated endogenously during oxidative metabolism and energy production by mitochondria in the body. While oxidative phosphorylation in the mitochondria generates superoxide anion, enzymatic oxidation of biogenic amines by monoamine oxidase in mitochondrial outer membrane produces H_2O_2. Damaged mitochondria not only produce more oxidants, but mitochondria are also vulnerable to oxidative stress. Additionally, alterations in mitochondrial membrane potential (MMP) are involved in both apoptotic and necrotic cell death. MMP creates an electrochemical gradient essential for ATP synthase activity in the oxidative phosphorylation pathway.

Objectives: To study whether there is mitochondrial dysfunction in autism, mitochondrial free radicals generation and membrane potential were analyzed in the lymphoblasts.

Methods: The lymphoblasts from autistic and control subjects were obtained from Autism Genetic Resources Exchange Program**,** and the cell lysates and mitochondria were prepared. MMP was monitored using the fluorescent dye rhodamine123, a cell-permeable cationic dye, which preferentially partitions into mitochondria because of the highly negative MMP. ROS generation in the mitochondria was measured by the oxidation of dihydrorhodamine 123 to fluorescent rhodamine 123, while RNS were measured by using nitric oxide fluorometric assay kit.

Results: Elevated ROS and RNS levels were observed in the mitochondria of autistic lymphoblasts as compared with control lymphoblasts suggesting increased free radical generation by mitochondria in autism. The mitochondrial membrane potential was also reduced in lymphoblasts from autism than in controls.

Conclusions: Our results suggest increased mitochondrial oxidative stress and reduced MMP in autism. Such mitochondrial abnormalities may lead to defects in oxidative phosphorylation and energy metabolism in autism.

93 146.18 AUTISM SYMPTOMS IN CHILDREN WITH DOWN SYNDROME: RELIABILITY OF DIAGNOSTIC TOOLS AND POTENTIAL IMPACT OF WITHIN-CHILD FACTORS ON SYMPTOM PRESENTATION. S. Hepburn*[1], N. R. Lee[1], A. Philofsky[1], A. Blakeley-Smith[1], K. Ridge[1], D. Fidler[2], C. DiGuiseppi[3], L. Miller[4] and C. Robinson[1], (1)*University of Colorado at Denver*, (2)*Colorado State University*, (3)*University of Colorado, Denver*, (4)*Colorado Department of Public Health and Environment*

Background: Children with Down syndrome (DS) may be at increased risk for autism. Whether this comorbidity reflects a true neurobiological vulnerability, with potential implications for the genetic underpinnings of autism, or the impact of a significant cognitive impairment is not yet understood. Our clinical observations suggest that child temperament,

executive function, and motor skills may also impact this apparent comorbidity.

Objectives: To examine agreement amongst diagnostic tools in this population and to explore how other child factors impact symptom presentation.

Methods: 87 children with DS (ages 2 -11) and their parents participated in evaluations for autism. Measures included: ADOS, developmental testing, ADI-R, VABS, Carey Temperament Scales, and BRIEF.

Results: 9 children (10.3%) met criteria for clinical diagnosis of Autism; 14 (16.1%) met criteria for PDD-NOS. Relying upon clinical diagnosis as the "gold standard", intraclass correlation coefficients were obtained for the ADI-R (Lifetime Codes: ICC = .87; Current Codes: ICC = .81) and for two modules of the ADOS: (Module I: ICC = .93; Module II: ICC = .53). Autism spectrum status on the ADI was strongly associated with diagnostic classifications on Module I of the ADOS (ICC=.84, Lifetime, .81 Current), but not on Module II (ICC= .64, Lifetime, ICC= .28, Current). Correlation of IQ to clinical diagnosis was .52. Discriminant function analysis was used to predict diagnostic status, without using measures from diagnostic tools. Receptive language, EF, and Motor Activity correctly classified 90.3% of cases as on/off the spectrum, and 82.3% of cases on specific diagnosis.

Conclusions: Current diagnostic tools are promising, but have limitations, particularly for children with DS with relatively better expressive language. Children with DS who met criteria for an ASD in this sample tended to demonstrate low activity levels, clinically significant problems in executive function, and poor language understanding.

94 146.19 Broader Autism Phenotype as a Predictor of Marital Quality in Parents of Toddlers with Autism Spectrum Disorder. N. A. Edwards*[1], S. A. Grossman[1], M. B. Kadlec[1] and A. S. Carter[2], (1)*Boston University*, (2)*University of Massachusetts, Boston*

Background: Parents of children with Autism Spectrum Disorder (ASD) have higher levels of broader autism phenotype (BAP) than parents of typically developing children. Because BAP involves traits of autism it can affect an individual's ability to relate to others. Parents of children with ASD already report lower levels of marital quality than parents of typically developing children, but no studies have looked specifically at whether BAP is associated with marital quality in parents of toddlers with ASD.

Objectives: Examine the association between BAP and marital quality in mothers and fathers of toddlers with ASD.

Methods: Parents of children with ASD between 30- to 45-months of age who participated in a longitudinal research study are included in this report. As part of a larger study, mothers and fathers completed questionnaires about themselves on the Autism Spectrum Quotient (ASQ; total score and 5 subscales) and about their marital relationship on the Dyadic Adjustment Scale (DAS; total score and 4 subscales).

Results: Correlations between ASQ total and subscale scores and DAS total and subscale scores for 84 couples showed that fathers who reported lower overall marital quality rated themselves as higher on the ASQ Social Skills scale ($r=-.34$, $p=.002$). This association was not present for mothers. Regression analyses indicated that after accounting for mothers' ratings of marital quality ($\Delta R^2=.25$), fathers' ASQ Social Skill scores accounted for an additional 11% of unique variance in fathers' DAS scores. Neither mothers' nor fathers' ASQ scores were associated with mothers' marital quality and mothers' ASQ scores did not significantly predict fathers' marital quality.

Conclusions: Results show that fathers' endorsement of challenges with social skills is predictive of lower levels of marital quality. Therefore, fathers' social ability should be taken into consideration when assessing marital well-being of parents with children with ASD.

95 146.20 Increased oxidative damage and free radical generation in lymphoblasts from autism. M. M. Essa*[1], B. Muthaiyah[1], V. Chauhan[1], W. T. Brown[2] and A. Chauhan[1], (1)*NYS Institute for*

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

Background: Recent studies have suggested increased oxidative stress in autism. Most of these studies were done with serum, plasma or erythrocyes. The studies with cell cultures are lacking in autism. Under normal conditions, a dynamic equilibrium exists between the production of free radicals (reactive oxygen species -ROS and reactive nitrogen species- RNS) and the anti-oxidant capacity of the cell. The free radicals are highly reactive, and their elevated levels lead to oxidative/ nitrosative stress and cell death.

Objectives: The aim was to study the status of oxidative/ nitrosative stress in lymphoblasts from autism by analyzing lipid peroxidation, generation of free radicals (ROS/RNS) and extent of membrane damage.

Methods: The lymphoblasts from autistic and control subjects were obtained from Autism Genetic Resources Exchange Program**,** and the cell lysates were prepared. Lipid peroxidation was assessed by measuring malonyldialdehyde, an end product of fatty acid oxidation. ROS levels (basal and upon induction by Fenton reaction) were determined by using dichlorofluorescin-diacetate (DCFH-DA) as a fluorescent probe. RNS levels were measured by nitric oxide fluorometric assay kit. Damage of the plasma membrane was evaluated by measuring the amount of intracellular lactate dehydrogenase (LDH) that was released into the conditioned medium.

Results: Lipid peroxidation was significantly increased in lymphoblasts from autism as compared with control lymphoblasts, suggesting increased oxidative damage in autism. The levels of ROS and RNS were significantly increased in the lymphoblasts from autism as compared with control lymphoblasts, suggesting increased generation of free radicals in autism. LDH leakage was also increased in lymphoblasts of autism as compared with controls, suggesting that membrane integrity is affected in autism.

Conclusions: Autism is associated with increased formation of free radicals (ROS and RNS), which leads to increased oxidative damage and membrane damage.

96 146.21 Etiologic Investigation of 654 patients with Autism Spectrum Disorder (ASD): the experience at Hospital Pediátrico de Coimbra in Portugal. G. Oliveira*[1], J. Almeida[1], R. Lontro[1], C. Café[1], S. Mouga[1], C. Lobo[1], T. Miguel[1], J. Saraiva[1], A. Coutinho[2], I. Carreira[3] and A. M. Vicente[4], (1)*Hospital Pediátrico de Coimbra*, (2)*Instituto Medicina Molecular*, (3)*Universidade de Coimbra*, (4)*Instituto Gulbenkian de Ciência/Instituto Nacional de Saúde Dr. Ricardo Jorge*

Background: ASD may be a neurodevelopmental syndrome with many different causes leading to the same final common pathway, a hypothesis supported by the multiple rare medical conditions associated with the disorder.

Objectives: This study assessed the diagnostic yield for autism in a large sample of children observed over several years at HPC.

Methods: Assessment of ASD entailed extensive interaction with patients in a clinical setting, the majority of whom return frequently for follow up. ASD was diagnosed using the ADI-R and CARS. A comprehensive clinical history was collected, including the pre and perinatal periods. Laboratorial assessment included testing for chromosomal abnormalities (karyotyping, 15q11-13 FISH analysis), neurocutaneous syndromes, endocrine, metabolic and genetic disorders.

Results: Of the 654 ASD patients who participated in the study (518 males, mean age 12.6±4.8), 17% were non-idiopathic. 4% presented chromosomal abnormalities: five patients on ch15q11-13, two on chromosome9, one each on chromosomes 1, 3, 5, 6, 7, 8; trisomy 21 was present in eleven ASD children. Nineteen cases had a genetic syndrome of unknown origin (2.9%). *FMR1* mutations were found in seventeen cases (2.6%) and Rett Syndrome was confirmed by molecular analysis in two cases; one additional *MECP2* non-synonymous variant was found in a male patient. *NLGN4* sequence analysis in 148 cases detected two non-synonymous

changes. Lactate levels were increased in 21% of the patients; mitochondrial disease was confirmed in 8 cases and probable in 3 cases out of 20 fully tested. Six patients presented a neurocutaneous syndrome, five had abnormalities in brain development. Fourteen patients had documented pre or peri-natal incidents, five post natal infections, one hypothyroidism and one brain tumour.

Conclusions: This study illustrates the etiological diversity associated with autism in an important percentage of cases, and supports the need of screening for specific medical disorders with implications in recurrence risk and medical support.

97 146.22 Alterations in the activities of antioxidant enzymes in lymphoblasts from autism. B. Muthaiyah*[1], M. M. Essa[1], V. Chauhan[1], W. T. Brown[2] and A. Chauhan[1], (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*New York State Institute for Basic Research in Developmental Disabilities*

Background: Recent evidence suggests that autistic subjects are under oxidative stress. Antioxidants enzymes scavenge the free radicals and play vital role in the intracellular defense mechanism against oxidative damage. Superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) are the primary enzymes involved in direct elimination of reactive oxygen species (free radicals), while glutathione reductase (GR) is a secondary antioxidant enzyme, which helps in maintaining a steady concentration of glutathione (GSH). GSH is the most important antioxidant for detoxification and elimination of environmental toxins. SOD protects from the damage caused by superoxide by catalyzing its conversion into hydrogen peroxide and oxygen, while CAT converts hydrogen peroxide to water and molecular oxygen, thereby reducing the amount of hydroxyl radical. GPx removes hydrogen peroxide in the presence of GSH.

Objectives: To understand the mechanism of oxidative stress in autism, the activities of antioxidant enzymes SOD, CAT, GPx and GR were analyzed in the lymphoblasts from autism and control subjects.

Methods: Cell lysates were prepared from lymphoblasts (control and autistic). SOD activity was measured by using assay kit from Calbiochem. CAT activity was measured spectrophotometrically by analyzing complex of ammonium molybdate with H_2O_2. Measurement of GPx activity was based on the oxidation of GSH to oxidized glutathione (GSSG) catalyzed by GPx. Activity of GR was measured by the method based on the reduction of GSSH by NADPH.

Results: Activites of SOD, CAT, GPx and GR were reduced in lymphoblasts from autism as compared with control lymphoblasts.

Conclusions: The activities of antioxidant enzymes SOD, CAT, GPx and GR are decreased in autism, suggesting that defense mechanism against oxidative damage is impaired in autism. Reduced antioxidant capacity of the cell will lead to increased oxidative damage in autism.

98 146.23 The Continuous STAT: Investigation of a New Coding System for the Screening Tool for Autism in Two-Year-Olds (STAT). C. R. McMahon*, B. Thompson and W. L. Stone, *Vanderbilt University*

Background: The STAT is an interactive measure for identifying children at risk for autism (Stone, Coonrod, & Ousley, 2000; Stone, et al., 2004). A scoring algorithm for 24-36 month olds has demonstrated strong psychometric properties for discriminating autism from developmental delay (DD). Modifying the existing STAT scoring algorithm to make finer discriminations of social-communicative functioning within the autism spectrum (e.g., autism vs. PDD-NOS) may increase the utility of the STAT.

Objectives: To design a more sensitive coding system and scoring algorithm for the STAT for use with toddlers with developmental concerns.

Methods: Videotapes from 11 children with ASD (7 autism, 4 PDD-NOS) and 11 children with DD during the STAT were coded.

Children were matched on CA (Mean: 32.7 months; Range: 29-35 months) and MA (Mean: 20.6 months; Range:13.5-30.25). The *Continuous STAT* differs from the STAT in that it provides separate scores for social engagement and task performance for each item; each score ranges from 0-2, rather than having a single dichotomous pass/fail score for each item. Item scores are averaged per domain (i.e., play, requesting, directing attention, and imitation) and summed to create "Social" and "Response to Press" (RTP) total scores. Means for the total and domain scores were compared across groups.

Results: Analyses reveal significant differences between the ASD and DD groups on both the Social and RTP scores. Moreover, children with PDD-NOS differed from children with autism on the Social score. Significant correlations were found between the two scores and other measures of autism symptomatology. Interestingly, different patterns of group differences emerged when scores were compared across domains.

Conclusions: This study provides preliminary support for the use of the *Continuous STAT* coding system and its ability to discriminate between diagnoses within the autism spectrum.

99 146.24 An Evaluation of the Psychometric Properties of the Social Responsiveness Scale in Two Groups of Children in Iceland. P. Magnusson*[1], E. Saemundsen[2], S. Steinberg[3], R. Fossdal[4], M. F. Olafsson[5], O. O. Gudmundsson[1], B. Lauth[1], K. Kristjansson[4], S. Hreidarsson[2], G. Bjornsdottir[4], J. Gulcher[4], H. Einarsdottir[4], H. Stefansson[4], T. E. Thorgeirsson[4] and K. Stefansson[4], (1)*Landspitali University Hospital*, (2)*State Diagnostic and Counseling Center*, (3)*deCODE genetics Inc*, (4)*deCODE genetics Inc.*, (5)*Midstod heilsuverndar barna*

Background: : In the context of a study of the genetics of autism a screening instrument was needed to assess symptoms in the relatives of probands.

Objectives: The reliability and construct validity of the Social Responsiveness Scale (SRS) was evaluated in two groups of Icelandic children.

Methods: The SRS, an instrument designed to assess autistic traits, consists of 65 items scored on a four-point Likert scale. The questionnaire was completed by the parents of 606 children aged 4-15 years, relatives of probands with autism and the parents of a random general population sample of 248 children aged 6-15 years. Median scores were compared by age and gender. In the group of relatives the familial aggregation of autistic traits was explored by considering both SRS high-scorers and individuals with autism as affected. Summary statistics of the relatives were compared with those of the general population sample. The relationships between SRS scores and scores on the Strengths and Difficulties Questionnaire (SDQ) were examined.

Results: Internal consistency measured by Cronbach´s alpha was .93-.96 according to group and gender. Median scores for males were higher than for females and the differences in scores between the group of relatives and the general population sample was in the expected direction. Autistic traits were elevated in closer relatives compared with more distant ones. An examination of the relationships of SRS total scores with subscale scores of the SDQ showed positive correalations with the Peer problems subscale and negative correlations with the Prosocial behaviour scale.

Conclusions: The results lend support to the reliability and validity of the Icelandic version of the SRS.

100 146.25 Identifying Emergent Phenomena in Autism. G. M. Anderson*, *Yale University School of Medicine*

Background: There is accumulating evidence that many autism-related phenomena are separable and fractionable. Thus, many of the phenomena and behaviors occur in isolation in family members and the general population, are not highly correlated within individuals, and appear to be inherited separately. However, some of the most characteristic and perplexing phenomena observed in individuals

diagnosed with autism do not run in their families. It has been suggested that these novel, "emergent", phenomena might arise in the individual from interacting configurations of co-occurring traits or from the interaction of genetic and biological factors underlying the traits (GM Anderson, Autism Research, in press, 2008).
Objectives: 1) To propose criteria for emergent phenomena in autism; and 2) to apply the criteria to a range of potentially emergent phenomena in order to rank their emergenic likelihood.

Methods: *Criteria:* A phenomenon is proposed to be emergent if: a) occurrence in probands>>relatives=general population; b) correlation or concordance in dizygotic twin pairs>>monozygotic twins; and c) monozygotic twin pairs are occasionally discordant. *Application of Criteria:* A systematic review of the literature was performed to determine the extent to which autism-related phenomena including intellectual disability (ID), seizures, persistence of primitive reflexes, stereotypies, self-injurious behavior, savant abilities, brain alaterality, morphological abnormalities, neurochemical alterations, gait disturbances and clumsiness, met the criteria.
Results: Supporting evidence and theoretical bases underlying the proposed criteria are discussed.
Systematic literature review indicated that all three criteria were met for ID. Persistence of primitive reflexes, stereotypies, and self-injurious behavior could be suggested to be emergent on the basis of *apparent* low occurrence in relatives.
Conclusions: Based on available family and twin data, ID (MR) can be put forth as likely to be emergent. Although the other phenomena examined remain plausibly emergent, additional family and twin studies are needed to estimate their emergenic likelihood.

101 146.26 Identifying Genetically Meaningful Phenotypes in Autism: A Childhood Profile of Language and Cognition in Parents. M. Losh*, *UNC, Chapel HIll*

Background: Language and cognitive delays are hallmarks of autism, and also appear to be genetically meaningful phenotypes that aggregate in families. However, knowledge of the precise linguistic and cognitive features of genetic significance is seriously lacking. Prior reports of early delays among parents have necessarily relied on retrospective reports obtained in adulthood. And, while sibling studies are proving highly informative, parental phenotypes are potentially more significant genetically, as they afford the opportunity to trace patterns of lineality and employ such characteristics in molecular genetic studies where phenotypic characteristics are examined in relation to transmission of specific molecular markers.

Objectives: This study examined directly assessed, detailed developmental language and cognitive phenotypes in parents of individuals with autism in an attempt to identify childhood profiles that may index genetic liability to autism, and which may be of use in molecular genetic studies.

Methods: Using archived language and cognitive testing records, we characterized the childhood language and cognitive skills of these parents from ages 5-10 years. Records were obtained from 48 parents of children diagnosed with autism. Archival data included summary scores for both language (e.g., vocabulary, grammar, discourse) and math (numerical representation/operations, fractions, decimals, geometry, etc.).

Results: Analyses revealed a significant split between composite language and math skill ($p<0.0005$). Thirty-five out of 48 parents showed composite language scores 20 points below their composite math score.

Conclusions: This fractionation in skills resembles a profile often observed in autism. Findings suggest that a dissociation in language and math/computational ability could represent a highly specific developmental cognitive-linguistic profile indexing genetic liability among parents.

102 146.27 GENDER DIFFERENCES IN AUTISM: EXPLORING SYMPTOM PRESENTATION AND EMOTIONAL COMORBIDITIES IN HIGHER FUNCTIONING CHILDREN WITH AUTISM. N. Kojkowski*[1], D. Coman[1], N. Zahka[2], A. P.

Inge[2], C. Schwartz[2], C. Hileman[2], L. Mohapatra[1], H. A. Henderson[1] and P. C. Mundy[3], (1)*University of Miami*, (2)*Graduate Student*, (3)*UC Davis*

Background: There is currently a paucity of research on the female expression of autism spectrum disorders (ASD) and therefore little is known about the specific diagnostic and treatment needs of girls with autism. Theoretically, it is important to examine gender differences in expression and patterns of comorbidity because of current theory that suggests autism may be a gender specific affect as suggested by the extreme male brain hypothesis.

Objectives: To investigate the associations between gender and symptom presentation and emotional comorbidities in a sample of HFA children and gender, age, IQ-matched neurotypical children. Primarily this study investigates the effects of diagnostic status and gender on symptom expression and emotional functioning.

Methods: Thirty-two children (8 HFA females, 8 HFA males, 8 neurotypical females and 8 neurotypical males) were included in the preliminary analyses. Parents completed the SCQ and each participant completed the BASC self report.

Results: Preliminary analyses indicate a significant interaction between diagnostic group and gender on the SCQ total score, $F(1) = 7.57$, $p < 0.5$. HFA males are reported as more symptomatic than HFA females, whereas gender was unrelated to symptom scores within the control sample. Additionally, analyses indicated a significant effect of gender on internalizing problems with the BASC-SRP, $F(1) = 5.42$, $p < 0.5$, such that females, regardless of diagnostic status, endorsed more internalizing problems than males.

Conclusions: These data suggest that while still meeting diagnostic criteria, HFA females are perceived by their parents as less impaired in social communication than HFA males. Given that all females self-reported greater internalizing symptoms, it may be that HFA females are more aware of, and sensitive to, their social environment and therefore present as less classically symptomatic in the social and communication domains. The results will be discussed with reference to implications for gender-specific diagnostic and intervention strategies.

103 146.28 Agreement among diagnostic instruments for autism spectrum disorders and clinical judgment in preschool aged children. C. Chlebowski*, H. Boorstein, M. Barton, T. Dumont-Mathieu, S. Hodgson and D. Fein, *University of Connecticut*

Background: Past research indicates that there is strong agreement between clinical judgment based on DSM-IV criteria, CARS, and ADOS-G when classifying toddlers with ASD; however, the agreement between the ADI-R, and the CARS, ADOS-G, and clinical judgment is poor (Ventola et. al., 2006). The diagnostic agreement rates when classifying older preschool children with ASD have not been sufficiently studied.

Objectives: To examine the diagnostic agreement rates among the ADOS, ADI-R, CARS and clinical judgment in older preschool children with ASD.

Methods: Participants were 107 children who initially screened positive on the M-CHAT (Robins, et al., 2001), and were evaluated, at age 2. At a second time point about two years later (mean age 53 months), all children were reevaluated, and classified as ASD or non-spectrum by the ADOS, ADI-R, CARS, and clinical judgment based on DSM-IV symptomatology. Current results are based on this second evaluation.

Results: Kappa analyses revealed very good agreement between the ADOS and clinical judgment ($k = .808$, $p = <.001$) as well as moderate agreement between the ADOS and CARS ($k = .553$, $p = <.001$) and the CARS and clinical judgment ($k = .442$, $p = <.001$). The ADI-R displayed fair agreement with the CARS ($k = .382$, $p = <.001$), the ADOS ($k = .236$, $p = .002$), and clinical judgment ($k = .262$, $p = <.001$).

Conclusions: This replication found that the ADI-R continues to have relatively weak

agreement with other diagnostic measures and clinical judgment in a sample of preschool aged children, suggesting limitations with its use in younger children. Among the factors affecting this lower agreement may be the measure's reliance on only parental report, the inclusion of past behaviors in the diagnostic algorithm, and its lack of PDD or ASD cut off scores.

104 146.29 THE EFFECT OF AUTISM ON PARENT REPORT: A PRELIMINARY INVESTIGATION OF PARENT REPORTED SYPTOMOTOLOGY OF NEUROTYPICAL SIBLINGS OF HIGHER FUNCTIONING CHILDREN WITH AUTISM. D. C. Coman*[1], N. Kojkowski[1], A. Inge[2], N. Zahka[2], C. Schwartz[2], C. Hileman[2], L. Mohapatra[1], M. Alessandri[1], H. A. Henderson[1] and P. C. Mundy[3], (1)*University of Miami*, (2)*Graduate Student*, (3)*UC Davis*

Background: Currently, there is a myriad of research on the development and the broader phenotype of autism (ASD) in typically developing (TD) siblings of children with ASD. This research is dependent upon the parent report for diagnostic, developmental, and behavioral information. Therefore, it is imperative to investigate the possible effects of autism on the parent report of these TD siblings.
Objectives: To investigate the effects of autism on the parent report of a TD child with an ASD sibling. Furthermore, to investigate whether the autism sibling group differs significantly than the TD sibling group on self-reports of internalizing symptoms.

Methods: 10 TD children (5 in ASD sibling group, 5 in TD sibling group) were matched on birth order, age (M = 149.4 (20.0)), and IQ (M = 109.0 (8.763)). Parents completed the SCQ and each participant completed the PAES-III.

Results: Preliminary analyses indicate a significant difference between the two sibling groups on the SCQ Communication Domain, $F(1) = 10.8$, $p < 0.5$ and the SCQ total score, $F(1) = 6.77$, $p < 0.5$. Parents from the autism sibling group reported significantly lower on the SCQ Communication Domain and the SCQ total score than caregivers of the TD sibling group. Further analyses indicated a significant difference between the two groups on the PAES-III Anger-In Domain, $F(1) = 6.00$, $p < 0.5$. The autism sibling group reported significantly higher than the TD sibling group.
Conclusions: Preliminary analyses suggest that parents of the autism sibling group may under report when asked to complete diagnostic measures for their neurotypical child. This implies that the presence of autism in one child may affect the way parents report symptomotology in their TD child. Additionally, siblings of ASD children self-reported greater internalizing symptoms than the TD sibling group.

109 146.30 The Tooth Fairy Project: Heavy Metal Concentrations in the "Baby Teeth" of Children with Autism Spectrum Disorders (ASD). M. M. Abdullah*[1], A. R. Ly[1], W. A. Goldberg[1], K. A. Clarke-Stewart[1], T. Chan[1], E. Kent[1], J. Dudgeon[2], M. A. Spence[1] and J. E. Ericson[1], (1)*University of California, Irvine*, (2)*California State University, Long Beach*

Background: The growing literature on exposure to heavy metals during sensitive periods of development is equivocal regarding the risk of neuropsychological disorders. Recent reports have suggested mercury exposure as a potential contributor to the development of ASD (e.g., Bernard et al., 2002); others have not found an association (e.g., Fombonne et al., 2007). Previous studies have been limited by the choice of biomarkers of blood, hair, and tooth dentin, which are redeveloping organic tissues that address only current levels of metals. The current study focuses on tooth enamel, which does not regenerate, yielding archival records during two important periods: prenatal and early postnatal brain development.
Objectives: To evaluate differences in concentrations of heavy metals in shed deciduous teeth of children with ASD and matched typically developing children.
Methods: Shed "baby teeth" were collected from 22 children with ASD and 22 typically developing children matched on gender (86% male) and chronological age ($M = 11.7$

years). Study children were participants in one of two multi-site studies and received comprehensive developmental and psychological evaluations. Trace metal spatial distributions of lead, mercury, manganese and other elements in tooth enamel were analyzed using laser ablation-inductively coupled plasma-mass spectrometry (LA-ICP-MS).
Results: Initial analyses do not indicate higher concentrations of lead, manganese, or mercury in either prenatal or postnatal regions of the teeth among children with ASD as compared to matched controls. The presentation will include final analyses and interpretations on the full sample and on other elements.
Conclusions: Based on preliminary results, concentrations of heavy metals do not seem to be higher in children with ASD. The type of biomarker used may be important, and it is also possible that prenatal and early postnatal exposure to heavy metals contributes to the development of ASD in some children, but not others.

105 146.31 COGNITIVE AND LANGUAGE DEVELOPMENT IN OLDER AND YOUNGER SIBLINGS OF CHILDREN WITH ASD. C. Montiel-Nava*, E. Bromberg, Z. González, V. Toledo, I. Montiel-Barbero, J. A. Chacín and J. A. Peña, *La Universidad del Zulia*

Background:, abnormalities in language development and cognitive deficits have been reported in siblings of children with autism spectrum disorders (ASD). However, the extent of such impairment depending on the birth order is still unclear.
Objectives:, to explore cognitive and language development in siblings of children with ASD, and to compare younger and older siblings on all the measures.
Methods:, 36 siblings of children with ASD, between the ages of 2 years, 6 months and 15 years (x=8.67; SD=3.91) participated in this study. 72% (n=26) were older than the affected sibling, whereas 28% (n=10) were younger. The Peabody Picture Vocabulary Test (PPVT) was administered to all participants. The IQ was estimated based on the administration of the WPPSI-III or WISC-III.The Social –Communication Questionnaire (SCQ) was used to assess autism-related symptoms; and the Vineland Adaptive Behavior Scales (VABS) as a measure of adaptive functioning.
Results:, PPVT scores were below normal limits (x=73.96; SD=38.49). On the contrary, IQ scores (FSIQ [x=91.52, SD=15.98], VIQ [x=94.8, SD=20.81], and PIQ [x=92.6, SD=12.73] were regarded as average. A more detailed analysis on the measures indicated that: 45% (n=16) exhibited language impairment (<79), while 28% (n=10) had borderline and intellectually deficient IQ scores (<79). In contrast, their adaptive functioning was within normal limits. Only 2.97% (n=1) had SCQ scores above 15. Younger siblings had poorer performance on the PPVT (U=0, $p<0.001$), and on the communication sub-domain of the VABS (U=58.500, $p<0.1$) when compared to older siblings.
Conclusions:, siblings of children with ASD might exhibit abnormal language development, which could be considered as features of the broader-autism phenotype. Although it has also been suggested that birth order could affect the language development of the unaffected siblings, the relationship between these variables remains unclear. These findings offer additional support for a familial association between ASD and language abnormalities.

106 146.32 The Extended Family History of Children with ASD. E. G. Schreiber*[1], E. E. Malesa[2] and T. A. Walden[2], (1)*Department of Psychology, Vanderbilt University*, (2)*Vanderbilt University*

Background: Given the growing evidence for genetic linkages within ASD, examination of the family history of heritable disorders that may contribute to the risk of ASD may be useful. Past research has found an increased risk of ASD for those with a parental history of a mental health disorders, however, much of the family research to date has examined only first-degree relatives. Thus, little is known about the prevalence of disorders in the extended families of individuals with ASD.

Objectives: To examine the prevalence of mental health disorders within first- and second-degree relatives of children diagnosed with ASD as compared to those of typically developing (TD) peers.

Methods: Participants included 48 children with ASD (mean CA=34.9 mos, range 30-40 mos) and 26 TD children (mean CA = 30.7 mos, range 29-44 mos). Family history was collected via semi-structured interview with one or both parents of each child. Parents were asked to report the presence of any mental health disorders in their extended families.

Results: Overall, similar rates of mental health disorders were found across ASD and TD families (68.75% vs 61.45%). A significantly higher prevalence of bipolar disorder (21% vs 4%, p=.5) and marginally higher prevalence of ADHD (33% vs 16%, p=.8) was found in the extended families of children with ASD in comparison to the extended families of TD children.

Conclusions: While overall rates of mental health disorders in extended families of children with and without ASD are comparable, those with an extended family history of bipolar disorder and/or ADHD may be at an increased risk for having a child with ASD.

107 146.33 DYSMORPHOLOGY EVALUATION USING PICTURES COMPARED TO PHYSICAL EXAM IN CHILDREN WITH AUTISM SPECTRUM DISORDERS. A. M. Reynolds*[1], E. R. Elias[1], A. Tsai[1], G. Bellus[1], K. Kaparich[2], A. Ribe[2], L. Miller[3] and S. Hepburn[4], (1)*University of Colorado Denver*, (2)*School of Medicine*, (3)*Colorado Department of Public Health and Environment*, (4)*University of Colorado at Denver*

Background: Autism is a heterogeneous disorder. Miles (2005) has described complex vs. essential autism based upon the presence of dysmorphic features and microcephaly. In large epidemiologic studies, it is not practical for each child to see a clinical geneticist. Relatively cost-effective methods for evaluating dysmorphology are needed.

Objectives: Compare dysmorphology exam by a clinical geneticist to proposed research evaluation of dysmorphology (Pictures and Measurements Approach-PMA).

Methods: Forty children (ages 2-5 years) with ASD were seen by a geneticist, who documented dysmorphic features observed during the exam. Each child was also seen by a non-geneticist clinician who administered the PMA (anthropometric measurements, description of specified features, and photographs of the face, head, hands, feet, and unusual physical features observed by examiner). A second geneticist reviewed the PMA data only and determined the number of dysmorphic features. The geneticists were alternately assigned to perform the clinical exam or review the PMA data.

Results: The intraclass correlation coefficient for the total number of dysmorphic features identified was .52 (CI: .9 - 0.74), suggesting moderate agreement across methods. Analysis of examiner effects suggested variability across geneticists viewing the pictures: Examiner A: ICC =0.32 (ns); Examiner B: ICC = 0.65 (ns). Agreement across methods was best for the mouth and ears and worst for the nose. In 16 of 40 subjects (40%), the geneticist found 1 or more features that would not be picked up by the PMA. These features included the chest (accessory nipple, pectus excavatum), teeth and palate (high narrow palate, small or wide spaced teeth), genitalia (shawl scrotum, hypospadias), and joints (laxity).

Conclusions: Although time-saving, assessing dysmorphic features via photographs results in missing some physical features. In epidemiology studies, the potential for PMA to miss important features is a concern that needs to be addressed, potentially through medical record review.

Sponsors: CDC/CADDRE/SEED.

108 146.34 Early Identification of Infants at Risk for ASD using Head Circumference and the Head Tilt Reflex. C. Samango-Sprouse*[1], E. Jobes[2], R. L. Jameson[3], K. Haskell[3] and T. Sadeghin[3], (1)*George Washington University / NDC for Young Children*, (2)*The Pediatric Group*, (3)*NDC for Young Children*

Background:

Autism Spectrum Disorder is a neurobiological disorder that occurs one in 150 children. Children have a triad of well known features including severe speech and language dysfunction, repetitive stereopathies and atypical social interactions. Early identification results in significant improvement in development and reduction in behavioral symptoms. Retrospective studies show that head circumferece (HC) in children with ASD accelerates between 6 and 12 months. Teitlebaum and associates have shown in a small study that children with ASD did not acquire head tilt reactions appropriately. This is a normative study in typical developing infants to assess the reliability of these two measures to identify infants at risk for ASD.

Objectives: This study focused on two possible risk factors which indicate vulnerability for ASD. They were abruptly changed from the 50^{th} percentile to above 75^{th} percentile and head tilt reflex.

Methods: 366 infants were enrolled in the study and HC was measured and head tilt responses were completed at 4, 6 and 9 months of age. Children had a neurodevelopmental evaluation if head circumference abruptly changed from the 50^{th} percentile to above 75^{th} percentile or if head tilt response was not established by 9 months.

Results: Sixteen infants had neurodevelopmental evaluations because of atypical head tilt reaction or accelerated head growth. Three children were determined "at risk" for ASD with developmental delay. All three infants were referred for EI services and will be followed to see if the diagnosis of ASD is confirmed.

Conclusions: Risk factors are a quick and efficient mechanism to assist PCP in identifying children who are at risk for ASD and other neurodevelopmental disorders. It appears to be an effective mechanism to facilitate early identification and treatment of children at risk for ASD and neurodevelopmental disorders by

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147 Autism Spectrum Disorders: policy and practice in Europe

Speaker: J. Fuentes*Child & Adolescent Psychiatry Unit*

Presentation by Joaquin Fuentes on behalf of Autism Europe and IACAPAP

Invited Educational Symposia Program

148 Sensory Processing: The Interface of Research and Clinical Practice

Moderator: G. T. Baranek*University of North Carolina at Chapel Hill*

Organizer: S. Hyman*University of Rochester*

Speakers: G. T. Baranek[1]L. Bennetto[2]C. Cascio[3](1)*University of North Carolina at Chapel Hill*, (2)*University of Rochester*, (3)*Vanderbilt University*

Sensory differences are commonly reported in people with autism. Often they are among the most problematic symptoms. This symposium will examine the phenomenon of sensory symptomatology, the research methodology used to characterize and explain the observed behaviors, and the treatments that are being used in the community. A translational approach will be emphasized to inform both basic researchers and clinicians on future avenues of study.

1 Introductory Remarks.

2 Characterizing Sensory Processing Features in Autism: Scope of the Problem and Clinical Measurement. G. T. Baranek*, *University of North Carolina at Chapel Hill*

Sensory processing research in autism has been hampered by myriad methodological issues such as the lack of consensus for terminology used across disciplines, controversies about the extent to which sensory processing problems exist, whether or not these issues relate to core features of autism, and debates surrounding the efficacy of sensory-based interventions. This presentation will describe recent findings on the nature of unusual sensory features, their

prevalence, specificity, and developmental course in autism. A variety of sensory processing patterns have been identified behaviorally and may take the form of hyper- and hyporesponsiveness to environmental stimuli, extreme sensory seeking behaviors or fascinations, and/or paradoxical responses across sensory modalities. These sensory features may have significant consequences on adaptive functioning, daily activities, and social participation for persons with autism and their families. Careful clinical characterization of the "sensory phenotype" is critical to understanding the pathogenesis of these features, as well as to designing sensitive and specific assessments, and evaluating intervention outcomes. Systematic translational research, integrating evidence across multiple disciplines and stakeholders, is needed to move the field forward in understanding these complex issues.

3 Interventions for Sensory Processing Problems in Autism. M. L. J. Miller*, S. A. Schoen and B. Brett-Green, *Sensory Processing Disorder Foundation*

The considerable literature that exists on the effectiveness of various treatments (e.g., pharmacological, behavioral, nutritional, sensory-based etc.) for children with autism has inconsistent findings. The array of possible treatments can be bewildering when parents and others are confronted with making decisions about what the "best" treatment is for their child. Given the prevalence of unusual sensory features in autism, "sensory-based" interventions are common yet controversial. These often hinge on the assumption that improving faulty underlying mechanisms (i.e., sensory processing) may ameliorate sensory symptoms, as well as facilitate broader developmental, behavioral, or adaptive outcomes such as increased social participation. This talk will discuss the evidence-base for common approaches used to treat sensory processing problems in autism and highlight one intervention, occupational therapy with a sensory integrative approach (OT/SI). The principles of OT/SI will be presented using video-taped examples of treatment, and OT/SI will be demystified using two clinical reasoning models: (1) the Sensory Matrix and (2) "A SECRET" (Miller, 2006). Controversial issues will be noted such as: To what extent does the child direct the treatment session? Should OT/SI be focused on changing underlying brain function or on functional outcomes? What is the "best" intensity of treatment? What is the "just right challenge"? Preliminary results of a randomized controlled trial on OT/SI highlighting two of the outcome measures used (i.e., psychophysiologic functions and Goal Attainment Scaling) will be presented, taking into consideration four key criteria for implementing rigorous outcome studies. The session will conclude with directions for future research using a translational approach to describe how studies of the behavioral features, neurophysiology, and treatment may interrelate.

Miller, L. J. (2006). Sensational kids: Hope and help for children with Sensory Processing Disorder. New York: Putnam.

4 Neural Mechanisms for Sensory Features in Autism. C. Cascio*, *Vanderbilt University*

Caregivers, educators and practitioners have long taken note of prevalent sensory features, such as hyper- and hyporesponsiveness to sensory stimuli and highly focused perceptual processing styles, that are shared by many people with autism. While the vast majority of autism research has proceeded using a "top-down" strategy (beginning with hypotheses related to the complex social-communication behaviors that define the disorder), a growing contingent of researchers have begun to address autism from the "bottom-up." A bottom-up approach starts with the premise that social-communication behaviors depend on complex and highly specialized sensory and perceptual functions that may also be compromised at lower levels of processing in persons with autism. Investigation of simple sensation and perception is a natural fit for neurophysiology and functional brain imaging techniques, which have already uncovered important clues to the disorder. This presentation will describe plausible neural mechanisms underlying myriad sensory features in autism and their relationship to core features. Recent findings from neurophysiological and fMRI methods will be discussed to highlight emergent themes such as: enhanced processing of simple auditory, tactile, and visual stimuli; specific deficits in

processing complex non-social sensory stimuli; and aberrant connectivity within and between brain regions as potential neural substrates of sensory features seen in autism. The convergence of these findings with fMRI studies of more complex social stimuli such as speech and faces will help to characterize various strengths and deficits along the continuum of sensory and perceptual processing complexity. Future directions for translational research that connects our understanding of neural mechanisms to clinical assessment and intervention for sensory features in autism will be discussed.

5 Neuropsychological Perspectives on Sensory Processing in Autism. L. Bennetto*, *University of Rochester*

There is a growing appreciation for the role that basic sensory processing problems in autism play in the development and presentation of core diagnostic symptoms and everyday functioning difficulties. Using neuropsychological theory and research, this talk will highlight how two common clinical features of autism (communication impairments, atypical eating patterns) may be explained in part by basic sensory difficulties in hearing, vision, taste, and/or smell processing. Within the domain of communication, research in autism reveals evidence of impaired perception of unimodal auditory and visual information during speech processing, as well as evidence for impairments in multimodal processing (e.g., the enhanced perception of speech when viewing the speaker's lips). This talk will further discuss how these deficits could be related to delays in language acquisition, as well as later impairments in the comprehension of verbal and nonverbal information in social and academic settings. Within the domain of eating behaviors, neuropsychological studies are beginning to reveal how differences in basic functions requiring chemosensory (taste and smell) processing may influence food selection in persons with autism. These recent findings provide empirical support for the long-standing concerns of parents about their children's unusual or restricted eating habits, and illustrate the importance of sensory processing functions as one component that may interact with myriad other biological or environmental factors to result in eating problems. This talk will describe both parent report and neuropsychological methods for evaluating sensory processing in autism and discuss how sensory processing across modalities can influence everyday functioning. Advantages and limitations of these types of modality-specific neuropsychological investigations will be presented, focusing on the translation of knowledge from this area of study to neurobiological or clinical studies in the future.

Roundtable Program

149 Strategies to Assay Communication Deficits in Animal Models of Autism: Roundtable Discussion

Moderator: J. Crawley*National Institute of Mental Health*

Speakers: A. Bailey[1]J. Bakker[2]R. J. Blanchard[3]P. Brennan[4]S. Brudzynski[5]N. Clayton[6]J. Crawley[7]U. Frith[8]M. L. Scattoni[9]S. E. Swedo[10](1)*University of Oxford*, (2)*University of Liège*, (3)*University of Hawaii*, (4)*University of Bristol*, (5)*Brock University*, (6)*University of Cambridge*, (7)*National Institute of Mental Health*, (8)*University College London*, (9)*Istituto Superiore di Sanita*, (10)*National Institutes of Health - National Institute of Mental Health*

The second diagnostic criterion for autism, qualitative impairments and delays in communication, is conceptually the most difficult to model in animals. While we have many tests for social and repetitive behaviors in model organisms, little is known in most non-primate species about signaling mechanisms that represent true communication in a social setting. Particularly for mice, a species useful for testing hypotheses about candidate gene mutations in autism, new approaches are needed to detect the communicative value of their olfactory signals, ultrasonic vocalizations, and the possible presence of Theory of Mind mentalization and empathy. Our Roundtable session is designed to generate ideas for optimal assays to evaluate communication in animal models of autism.

Behavioral neuroscientists expert in mouse, rat, and bird communication will present photographs, videos, and audioclips of their tests for olfactory, auditory, visual, gustatory, and tactile signaling between individuals. Clinical experts will critique the relevance of each task to the qualitative and quantitative communication deficits seen in autism and autism spectrum disorders. Back-and-forth discussion between the basic and clinical roundtable participants, along with input from members of the audience, will focus on identifying tasks with optimal face validity to the second diagnostic symptom of autism.

Oral Presentations Program

150 Brain Imaging 1

150.1 Cortical Maturation in Autism Spectrum Disorder. A. Raznahan*[1], R. Toro[2], E. Daly[1], P. Bolton[3], T. Paus[2] and D. G. Murphy[1], (1)*Institute of Psychiatry, King's College London*, (2)*University of Nottingham*, (3)*Institute of Psychiatry*

Background: Structural neuroimaging studies have identified early overgrowth and regional abnormalities of the cerebral cortex in autism spectrum disorders (ASD). However, most reports have only examined differences in cortical volume (CV) - but CV is a product of surface area (SA) and cortical thickness (CT). Because SA and CT differ phylogenetically and ontologically– their study could help us better understand the neurobiological underpinnings of ASD.

Objectives: (1) To differentiate cortical abnormalities in autism according to CV, CT and SA. (2) To examine the age-dependency of group differences in regional cortical anatomy.

Methods: We used FreeSurfer to measure global and regional CV, CT and SA in a large sample of children and adults with ASD (n=76) and healthy controls (n=51).

Results: We found abnormalities in ASD of specific cortical systems known to be involved in language, social cognition and executive function. But, the distribution of GMV, CT and SA differences did not overlap – suggesting that not all ASD-related brain differences come about in the same way. Furthermore, we found preliminary evidence that in some brain regions, differences in cortical CV between subjects with ASD and controls seem to depend on the subject's age. This effect was most pronounced in the temporal lobes (Age by Group interaction for Bilateral Temporal CV: F=10.95, p=0.001), and was mirrored in age by group interactions for CT (F=6.60, p=0.1), but not for SA (p=0.36). The most prominent age by group interactions for CT was found in the fusiform region - which is known to be involved in face processing and shows functional abnormalities in ASD.

Conclusions: This is the first evidence to date that abnormal brain maturation in ASD is not limited to early life and is regionally specific. We predict that other areas of the social brain will also show evidence of dysmaturation in ASD.

150.2 Increased cortical thickness and gray matter volume in young children with Autism. R. K. Lenroot*, D. Nielsen, A. Willment, C. Draper, D. O. Black, S. J. Spence, A. Thurm, S. E. Swedo and J. N. Giedd, *NIMH*

Background: Increasing evidence indicates that brain growth in children with autism may be accelerated early in life and then slow, resulting in more significantly enlarged brain volumes in younger children(Courchesne, Neuron 2007). One previous report in older children has found increased cortical thickness (Hardan, AJP, 2006), however cortical thickness has not been characterized in younger children with autism.

Objectives: Assess cortical thickness and brain volumes in a cohort of young children with autism.

Methods: 20 subjects meeting strict criteria for Autistic Disorder (18 males, age 4.5(sd1.2)); 31 healthy controls matched on age and sex. Diagnoses were established by trained raters using the ADOS and ADIR. Autistic subjects were sedated during MRI procedure; controls were not sedated. All subjects were scanned using the same 1.5T scanner and protocol (Giedd, Cerebral Cortex 1996). Volumes for

total brain volume and white and gray matter lobar regions and cortical thickness at 40,973 vertices were obtained using fully automated methods developed by the Montreal Neurological Institute (MNI) (Zijdenbos, IEEE TMI, 2002; Lerch, Neuroimage, 2005). 2-tailed t-tests were used to compare brain volumes; effects of diagnosis on cortical thickness at each vertex were determined using linear regression followed by adjustment for multiple comparison using FDR.

Results: Total gray matter was significantly larger in subjects with autism (780.78cc ± 78.0 vs 732.5cc ± 74.5, $p < .31$); gray matter was larger in frontal, temporal, and parietal but not occipital lobes; total brain volume and white matter were not different. The cortex was significantly thicker in individuals with autism across broad regions with most pronounced effects in frontal and temporal regions.

Conclusions:Increased cortical thickness contributes to larger gray matter volumes in young children with autism. Future directions include comparison of brain structures in regressive and nonregressive autism subtypes.

150.3 Structural brain correlates of autism. K. L. Hyde*[1], F. Samson[2], A. C. Evans[1] and L. Mottron[2], (1)*Montreal Neurological Institute, McGill University*, (2)*Hôpital Rivière-des-Prairies*

Background:

There is currently no consensus on the neuroanatomical brain correlates of autism. This lack of consensus is likely due to the fact that available studies on the structural brain basis of autism differ in diagnostic criteria, age and IQ of participants with autism, and have utilized different brain imaging methods.

Objectives:

The aim of the present study was to investigate the neuroanatomical correlates of high-functioning autism by novel cortical thickness methods in well-defined and closely matched subject groups.

Methods:

Subjects were 19 participants diagnosed with autism via ADI-R and ADOS (mean age 23.4 years, 6.6 SD, mean global IQ 100.4, 12.4 SD), and 15 controls who had no neurological history, and were closely matched to participants with autism in age and global IQ. All participants were right-handed. T1-weighted MR images were obtained for all subjects on a 3 Tesla scanner. Cortical thickness maps were derived from these MRI data for each subject as described elsewhere (Lerch and Evans, 2005) and between-group statistical analyses were then performed. Ethical approval for the present work was obtained in accordance with the National Institute of Health guidelines.

Results:

Region specific differences in cortical thickness between groups were found in predicted distributed cortical areas such as brain areas implicated in auditory (right Heschl's gyrus) and visual perception (middle occipital gyrus), and in social cognition (bilateral frontal cortex, right cingulate gyrus).

Conclusions:

Our findings demonstrate that cortical thickness is a viable method to detect differences in brain regions implicated in the perceptual (Mottron et al, 2006), social and emotional (Schultz et al, 2005) domains, and thus in the important processing domains in which autistic demonstrate atypicalities.

150.4 MRI Longitudinal Study of the Cerebral Cortex through Early Childhood in Autism. C. Schumann*[1], G. Wideman[1], C. Carter Barnes[1], T. Kao[1], R. Carper[1], C. Bloss[2], D. Hagler[1], C. Lord[3], N. Schork[2] and E. Courchesne[1], (1)*University of California, San Diego*, (2)*Scripps Research Institute*, (3)*University of Michigan Autism and Communication Disorders Center*

Background: A recent hypothesis has emerged that toddlers with autism undergo abnormal neuroanatomical development that includes a period of early brain overgrowth. Cross-sectional MRI and head circumference studies suggest that the overgrowth occurs before the diagnosis is typically given in the fourth year of life. MRI studies that further

partition the cerebrum into lobes find that the more anterior and higher association areas exhibit the highest degree of enlargement.

Objectives: We carried out a longitudinal MRI study of the cerebral cortex in toddlers 18 months to five years of age in order to 1) identify aberrant growth patterns in specific regions of the cerebral cortex that may contribute to early enlargement and 2) correlate behavioral and clinical features with affected cortical regions in toddlers with autism.

Methods: Clinical evaluations and MRI scans (total=220) were collected at ~12 month intervals from ~18-60 months from typically-developing toddlers (n=48) and those with provisional autism spectrum disorder (n=43). Final diagnosis was given at ~4 years of age upon completion of the study with the Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview-Revised (ADI-R). For each T1-W MRI, a semi-manual segmentation program was used to delineate cerebral gray and white matter and then the program Freesurfer further parcellated the cortex into subregions.

Results: Preliminary regression analyses revealed significant enlargement in cerebral, frontal, and temporal gray matter volumes ($p<.5$) in toddlers with autism relative to typically-developing controls.

Conclusions: In this first longitudinal MRI study of toddlers with autism, growth trajectories of total cerebral, frontal and temporal gray were significantly different from typical toddlers. Aberrant growth patterns observed in longitudinal MRI's at early ages provide a developmental anatomical phenotype for autism spectrum disorder.

150.5 STRUCTURAL ABNORMALITIES IN THE AUTISTIC BRAIN REVISITED – A SURFACE-BASED TOPOGRAPHIC ANALYSIS. C. Ecker*, P. Johnston, E. Daly and D. Murphy, *Institute of Psychiatry*

Background: The investigation of brain structure in autism has traditionally focused on volumetric differences by employing techniques such as voxel-based morphometry (VBM). VBM is, however, highly unspecific as observed differences might be attributed to several parameters related to cortical surface topography (e.g. cortical thickness or pattern of gyrification).

Objectives: The aim of this study was to identify which structural parameters in particular elicit the differences in brain anatomy previously observed in autism by employing both volume-based and surface-based topographic analysis.

Methods: Structural MRI scans were collected on 29 well-characterized individuals with autism (mean age = 32 yrs, mean IQ = 105, right-handed) and 27 age/gender matched healthy controls. A set of 4 measures (grey matter volume, cortical thickness, curvature index, folding index) were obtained for each anatomical region using FreeSurfer software, and subsequently compared across subject groups.

Results: Across all investigated areas, most differences were observed in curvature index and cortical folding including several areas of the frontal, parietal and temporal lobe, with individuals with autism displaying reduced parameter values. No significant group differences were observed in cortical thickness. A significant reduction in grey matter volume in the autistic group was observed in the left lateral orbitofrontal cortex and the bilateral rostral middle frontal area only.

Conclusions: The data shows that the previously observed differences in brain structure in the autistic brain are predominantly due to shape rather than volume abnormalities suggesting an abnormal pattern of regional neuronal connectivity. This finding is in agreement with a recent study demonstrating that individuals with autism display cortical folding abnormalities in parietal and frontal regions (Nordahl et al., 2007).

150.6 The relation between connection length and degree of connectivity in autism: Measuring the impact of brain overgrowth with DTI. J. D. Lewis*[1], R. J. Theilmann[1], M. I. Sereno[2] and J. Townsend[1], (1)*UCSD*, (2)*UCL/Birkbeck College*

Background: Ringo et al (1991) hypothesized that, due to the larger metabolic costs and conduction delays associated with long-distance connections, larger brains would show decreased long-distance connectivity. That hypothesis is supported by computational modeling (Ringo, 1991), MRI across species with a wide range of brain sizes (Rilling and Insel, 1999), and MRI from adults and children (Jancke et al, 1997; 1999). Recent research has, moreover, shown that this scaling relationship develops during childhood (Lewis *et al,* 2007).

Objectives: This motivates the hypothesis that the abnormal early brain overgrowth seen in autism (Courchesne *et al,* 2001; Hazlett *et al,* 2005) will lead to a lesser degree of connectivity — consistent with findings of underconnectivity in autism (Lewis et al, 2003, 2004; Just et al, 2004; Herbert et al, 2005). The prediction tested here is that individuals with autism should show a scaling relation between connection length and degree of connectivity, as do controls, but should show a lesser degree of connectivity, overall.

Methods: Using diffusion tensor imaging (DTI) and tractography to detail the patterns of connectivity of the corpus callosum, and to estimate the length of interhemispheric connections in each of five sub-regions, we investigated the relation between the length of the connections and the degree of connectivity in 9 individuals with autism and 22 controls. Regression analyses were used to assess the scaling relation in each of the five sub-regions in both groups, and between group differences were assessed with analysis of variance tests.

Results: Regressions between connection length and degree of connectivity were significant in anterior and posterior regions in both individuals with autism and in controls. Anterior regions showed a significantly reduced degree of connectivity in the autistic group.

Conclusions: The results support the hypothesis that the early brain overgrowth in autism leads to reduced connectivity.

150.7 Amygdala Activation and Connectivity to Emotional Faces in Autism Spectrum Disorders. C. S. Monk*, S. J. Weng, J. A. Lee, N. Kurapati, J. Maslowsky, H. M. C. Louro, S. Risi and C. Lord, *University of Michigan*

Background: Although many investigations have examined the brain basis of face processing in autism spectrum disorders (ASD), results are inconsistent. The inconsistency may be partly due to variations in attention to faces that were presented over long durations (2-3 secs).

Objectives: Using event-related functional MRI (fMRI) and a task that provided a behavioral measure of attention to briefly presented faces, we evaluated differences in brain function between adults with ASD and controls. We hypothesized that participants with ASD relative to controls would show greater amygdala activation to emotional faces.

Methods: During fMRI acquisition, a probe detection task was used to derive a measure of attention to faces. Participants (12 with ASD and 12 controls) viewed pairs of faces (angry/neutral, sad/neutral, happy/neutral, and neutral/neutral) for 500 msec. They then pressed a button to an asterisk that was either on the same or opposite side as the emotional face. ASD participants were recruited through the UM Autism and Communications Disorders Center. ASD was diagnosed with the ADOS and ADI-R.

Results: There were no group differences in the behavioral measure of attention. Relative to controls, participants with ASD showed greater right amygdala activation to sad faces ($p<.5$ small volume corrected) and trends in the same direction to other emotions. Moreover, amygdala activation to sad faces positively correlated with severity of social impairment. Finally, a connectivity (psychophysiological interaction) analysis showed that adults with ASD, relative to controls, had greater positive coupling between the right amygdala and visual processing structures (visual cortex and temporal lobe) and less positive coupling between the right amygdala and ventral prefrontal cortex.

Conclusions: When emotional faces are briefly presented and there are no group differences in attention, adults with ASD show greater

amygdala activation than controls. Furthermore, ASD is associated with altered amygdala-cortical interactions.

150.8 AGE-RELATED DIFFERENCES IN NEUROTRANSMITTER LEVELS IN THE HUMAN AMYGDALA DURING TYPICAL ADOLESCENT DEVELOPMENT. B. Nacewicz*, K. M. Dalton, L. A. Angelos, M. J. Sutterer, A. L. Alexander and R. J. Davidson, *University of Wisconsin*

Background:Recent work suggests abnormal amygdala development may relate to social impairments in autism. However, this is based on differences in amygdala volume and has yet to be related to underlying neural or histological differences. Magnetic Resonance Spectroscopy (MRS) holds promise for understanding differences in neurochemistry both in pathology and normal development. Initial MRS studies in adolescents with autism suggest that neurochemical differences in the medial temporal lobe may also relate to social impairments, but whether these represent amygdala or hippocampus is unclear. As a further confound, amygdala volume increases rapidly throughout adolescence and some metabolites may show similar age-related differences.
We recently developed an MRS technique that can reliably measure GABA levels specifically in amygdala. With this novel technique, we aim to characterize normal neurochemical development and to look for changes that parallel the rapid growth during this period. An understanding of normal amygdala neurochemistry will provide a reference for future studies of adolescents with autism, allowing models of hypersensitivity and hyposensitivity to be framed in terms of low and high GABA/glutamate levels.

Objectives:To characterize the typical neurochemical development of the human amygdala from age 10 to 25 using amygdala-specific MRS.

Methods:Twenty-two typically developing males aged 10-25 y were recruited in an ongoing effort to uniformly sample the age range (2 subjects per year of life). Amygdala-specific MRS was performed at 3T. Metabolite levels calculated with LCModel were corrected for acquisition volume by linear regression.

Results:Of all measured metabolites, only GABA showed a significant linear change with age ($r = -0.52$, $p = 0.2$).

Conclusions:While maturation of the amygdala during typical development includes increasing volume, GABA levels may be decreasing in this process. Future studies aiming to characterize amygdalar GABA in autism should take into account age effects.

Oral Presentations Program

151 Sibling Studies

151.1 Mother-Infant Interactions in High-Risk Infant Siblings of Children with Autism. M. W. Wan*[1], J. Green[1], M. Elsabbagh[2] and M. Johnson[3], (1)*University of Manchester*, (2)*Centre for Brain and Cognitive Development*, (3)*Birkbeck College, University of London*

Background: Recent studies, based on structured assessment and parent report, suggest that infant siblings of children with autism spectrum disorder (A-sibs) are more likely than typically developing siblings (TD-sibs) to exhibit social and communicative deficits and autism symptoms. Such early atypicalities may adversely affect the mother-infant interactions in A-sibs, particularly in those at high phenotypic risk.

Objectives: To compare the quality of mother-infant interaction between young A-sib infants, with and without phenotypic autism risk, and TD-sib controls.

Methods: Mother-infant play interactions involving 30 6-9-month-old A-sibs and 30 TD-sib controls were rated, blind to dyad characteristics. A global rating scale was developed for this purpose by combining appropriate elements of two validated mother-child interaction measures.

Results: A-sibs at high phenotypic risk were less attentive to mother, had fewer positive vocalisations and showed more neutral affect than A-sibs at low phenotypic risk. Their mothers exhibited less sensitive responsiveness and less acceptance, and their overall interactions were rated as slightly less dyadic. However, low-risk A-sibs tended to

show similar interaction scores as TD-sibs. A-sibs at high phenotypic risk were also more likely to show behavioural atypicalities during the interaction session than the other infants.

Conclusions: This study is the first to demonstrate that A-sib infants at high phenotypic risk *and* their mothers tend to differ in their interactions from others dyads. Based on a gene-environment transactional model, and on developmental research in non-ASD contexts, the findings suggest that such mother-infant relations in high-risk A-sibs may exacerbate their social and communicative difficulties. We also report on preliminary 12-15 month follow-up data. Our findings have implications for early preventative intervention.

151.2 Prospective Evaluation of Head Growth in Infants at Increased Risk of Autism. L. Zwaigenbaum*[1], W. L. Stone[2], K. Dobkins[3], R. Urbano[2], W. Lambert[2], S. Bryson[4], K. Chawarska[5], J. N. Constantino[6], G. Dawson[7], A. Klin[8], R. Landa[9], S. Ozonoff[10], S. J. Rogers[11], M. Sigman[12] and T. B. S. R. C. (BSRC)[13], (1)*University of Alberta*, (2)*Vanderbilt University*, (3)*UC San Diego*, (4)*Dalhousie University/IWK Health Centre*, (5)*Yale University School of Medicine*, (6)*Washington University School of Medicine*, (7)*University of Washington*, (8)*Yale School of Medicine*, (9)*Kennedy Krieger Institute, Johns Hopkins Medical School*, (10)*University of California at Davis*, (11)*University of California at Davis MIND Institute*, (12)*UCLA*, (13)*Autism Speaks/NICHD*

Background: Increased head circumference is the most consistently replicated biological marker of autism since the disorder was first described by Kanner in 1943. Recent analyses of data from medical records have suggested that accelerated head growth has an onset during the first year of life, although the apparent timing of this phenomenon varies between studies. To date, there are no *prospective* data on whether atypical trajectories of head growth are predictive of ASD.

Objectives: To assess prospectively whether children with ASD identified from a cohort of high-risk infants (siblings of children with ASD) exhibit accelerated head growth relative to non-diagnosed high-risk infants and low-risk comparison infants (no family history of ASD).

Methods: Head circumference (HC) was measured prospectively on a total of 761 high-risk and 400 low-risk infants from 11 sites across North America and supplemented by data from health records (25% of total dataset). Analyses compared head growth between high-risk infants diagnosed with ASD at age 24 months (DSM-IV clinical best estimate based on developmental history and symptoms observed on the ADOS) to non-diagnosed high-risk and low risk infants. Growth trajectories were assessed using mixed longitudinal models, assessing change in HC as a function of time (linear growth) and time-squared (acceleration/deceleration), including sex as a fixed covariate, and height as a time-varying covariate.

Results: Mean HC at birth (model-based estimates) did not differ significantly between the three groups ($p=0.8$). However, there were significant differences between the ASD and both non-ASD groups in HC growth rate (growth rate 0.6 cm/month faster in ASD group compared to non-diagnosed high-risk and low-risk infants; $p=.21$ and $p=.17$, respectively), and in deceleration rate (deceleration rate 0.002 cm/month higher in ASD group; $p=.18$ and $p=.21$, respectively).

Conclusions: Prospectively measured head growth rates differentiate infants subsequently diagnosed with ASD from non-diagnosed high-risk and low-risk infants.

151.3 Action and Speech Monitoring Delays in 3-month-old Infants at Risk for ASD. K. Chawarska*[1], F. Shic[2], S. Macari[1], J. Bradshaw[1], A. Klin[1] and F. Volkmar[1], (1)*Yale University School of Medicine*, (2)*Yale University*

Background: Limited monitoring of others' activities and a lack of attention to faces are hallmarks of ASD in toddlers. Due to the congenital nature of ASD and its strong genetic component, it has been hypothesized that deficits in social perception might be present in the first months of life, and that even unaffected siblings might share some

phenotypic similarities with their affected siblings.

Objectives: Visual scanning trajectories serve to obtain specific task-relevant information and are highly influenced by the perceptual and semantic content of the scene, and thus can be used to characterize deficits in social perception. This study examined action and speech monitoring in low risk (LR) infants and infants at high risk (HR) for ASD (siblings of children with ASD).

Methods: Participants included 10 LR and 18 HR 3-month-old infants. Infants were presented with two videos in which an actress: (1) spoke directly to the camera in motherese ("Speech"), or (2) engaged in making a sandwich ("Sandwich"). Visual scanning trajectories were recorded using an eye-tracker.

Results: In both video conditions HR infants, in comparison to LR infants, spent significantly more time examining objects and less attending to the actress. Notably, while LR infants modulated their attention to the face and hand area in accord with the actress's activities, the distribution of visual attention in HR infants was less sensitive to the experimental manipulation.

Conclusions: These results suggest that delays in human action monitoring and attention to speech can be demonstrated within the third month of life in infants at risk for developing ASD. While relatively few children in HR group are expected to develop ASD, results from this study suggests that an innate or early-emerging perceptual mechanism that support detection and monitoring of behaviors in others is impaired in 3 month old infants at high risk for ASD.

151.4 What do Infants See in Faces?: Evidence From Infants at Low and High Risk for Autism. A. P. F. Key*, W. Stone and S. M. Williams, *Vanderbilt University*

Background: Atypical attention to faces is one of the characteristics of autism, and retrospective parental reports often mention deficits in eye contact in infants later diagnosed with autism. While many studies examined general face processing in infants, few assessed the role of individual features.

Objectives: The purpose of this study was to investigate whether infants siblings of children with autism process facial features differently from typical infants and whether attention to faces and their individual features is associated with infants' social and communicative behaviors.

Methods: Visual event-related potentials (ERPs) and eye tracking data were recorded in 20 infants with no family history of autism and 10 infant siblings of children with autism (age 9 months +/- 15 days). Infants viewed photographs of smiling unfamiliar female faces. On 30% of the trials, the eyes or the mouth of the standard face were replaced by corresponding parts from a different female face. Mothers completed Receptive and Expressive Communication, and Interpersonal Relationships subscales of VABS-II.

Results: Both eye and mouth changes were detected, but associated with distinct response patterns. In typical infants, eye changes affected the face processing mechanisms and were not correlated with social or communication development, whereas mouth changes had a minimal impact on the face processing mechanisms but correlated with levels of receptive and expressive communication. In infants at risk for autism, responses to mouth changes correlated with interpersonal scores while responses to eyes correlated with receptive communication.

Conclusions: Infants with low and high risk for autism may utilize similar brain mechanisms for face processing, however (1) they derive different information from eyes vs. mouth regions of a face, and (2) individual differences in processing of these features are related to social and communicative skills.

151.5 DEVELOPMENTAL ABNORMALITIES IN THE FIRST YEAR OF LIFE IN CHILDREN LATER DIAGNOSED WITH ASD. M. Jonge*, C. Dietz, E. Daalen, Van and H. Engeland, *UMC Utrecht*

Background:
General agreement exists on the need to identify ASD early in life. In the Netherlands nearly all children (about 98%) visit well baby

clinics, where growth and development of children between age 0-4 is monitored by means of the Van Wiechen Schedule. This is a screening measure in which behavior within several domains of development (e.g. fine/gross motor skills, social behaviour, language abilities and adaptation) is evaluated.
Objectives:
To evaluate at which point in development (within the first year of life) children that are later diagnosed with ASD, show deviations in development in comparison with population norms. Furthermore, children with ASD and other developmental disorders will be compared.
Methods:
Schedules covering the first two years of development were studied retrospectively of 129 children diagnosed with ASD, 56 children diagnosed with other developmental disorders and compared to population norms.
Results:
The first results show abnormalities in development of children with ASD as early as the second month. Areas of abnormal development pertain to all developmental areas in the first year and to social and communication items in particular. Although the surveillance method with the Van Wiechen Schedule seems helpful in identyfing at risk children, the instrument can not discriminate children with ASD from children with other developmental problems, as these children also fail the Van Wiechen items.
Conclusions:
Surveillance with the Van WiechenSchedule can be helpful in identifying children at risk. Additional and specific ASD screening will be needed within the at risk group. The results will be replicated in an independent sample of 143 children with ASD and also in the siblings of these children, in order to assess early signs of the broader phenotype of autism. The replication study is in progress and the results will be presented at the IMFAR conference in may 2008.

151.6 Emotion, Attention, and Joint Attention in Infants at Risk for Autism. D. S. Messinger*, L. Ibanez, T. D. Cassel, J. D. Haltigan and K. M. Kelley, *University of Miami*

Background: The development of infant siblings of children with autism offers insight into the development of ASDs and subclinical manifestations of autism-related symptomatology ('the broad phenotype').

Objectives: To compare infant siblings of children with autism (ASD sibs) and infant siblings of typically developing children (TD sibs) with respect to attention and rated emotional valence (affect) during interaction with a parent, and subsequent joint attention with an examiner.

Methods: 17 ASD and 17 TD sibs (both groups split almost evenly by gender) interacted with their parents in a face-to-face/still-face (FFSF) procedure at six months. A slightly smaller number of siblings participated in the Early Social Communication Scales (ESCS) at 8, 10, 12, 15, and 18 months. Coding was standard except that emotional valence was rated by non-expert students to determine if potential deficits were perceivable by untrained individuals.

Results: Male ASD sibs were rated as expressing more negative (less positive) emotional valence than male TD sibs in the FFSF. As a whole, the mean duration of ASD sibs' gazes directed away from their parents' faces were longer than those of TD sibs. ASD sibs also exhibited less frequent shifts between gazing at and away from the parent's face. Gaze shift frequency was positively associated with initiating joint attention in the ESCS. ASD Sibs showed deficits in initiating joint attention and responding to joint attention in the ESCS between 8 & 18 months.

Conclusions: The results suggest male-specific attenuations of positive affect in ASD sibs, consonant with the heightened risk status of these boys. ASD sibs show a general pattern of difficulty in disengaging from non-social stimuli at 6 months. This difficulty may be manifested between 8 & 18 months as a reduction in initiating and responding to joint attention (both of which require disengaging from a non-social stimulus).

151.7 Clinical Assessment of Autism in High-Risk 18-Month-Olds. J. Brian*[1], S. Bryson[2], N. Garon[3], W. Roberts[4], I. M. Smith[2], P. Szatmari[5] and L. Zwaigenbaum[6], (1)*Hospital for Sick Children/ Bloorview Kids Rehab*, (2)*IWK Health Centre/ Dalhousie University*, (3)*IWK Health*

Centre, (4)*University of Toronto*, (5)*Dept of Psychiatry and Behavioural Neurosciences*, (6)*Glenrose Rehab Hospital/ University of Alberta*

Background: Evidence that earlier intervention improves the outcomes of children with Autism Spectrum Disorder (ASD) has spurred efforts at earlier identification. However, existing tools are at the limits of their standardization with 18-month-olds.

Objectives: To assess the predictive validity of items from the Autism Observation Scale for Infants (AOSI) and Autism Diagnostic Observation Schedule (ADOS) at 18 months.

Methods: Prospective data were collected on 155 infant siblings of children with Autism Spectrum Disorder (ASD) and 73 low-risk controls using the AOSI and ADOS at 18 months. Infants were classified into 3 groups (ASD sibs, non-ASD sibs, controls) based on blind best-estimate diagnosis at age 3 years.

Results: Discriminant Function Analyses, using items identified through Fisher's Exact Tests, yielded two discriminant functions for each tool. Discriminant Function 1 from the ADOS made a significant unique contribution to the model, χ^2 (2) = 49.29, $p < .001$. Both AOSI Discriminant Function 1, χ^2 (2) = 7.91, $p < .1$, and AOSI Discriminant Function 2, χ^2 (2) = 11.69, $p < .1$, made significant unique contributions. At 18 months, ADOS items from the Social and Behavioural domains were most informative, while AOSI items measuring behavioural reactivity and motor control contributed additional information to ASD diagnoses at 36 months (all p's < .5).

Conclusions: Findings highlight the importance of considering not only social-communication deficits, but also dimensions of temperament/state regulation and motor control when assessing toddlers with suspected ASD.

151.8 Early Cognitive, Communicative and Social Development in Infants Siblings of Children with Autism Spectrum Disorders (ASD). K. Dobkins*, N. Akshoomoff, L. Carver, E. Dohrmann and J. McCleery, *UC San Diego*

Background: Previous research has identified a broader phenotype of cognitive, social, and communicative atypicalities in first-degree relatives of individuals with ASD.

Objectives: Investigate cognitive and language development in infant siblings of children with autism ("high-risk infants"; HR) to determine whether: 1) infants who go on to develop ASD ("ASD infants") perform below unaffected HR infants, and 2) unaffected HR infants nonetheless exhibit a broader phenotype, i.e., perform below infants from families without autism history ("low-risk infants"; LR).

Methods: Assessments administered between 6 and 36 months included: the Mullen Scales of Early Learning, which measures gross motor, fine motor, visual reception, receptive language, and expressive language, the Ages & Stages Questionnaire (ASQ), which measures communication, gross and fine motor, problem solving, and personal-social development, and the MacArthur-Bates Communicative Development Inventory (CDI), which measures gesture and language skills.

Results: On the Mullen, the three groups (LR: n=140, HR: n=35, ASD: n=8) were indistinguishable at 6 months, but by 24 months, ASD infants underperformed HR infants on all subscales (with no differences observed between LR and HR infants). On the ASQ, ASD infants underperformed HR infants by 10 months in communication, personal-social and problem-solving behaviors. At all ages tested, HR infants underperformed LR infants. On the CDI (10-14 months, Words & Gestures), in all categories, ASD infants underperformed HR infants, who underperformed LR infants. On the CDI (18-36 months, Words & Sentences), the underperformance of the ASD infants continued; however, the HR infants caught up with the LR infants in language skills.

Conclusions: The differences observed between LR and HR infants support an early broader phenotype in ASD, while those observed between HR and ASD infants provide potential early markers for developing ASD. Such findings complement those from other laboratories using this HR infant approach.

Oral Presentations Program

152 Brain Imaging 2

152.1 FACE PROCESSING IN INDIVIDUALS WITH AUTISM: A LONGITUDINAL MAGNETOENCEPHALOGRAPHIC STUDY. S. Braeutigam*[1], A. Kylliainen[2], S. Swithenby[3] and A. Bailey[1], (1)*University of Oxford*, (2)*University of Tampere*, (3)*The Open University*

Background: Behavioural data suggest that individuals with autism use anomalous cognitive strategies when processing faces. Recent neurophysiological and neuroimaging data points to different-from-normal neural activity in able adults with autism when viewing faces. The development of face processing skills, however, is still rather poorly understood both under typical and atypical conditions.

Objectives: To investigate the developmental trajectory of neural systems associated with face processing.

Methods: 8 male individuals with autism and 8 typically developing male subjects participated in this study. Participants were matched on age (mean 12 years) and IQ. All measurements were taken at the Brain Research Unit, Helsinki University of Technology, using a VectorView(TM) system providing first-order gradiometers most sensitive to directly underlying neuronal currents. The participants performed a matching task that required attention to be paid to the face, where pairs of images of adolescents and motorbikes were presented sequentially. These brain data were compared to data measured with the same scanner in the same individuals who had performed the same task 3 years earlier. All participants and their parents gave informed consent (Helsinki Declaration) before experimentation.

Results: In both subject groups, by the age of 12, very early (< 60 ms) neural responses to faces exhibit amplitudes similar to those observed in adults. Adult-like signal topographies, however, are only observed in typically developing subjects at early latency. At 100 ms, responses to motorbikes (age 9) and to face and motorbike images (age 12) are observed over right inferior occipito-temporal regions in individuals with autism but not in typically developing subjects.

Conclusions: The development of neural systems associated with face processing has not reached adult level by early adolescence in autism. In particular, neural responses at very early latency that have received little attention previously may hold vital clues to understand atypical development.

152.2 The Effect of Task Differences on FFA Activity in Autism Spectrum Disorders. R. T. Schultz*[1], D. W. Grupe[2], E. Hunyadi[1], W. Jones[2], J. Wolf[2], E. G. Hoyt[2], D. Lin[2] and L. E. Herlihy[2], (1)*Children's Hospital of Philadelphia and the University of Pennsylvania*, (2)*Yale School of Medicine*

Background: Hypoactivation of the fusiform face area (FFA) among persons with an autism spectrum disorder (ASD) is a very well replicated neuroimaging finding; however, a few studies have reported normal levels of activation. Inconsistent findings may be due to ASD sample heterogeneity and/or differences in experimental procedures, with negative studies employing passive face viewing tasks that are not well controlled. Objectives: We studied modulation of the FFA in ASD and typically developing controls (TDC) by directly comparing several different face task paradigms commonly used in the literature. We predicted that FFA hypoactivation would be modulated by attentional and perceptual processing "load", with larger group differences for more attentionally challenging tasks. Methods: FMRI scanning was done on 19 children with an ASD (ADI & ADOS diagnosed) and 17 age-matched TDCs. Participants completed a series of five face tasks that varied in their processing demands and with stimuli that varied systematically with respect to social-emotional salience. We utilized whole-brain and ROI analyses to investigate main effects of group and task, and their interactions. Results: TDCs showed greater overall FFA activation relative to ASD participants, and more demanding tasks/more salient stimuli showed greater FFA activation than less demanding/salient tasks. Additionally, several parts of the FFA and related social nodes exhibited greater group differences for more engaging tasks. Passive viewing tasks, including tasks which focused attention on the eye region via a crosshair fixation, showed less FFA activation overall

and smaller group differences than active tasks. Conclusions: There are likely two factors modulating FFA activity: depth of processing and stimulus salience. Passive tasks appear to not drive the underlying neural systems hard enough to consistently reveal TDC-ASD group differences. Moreover, active tasks are theoretically preferred, since the real life behavioral phenomena of interest involve active social perceptual judgments.

152.3 Effect of Serotinin on Processing of Emotional Faces in Asperger's Syndrome. fMRI and Acute Tryptophan Depletion. E. Daly*, Q. Deeley, S. Surguladze, M. Phillips, M. Craig and D. Murphy, *Institute of Psychiatry, King's College London*

Background: One of the difficulties found in Autistic Spectrum Disorder is the processing of emotional faces. Modulation of the Serotonergic system by Acute Trypthophan Depletion (ATD) has shown an affect on the detection of fearful and disgust emotional faces in adult male controls.

Objectives: To elucidate the role of the serotonergic system in the neuroprocessing of emotional faces in people with Asperger's Syndrome, we employed the methods of functional Magnetic Resonance Imaging (fMRI)and Acute Tryptophan Depletion (ATD).

Methods: We studies 10 adult males with Asperger's Syndrome and 10 gender, age and IQ matched control subjects. Subjects were scanned on two separated occasions. On one visit a sham amino acid drink was consumed. On the other visit a Tryptophan depleted amino acid drink was consumed. fMRI scanning on both days employed implicit emotional face processing tasks with an explicit gender identification response to the stimuli. Separate runs were performed on disgust and fearful faces.

Results: There was a >70% blood Tryptophan reduction on consumption of the depleted drink. Aspergers showed different brain activation patterns than controls in the serotonin modulated experiments. For the processing of fearful faces the regions affected were Inferior Frontal and Precentral Gyrus. For disgust faces the activation changes were found in regions that extended to the Fusiform Gyrus. These regions are known to be involved in the processing of emotional faces.

Conclusions: Modulation of serotonin levels in the brain by Acute Tryptophan Depletion leads to differential effects on the processing of emotional faces in controls and males with Asperger's Syndrome.

152.4 MINDREADING, MIRROR NEURONS, AND CORTICAL MIDLINE STRUCTURES IN AUTISM. R. K. Kana*[1], T. Keller[2], D. L. Williams[3], V. Cherkassky[2], N. J. Minshew[4] and M. A. Just[2], (1)*University of Alabama, Birmingham; Carnegie Mellon University*, (2)*Carnegie Mellon University*, (3)*Duquesne University*, (4)*University of Pittsburgh School of Medicine*

Background: The Mirror Neuron System (MNS) and the Cortical Midline Structures (CMS) may play an important role in Theory of Mind (ToM) processing. While CMS has been found to be involved in self processing, MNS is involved in self recognition and social understanding. Functional and anatomical abnormalities in MNS have been found in autism. Similarly, CMS underactivation and underconnectivity were found in autism.

Objectives: The main objective was to examine the brain activation and synchronization of MNS, CMS and ToM networks in mental state attribution in high-functioning children with autism.

Methods: Thirteen children with high-functioning autism (mean age 12.5 years) and thirteen age- and IQ- matched controls (mean age 12.9 years) participated in this study. Nine silent animations, lasting 34-45s each, were shown on a computer screen. All featured a big red triangle and a small blue triangle moving about on a framed white background. Participants were asked to watch the animation and comprehend the meaning of the actions.

Results: The participants with autism activated less relative to controls in two key networks, the Theory of Mind (ToM) network (medial frontal and superior temporal cortex), and an anterior component of the MNS (bilateral inferior frontal gyrus). The autism group activated more in areas associated with the

"default network" (CMS: the anterior and posterior cingulate cortices, and the precuneus). In addition, the components of ToM network were less synchronized in participants with autism relative to controls.

Conclusions: Mental state attribution is a complex function involving simulation, self-other understanding, evaluation, and reasoning; and the components of this network function atypically in autism. It is possible that the functions mediated by the CMS, MNS and ToM structures may not be perfectly distinct. Perhaps what matters more is the functional synchrony of these structures and that is where people with autism falter.

152.5 Cognitive and Emotional Empathy and their Neurofunctional Correlates in Autism Spectrum Conditions. I. Dziobek*, I. Wolf, M. Bahnemann, J. Kirchner and H. R. Heekeren, *Max-Planck-Institute for Human Development*

Background: According to recent conceptions, empathy can be seen as multidimensional construct consisting of cognitive (inferring mental states) and emotional (empathic concern) components. The neuronal correlates of empathy are largely unknown. Despite a lack of research into its different components, individuals with autism spectrum conditions (ASC) are generally believed to lack empathy.

Objectives: To compare cognitive and emotional empathy and their neuronal correlates of adults with ASC with those of controls.

Methods: A group of 20 adults with ASC (7 women) and 18 controls (5 women) matched for age and IQ underwent fMRI scanning while taking an adaptation of the Multifaceted Empathy Test (MET; Dziobek et al., in press). Using photographic stimuli showing distressed individuals, the test allows for the multidimensional assessment of empathy by demanding mental state inferences (cognitive empathy) and self-evaluation of levels of compassion (emotional empathy).

Results: Between-group analyses of behavioral data revealed that while the ASC group scored lower on the MET's cognitive empathy scale, there were no differences between groups in the emotional empathy scale. Imaging analyses showed that both groups activated the same differing neuronal networks for cognitive and emotional empathy, respectively: while the superior temporal sulcus region was selectively involved in cognitive empathy, the medial prefrontal cortex, temporoparietal junction, and precuneus were selectively involved in emotional empathy. Group comparisons showed that during the cognitive empathy condition, the ASC group showed significantly more activation in a network encompassing the right amygdala, anterior insula, and orbitofrontal cortex.

Conclusions: On the behavioral as well as brain level, cognitive and emotional empathy represent dissociable functions. Individuals with ASC activate an emotional network including the amygdala when asked to appreciate other's distress. This activation might reflect aversion and arousal, respectively, when confronting a task demanding the processing of other's emotions and focusing on another person's eyes.

152.6 MEG INVESTIGATIONS OF NEURAL SYNCHRONY IN AUDITORY LANGUAGE CORTEX IN CHILDREN WITH AUTISTIC DISORDER, THEIR UNAFFECTED SIBLINGS, AND TYPICALLY DEVELOPING CONTROLS. N. M. Gage*, A. L. Isenberg and M. A. Spence, *University of California, Irvine*

Background: we have provided evidence for impaired feature extraction processes in auditory language cortex in children with autistic disorder (AD) vs. typically developing (TD) controls (Gage et al., 2003).

Objectives: to assess temporal acuity within auditory language cortex and neural synchrony across hemispheres to determine if feature extraction impairments were due to reduced neural synchrony within- and across-hemispheres in children with AD.

Methods: in healthy adults, M100 latency is prolonged in a near-linear manner by brief discontinuities (silent gaps 0-20 ms) at the onset of sounds (Gage et al., 2006), demonstrating the high temporal resolution of auditory language cortex. We used identical stimuli and measured M100 latency to 1kHz tones with gaps (0, 5, 10, 20ms) in 17 (15

male, 7-14 yrs) children with AD, and 17 (15 male, 7-14 yrs) controls. Within the control group, 8 (6 male) were unaffected siblings (SIB) of the AD group and 9 (all male) were unrelated TD controls.

Results: M100 dynamic range (DR) was calculated (20-gap – 0-gap) to assess magnitude of within-hemisphere modulation by gaps, a measure of temporal acuity. Laterality index (LI, (2*(L-R)/(L+R)) was calculated for the 0-gap and 20-gap conditions to assess the magnitude of between-hemispheres temporal offsets, a measure of neural synchrony. DR - AD: LH 13.8ms, RH 7.8ms; SIB: LH 25.1, RH 26.6; TD LH 18.5, RH 30.4. LI - AD: 0-gap 0.111, 20-gap 0.129; SIB: 0-gap 0.79, 20-gap 0.81; TD: 0-gap 0.64, 20-gap 0.89.

Conclusions: Children with AD evidenced reduced within-hemisphere temporal acuity to fine-grained features, particularly in RH, and increased between-hemisphere asynchrony vs. TD or SIB groups. Together these findings provide evidence for impairments in temporal resolution and neural synchrony within- and across-hemispheres in auditory language cortex for children with AD that are not present in their unaffected siblings or unrelated controls.

152.7 fMRI Investigation of Visual Search in Autism Spectrum Disorder. B. M. Keehn*[1], L. Brenner[2], E. Palmer[3], A. J. Lincoln[4] and R. A. Müller[3], (1)*San Diego State University and University of California, San Diego*, (2)*University of California, Los Angeles*, (3)*San Diego State University*, (4)*Alliant International University*

Background: Previous studies investigating visual search in autism spectrum disorders (ASD) have demonstrated accelerated response times (RT) and enhanced search efficiency. However, the underlying neural mechanisms remain unknown.
Objectives: To investigate the neurofunctional correlates of visual search in children with ASD and typically developing (TD) children, using an event-related functional magnetic resonance imaging (fMRI) design.
Methods: Participants were 13 individuals diagnosed with ASD and 13 age- handedness- and IQ-matched typically developing (TD) individuals. Four children with ASD, but none in the TD group, were excluded from the final sample due to excessive movement during fMRI scanning. We used an event-related visual search paradigm, manipulating search difficulty by varying set size (6, 12, or 24 items), distractor composition (heterogeneous or homogeneous), and target presence (absent, present) to identify brain regions associated with efficient and inefficient search.
Results: Groups did not differ significantly in error rate. While the ASD group did not demonstrate accelerated response time (RT) compared to the TD group, they did evidence increased search efficiency, as measured by RT by set size slopes. fMRI results showed occipitotemporal activation in both groups. However, the ASD showed additional frontoparietal activation, which was not seen in the TD group. Direct group comparisons (for both homogeneous and heterogeneous search conditions) confirmed greater frontoparietal activation in ASD compared to TD participants.
Conclusions: Enhanced activation in superior parietal and superior frontal regions in individuals with ASD suggests that accelerated performance in ASD may be related to enhanced top-down modulation of visual attention. While our finding of increased frontal recruitment during visual search in ASD may be consistent with enhanced top-down control of visual attention, it is surprising given previous theories of reduced prefrontal control in autism.

152.8 Neural Underpinnings of Autistic Reasoning and Novel Problem Solving. I. Soulieres*[1], M. Dawson[2], F. Samson[3], E. B. Barbeau[3], C. Sahyoun[4], T. A. Zeffiro[5] and L. Mottron[6], (1)*Massachusetts General Hospital/ Harvard Medical School*, (2)*Hopital Riviere-des-Prairies*, (3)*Riviere des Prairies Hospital, University of Montreal*, (4)*Harvard/ MIT*, (5)*Neural Systems Group, Massachussetts General Hospital*, (6)*Université de Montréal*

Background: Raven's Progressive Matrices (RPM) is a pre-eminent measure of fluid intelligence, assaying abilities to infer rules, manage goal hierarchies, and form high-level abstractions. Autistics perform significantly better on RPM than on Wechsler intelligence scales, while no such discrepancy is found in

nonautistics (Dawson et al., 2007). Neuroimaging studies of matrix reasoning and novel problem solving in nonautistics have demonstrated task-related activity in a bilateral frontoparietal network.

Objectives: To investigate the neural basis of autistics' RPM performance using fMRI.

Methods: Fifteen autistics and 18 nonautistics participated, matched on age (mean 22 years), Wechsler IQ (mean 103), sex and manual preference. The 60 RPM problems were presented in random order in one continuous self-paced run using echoplanar imaging on a 3T MRI system. Sixty visual pattern matching problems, similar in format to RPM, but not involving complex reasoning, were presented in a separate session. Performance and task related activity were compared between groups for both problem types.

Results: While accuracy for the RPM and pattern matching problems was equal in both groups, nonautistics were 40% slower in solving RPM problems. For the RPM problems, both groups exhibited similar patterns of task-related activity in occipital cortex, posterior parietal cortex, lateral premotor cortex, insula and cerebellum; with higher activity in nonautistics in the left middle frontal gyrus and medial posterior parietal cortex, and higher activity in autistics in a left extrastriate area (cuneus, BA19). This extrastriate region was active in both groups during pattern matching problems, but only in the autistic group during the RPM problems.

Conclusions: Autistics' faster performance in solving randomly-ordered RPM problems may indicate a net processing efficiency resulting from increased use of posterior and decreased use of frontal processing mechanisms. Areas primarily involved in perceptual processing in nonautistics may be utilized in reasoning and complex problem solving in autistics.

Oral Presentations Program

153 Repetitive Behaviour

153.1 Stability of Individual Restricted and Repetitive Behaviors in Children with Autism Spectrum Disorders. J. Richler*[1], M. Huerta[2], S. L. Bishop[3] and C. Lord[4], (1)*University of Minnesota*, (2)*University of Illinois - Chicago*, (3)*Waisman Center, University of Wisconsin-Madison*, (4)*University of Michigan Autism and Communication Disorders Center*

Background: Little is known about the stability of individual restricted and repetitive behaviors (RRBs) in children with autism spectrum disorders (ASD) (i.e., how commonly behaviors are lost or improve and how often they are acquired or worsen over time.) There is evidence that 'repetitive sensorimotor' (RSM) behaviors (e.g., motor mannerisms) follow different developmental trajectories than 'insistence on sameness' (IS) behaviors (e.g., rituals).

Objectives: We examine the stability of individual RRBs over time in children with ASD, and which factors are associated with stability.

Methods: Data were collected as part of a longitudinal study of toddlers referred for possible autism. There were 214 participants in the first cohort, 192 of whom were referred because of concerns about ASD. The nonspectrum developmental disorder (DD) referral group consisted of 22 developmentally delayed children who had never been referred for or diagnosed with autism. At each wave, children completed a battery of cognitive and diagnostic measures, and parents completed the Autism Diagnostic Interview-Revised. At ages 2, 5, and 9, each child was assigned a consensus best-estimate clinical diagnosis of autism, pervasive developmental disorder-not otherwise specified, or a nonspectrum developmental disorder.

Results: Once children with ASD had a particular RSM behavior, they were likely to continue having it, and children who did not have the behavior often acquired it. However, these behaviors often improved in children with higher nonverbal IQ (NVIQ) scores and/or milder ASD. Many children who did not have IS behaviors at a young age acquired them as they got older, whereas children who had these behaviors sometimes lost them. Trajectories of IS behaviors were not closely related to diagnosis and NVIQ.

Conclusions: Individual RRBs show different patterns of stability in children with ASD, based partly on the 'subtype' they belong to. Young children with low NVIQ scores often have persistent RSM behaviors.

153.2 'Over and Over Again': Comparing Repetitive Behaviours in Typically Developing Children and Children with Autism Spectrum Disorder, at a Two Year Language Age. N. Burton[1], H. McConachie*[1], S. Leekam[2], E. Meins[2], K. Parkinson[1], B. Arnott[2] and A. S. Le Couteur[1], (1)*Newcastle University*, (2)*University of Durham*

Background:

Repetitive behaviours are one of the defining features of autism. Research suggests two groupings: 'low-level' (eg. repetitive motor movements) and 'high-level' (eg. insistence on sameness), and that the range and severity of repetitive behaviours are related to age and cognitive ability. Repetitive behaviours are also commonly seen in typically developing young children, but are they the same or different?

Objectives:

The aim was to compare the frequency and factor structure of repetitive behaviours in typically developing children and children with autism/ASD, at a comparable language level.

Methods:

Eleven items from the Repetitive Behaviours Questionnaire (RBQ2 - Leekam et al 2007) had been answered by parents in two studies. Study 1 included 53 children (31 Autism, 22 ASD) aged between 35 and 67 months. Study 2 included 192 typically developing (TD) children aged 24 to 28 months.

Results:

Principal components analysis showed a similar two-factor structure for the TD and Autism/ASD groups. The Repetitive Motor Behaviours Factor accounted for a larger proportion of the variance in responses from the TD group than the Autism/ASD group (33% vs 19%) and vice versa for the Rigidity/Sameness Factor (TD 16% vs Autism/ASD 34%).

The TD and Autism/ASD groups did not differ in frequency and severity of their repetitive behaviours for either factor. Age and better language were related to more high-level behaviours in the TD group, but not in the Autism/ASD groups.

Conclusions:

Repetitive behaviours seem to be much the same in children with autism as they are in TD children at two years of age. The difficulty for families lies in the degree to which these behaviours continue long after the "terrible twos". The findings reinforce the suggestion that repetitive behaviours may not act as early diagnostic markers, though more research is required on infants with autism before the age of two.

153.3 Repetitive behavior, basal ganglia and thalami changes in ASD from 3 to 6 years of age. A. M. Estes*, J. Munson, G. Dawson, D. Shaw, V. Hus and S. Dager, *University of Washington*

Background: Abnormalities of the thalami and basal ganglia may contribute to symptom expression in autism spectrum disorders (ASD). Some 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).

Objectives: RB subtypes were investigated in children with ASD and developmental delay (DD) at 3 years. Basal ganglia and thalami volumes were compared in children with ASD, DD and typical development (TD) at 3 years. Longitudinal relationships between RB and volumetric measures were examined from 3 to 6 years.

Methods: Children were assessed at 3 and 6 years for RB with ADI, ADOS and ABC (ASD n=75, DD n=39). A subgroup was also assessed with 3-D T1 MRI (ASD n=45, DD n=14) with an additional MRI-only typical development (TD) group (n=24). Structures assessed include thalami and basal ganglia (striatum, globus pallidus, putamen and caudate).

Results: RB subtypes were identified and were elevated in the ASD group relative to the DD group at age 3. However, self-injurious behavior did not differ between groups. Volumetric findings indicate enlargement of most structures in the ASD relative to the TD group. Enlargement was proportional to overall brain volumes. Comparing the DD to both ASD and TD groups revealed disproportionately smaller volumes in selected structures. There does not appear to be a systematic relationship between levels of RB and volumetric measures at age 3. Developmental changes in RB will be presented in relation to morphometric findings between 3 and 6 years of age.

Conclusions: At age 3, RB was elevated in the ASD relative to the DD group, with the exception of self-injurious behavior. Basal ganglia and thalami were enlarged in the ASD group compared with the TD group and enlargement was in proportion to overall brain volume.

153.4 RESTRICTED AND REPETITIVE BEHAVIORS IN CHILDREN BETWEEN 8 TO 57 MONTHS WITH AUTISM BASED ON AUTISM DIAGNOSTIC OBSERVATION SCHEDULE (ADOS). S. H. Kim*[1], W. Guthrie[2] and C. Lord[2], (1)*University of Michigan*, (2)*University of Michigan Autism and Communication Disorders Center*

Background: There has been a great interest in the restricted and repetitive behaviors (RRBs) in children with autism. However, there have been only few studies on the RRBs in children under preschool age especially based on observations.

Objectives: Describe differences in the RRBs based on the ADOS at different developmental levels across different diagnostic groups of autism, pervasive developmental disorders not otherwise specified (PDD-NOS), typical development (TD), and developmental delay (DD).

Methods: Participants were included from projects 1) one in which they entered the study at 12 months and were assessed by the ADOS–Toddlers, 2) one in which they entered the study at 24 months and were assessed by the Pre-Linguistic-ADOS, the previous version of the ADOS-T.

Results: 655 cases (mean age of 28.26 months) were categorized into 7 cohorts by chronological age. A Poisson Generalized Estimating Equations (GEE) model was used with age, diagnosis at age 2, and full scale IQ scores as predictors, and the ADOS algorithm domain score for the RRBs as the outcome. Preliminary results revealed that the diagnosis, chronological age, and full scale IQ scores were significant predictors of the RRBs. The estimated marginal means for children with autism were significantly higher than for children with DD and TD in all the cohorts. Additional analyses for each item in the domain of the RRBs showed different trajectories and cross sectional differences.

Conclusions: Not surprisingly, children with autism show significantly higher RRBs scores than children with TD and DD. Additionally, different trajectories and cross sectional differences for each item also reveal that lumping different types of RRBs together under one criterion of RRBs could be problematic.

153.5 Co-morbid Anxiety in Autism Spectrum Disorders. H. M. G. Hsu[1], D. Pearson[2], R. Mansour[2] and K. Loveland*[2], (1)*Fu Jen Catholic University*, (2)*University of Texas Health Science Center, Houston*

Background:

Autism Spectrum Disorders (ASD) involve impairments in social-emotional skills, communication, and repetitive behaviors. Many persons with ASDs also have symptoms of anxiety, resembling OCD, since individuals with ASD and those with OCD both have repetitive or compulsive behaviors.

Objectives:

This study had three goals: 1) classifying youth with ASD into those with and without clinically significant symptoms of OCD, 2) determining if those with ASD and OCD differ in anxiety from those without OCD, and 3) examining group differences in repetitive/stereotyped behaviors.

Methods:

Participants were 106 children and adolescents with (ADI-R/ADOS) ASD aged 7-18 years, IQ ³ 40, assessed with the Diagnostic Interview for Children and Adolescents (DICA) and classified significant symptoms of Obsessive Compulsive Disorder (OCD). 33 met criteria for OCD and 73 did not. These groups were both >80% males, with no significant differences in age and IQ. Differences in anxiety were examined using the Conner's Parent Rating Scale-Revised (CPRS-R). Differences in repetitive/stereotyped behavior were compared using the ADI-R.

Results:

On the CPRS-R, the ASD-OCD group had significantly higher anxiety and shyness than the ASD-only group (t (72) =2.69, p=.003), and more of them met criteria for Specific Phobia ($c^2(1)$ =18.38, p<.001) and Social Phobia ($c^2(1)$ =8.18, p<.2).

The ASD-OCD group also had significantly greater compulsions or rituals (t (101) =3.47, p=.001) and difficulties with minor change (t (98) =2.97, p=.004).

Conclusions:

This study identified a subset of individuals with ASD who met criteria for OCD and who also had more anxiety, phobias, compulsions, and difficulties with change. These results suggest there is a significant subgroup of persons with ASD who can be considered to have co-morbid OCD, and that these persons exhibit greater symptoms of anxiety and anxiety disorders more generally. Further studies should address specific risk factors for co-morbid OCD in persons with ASDs.

153.6 Examining the Structure of the Repetitive Behavior Scale-Revised in Young Children with Autism Spectrum Disorder. S. Georgiades*[1], E. Duku[1], I. Smith[2], P. Mirenda[3], P. Szatmari[1], S. Bryson[2], E. Fombonne[4], W. Roberts[5], T. Vaillancourt[1], J. Volden[6], C. Waddell[7], L. Zwaigenbaum[8] and P. I. ASD Study Team[9], (1)*Offord Centre for Child Studies & McMaster University*, (2)*IWK Health Centre, Dalhousie University*, (3)*University of British Columbia*, (4)*Montreal Children's Hospital & McGill University*, (5)*The Hospital for Sick Children & University of Toronto*, (6)*University of Alberta*, (7)*Simon Fraser University*, (8)*Glenrose Rehabilitation Hospital & University of Alberta*, (9)*N/A*

Background: The Repetitive Behavior Scale-Revised (RBS-R; Bodfish et al., 2000) was designed to examine restricted/repetitive behaviors in ASD. A recent factor analytic study by Lam and Aman (2007), using a sample of older children and adults (mean CA=184 months), revealed five factors. **Objectives:** To examine the factor structure and correlates of the RBS-R in preschool children with ASD. **Methods:** The RBS-R was completed by parents of newly-diagnosed children with ASD, participating in a Canadian longitudinal study (Pathways in ASD). Our sample consisted of 225 children (193 males; mean CA=39.80 months; mean MA=26.00 months; 69.8% Caucasian). Principal axis factor analysis was used to examine the structure of the RBS-R. Pearson correlations were calculated to examine relationships between derived factors and other ASD symptoms, as well as cognitive and adaptive function. **Results:** A three-factor solution explaining 40.2% of the variance was selected, using scree plot and goodness-of-fit criteria. The three factors were: Compulsive Ritualistic Sameness Behaviour (CRSB), Self Injurious Behaviour (SIB), and Stereotyped Restricted Behaviour (SRB). Children with higher CRSB scores were significantly older (r=.22), showed more severe autism symptoms (SRS and ADI-R, r=.15 to .58), and had poorer adaptive behavior (Vineland II, r=-.29). High scores on SIB were associated with higher SRS scores (r=.21). Children with high scores on SRB were younger (r=-.15), had more severe autism (ADI-R, ADOS & SRS, r=.11 to .23), and were more impaired on both cognitive (M-P-R) and adaptive (Vineland II) skills (r=-.17 to -.33). Males scored higher on the SRB factor (p<.1). **Conclusions:** The structure of the RBS-R is best captured using fewer, more inclusive factors in a population of preschool children, compared with a previous factor analysis in an older sample. This ongoing longitudinal study may reveal useful information on increasing differentiation of repetitive behaviours, as well as potential factors associated with their development.

153.7 Assessment of Restrictive/Repetitive Behaviors in Probands and Parents. R. K. Abramson*[1], A. Hall[2], M. L. Cuccaro[3], J. Gilbert[4], M. Pericak-Vance[4] and H. H. Wright[1], (1)*Univ. S. Carolina Sch. Med.*, (2)*Univ. S. Carolina Sch. Public Health*, (3)*University of Miami School of Medicine*, (4)*Miami institute of human genomics*

Background: The relationship between restrictive/repetitive behaviors (RRBs) in individuals with autism spectrum disorders (ASDs) and their parents remains a subject of interest stemming from characterization of the broader autism phenotype (BAP) in parents, the range of RRBs in the child, and the familiality of this trait as an endophenotype.

Objectives: To characterize the broader range of RRBs in children with an ASD with a parent with RRBs.

Methods: Parents (n=142) and children (n=174) were enrolled from a genetic study of ASDs. In multiplex families, the first affected proband was included in the analysis. Parents completed the YBOCS for themselves and the Repetitive Behavior Scales Revised (1999) for their children.

Results: A majority of parents (60.5%) did not have clinically significant YBOCS scores; 14.8% had mild, 9.9% moderate and 3.5% severe scores. Level of severity of YBOCS and RBS-R scores were evaluated by one-way ANOVA. Parents with clinically severe YBOCS scores (24 or greater) reported significantly more RRBs in their children ($F=4.471$, $df=2$, $p=0.2$). Pearson correlations were significant for YBOCS total score and RBS-R total score ($r=0.304$**), and subscale scores: Compulsive Behavior ($r=0.207$*), Ritualistic Behavior ($r=0.296$**), Sameness Behavior ($r=0.308$**) and Restricted Behavior ($r=0.229$*). RBS-R Stereotyped and Self-Injurious behavior subscales were not correlated with parental YBOCS total score. Seventeen multiplex families had 2 or more sibs with an ASD. The difference in RBS-R total scores, whether high or low, between sibs was less than 5-7 points for 53% and 10-14 points for 76%.

Conclusions: Parents with clinically severe YBOCS scores report higher levels of RRBS in their children with an ASD. We found significant RRBs in 3.5% of parents, similar to Dawson (2007) who reported 4% of parents with significant RRBs from the BPASS. BAP parents need to be assessed for comorbid OCD.**$p<0.1$ *$p<0.5$ supported by NIH grant 2R01 NS16768-08

153.8 Familial Associations of Intense Preoccupations, an Empirical Factor of the Restricted, Repetitive Behaviors and Interests Domain of Autism. C. J. Smith*[1], C. M. Lang[2], L. M. Kryzak[2], E. Hollander[2], R. Melmed[1] and J. M. Silverman[2], (1)*Southwest Autism Research & Resource Center*, (2)*Mount Sinai School of Medicine*

Background: Clinical heterogeneity of autism likely hinders efforts to find genes, but promising results were obtained when samples were restricted to subjects that shared a common familial trait. Previous studies have analyzed the factor structure of the restricted, repetitive behavior and interests (RRBI) domain and found a two-factor model, 'insistence on sameness' (IS) and repetitive stereotyped motor behaviors,' (RSMB) that accounted for a relatively small amount of variance. Identifying additional familial factors that account for more variance may provide an approach to reduce heterogeneity in future studies.

Objectives: To a) replicate previous findings; b) identify new factors in the RRBI domain; c) examine their familiality among affected siblings; and, d) measure the association with broader autism phenotype (BAP) traits in their parents.

Methods: Our sample included 310 verbal subjects (age 5 to 22) who met DSM-IV criteria for autism. We factor analyzed the RRBI 'ever' items from the Autism Diagnostic Interview-Revised to replicate previous findings and then in a separate analysis we included the communication item, 'verbal rituals.' We examined the familial aggregation of factors and their association with BAP traits.

Results: The IS and RSMB two factor model was replicated in our sample. In the second factor analysis (RRBI + verbal rituals) we observed a four factor model: IS, 'simple' RSMB, 'complex' RSMB, and a fourth factor including symptoms associated with intense

preoccupations (IP). IS and IP were each significantly familial ($p < .001$ for both), but only IP was significantly correlated with the BAP traits of rigidity ($r = .39$, $p = .007$) and aloofness ($r = .39$, $p = .005$) in fathers.

Conclusions:The results support previous evidence for the familiality of IS and identify IP as an additional strong candidate trait for genetic studies of autism.

Poster Presentations Program

154 Language Posters

1 154.1 Prosodic processing: the effect of semantic context and relationship with "autistic" traits on the perception of contrastive stress. S. Peppe[1], J. McCann[1], M. Ota[2] and M. Stewart*[3], (1)*Queen Margaret University*, (2)*University of Edinburgh*, (3)*Heriot-Watt University*

Background:

Prosody, the intonation and inflection of spoken language, serves to change or enhance the meaning of what is being said, through elements such as pitch, loudness, speech rate and rhythm. "Contrastive stress" is an area of particular difficulty for those with autistic spectrum disorders (ASD; Paul et al., 2005; Peppé et al., 2007).

Objectives: This study asks whether processing of prosodic information in ASD is affected more by semantic context or by the prosodic forms of speech.

Methods:

Typically developed (TD) young adults completed the Autism-Spectrum Quotient (Baron-Cohen et al., 2001) and tests of receptive prosody assessing the impact of semantic/lexical information and prosodic factors (n=22, 8 males, 14 females).We assessed whether the context of speech would influence the time taken and the accuracy of listeners' ability to identify stress on words. In addition, we assessed the listeners' ability to identify stress in a phrase without any semantic or lexical information using laryngeal recordings.

Results: Participants were less accurate and slower at identifying which word carried stress when it was on a word that was incongruent with the semantic context of the sentence than when it was congruent. Those with more autistic traits were however less influenced by the semantic context of the sentence.

When the semantic context was removed from the sentence and a laryngeal recording was used we found that as autistic traits increased accuracy scores decreased, suggesting that an increased amount of autistic traits is associated with worse performance on the prosody test.

Conclusions:

Our study suggests that prosodic processing in typically developed young adults is significantly influenced by semantic context. As autistic traits increase it appears that identification of where stress lies in a sentence is more difficult, and that the semantic context of a sentence has less influence.

2 154.2 Pragmatic inferences in high-functioning adults with autism and Asperger syndrome. J. Pijnacker*[1], P. Hagoort[1], J. Buitelaar[2], J. P. Teunisse[3] and B. Geurts[3], (1)*F.C. Donders Centre for Cognitive Neuroimaging*, (2)*Radboud University Nijmegen Medical Centre*, (3)*Radboud University Nijmegen*

Background: Although high-functioning people with autism possess relatively intact core language skills they often have severe deficits in pragmatic aspects of language. Despite a considerable amount of research on pragmatics in autism, very few studies have assessed pragmatic reasoning in autism.

Objectives: To investigate whether high-functioning adults with autism are capable of deriving scalar implicatures, which are generally considered as pragmatic inferences.

Methods: We carried out a behavioral experiment on high-functioning adults with autistic disorder (n=11) or Asperger syndrome (n=18) and matched controls (n=28). Participants were presented with underinformative sentences like "Some

sparrows are birds" and "Zebras have black or white stripes". These sentences are logically true, but pragmatically infelicitous if the scalar implicatures "Some *but not all* sparrows are birds" and "Zebras have black or white stripes *but not both*" are derived. The task was to judge whether the presented sentences were true or false. Responses and reading times were measured.

Results: Participants with autistic disorder derived fewer scalar implicatures than participants with Asperger syndrome, but they did not differ in response pattern from the control group. However, reading time data suggest that the autistic disorder group needed more time to perform the task. In contrast, participants with Asperger syndrome performed at normal levels and even better. Moreover, in the autistic disorder group the number of derived implicatures correlated with verbal intelligence. In the Asperger syndrome and group control group no such correlations were found.

Conclusions: Our findings indicate that a differentiation between high-functioning autistic disorder and Asperger syndrome is relevant. Moreover, our results suggest that verbal intelligence is a constraint on task performance in autism.

3 154.3 The Influence of the Frequency of Maternal Speech Acts vs. Children's Responsiveness to Those Speech Acts in Typically Developing Children and Children with Autism. L. D. Swensen*[1], D. Fein[2] and L. Naigles[2], (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*University of Connecticut*

Background: Mothers use various speech acts during children's second and third year of life that facilitate language development (Ninio & Snow, 1996). For example, mothers who ask more Y/N- Questions have children who later use more auxiliary verbs (Newport, Gleitman, & Gleitman, 1977). We know that joint attention facilitates language growth in typically developing children and children with autism (Rosenthal-Rollins and Snow, 1998). Little research has explored whether different types of maternal speech acts facilitate language in children with autism.

Objectives: To investigate how specific maternal speech acts, and children's responsiveness to these, influence their language development.

Methods: 10 boys with Autism Spectrum Disorder (ASD) and 14 typically developing children (TYP) were studied longitudinally. Every four months (ASD: 33-45 months old; TYP: 17-29 months old), mother-child dyads participated in 15 minute free play sessions, which were transcribed and analyzed. The groups were roughly equivalent in language production at visits 2 and 3.

Results: Few relationships emerged between the frequency of maternal speech acts and children's subsequent language. Many relationships were found between children's responsiveness to specific speech acts and their subsequent language. Additionally, at visit 2, responsiveness to all types of maternal speech acts influenced children's language for the TYP group. These widespread responsiveness effects were not seen for the ASD group until visit 3.

Conclusions: Findings suggest that it is not mothers' usage of specific speech acts that facilitates language, but instead how children responded to these speech acts. By responding to certain speech acts, the children may have been forced to use certain elements of speech. Certain speech acts may only influence children's language when the children are "engaged" during that utterance. Therefore, although there are differences in the influence of discourse elements in maternal input for ASD and TYP children, these elements are informative for both groups.

4 154.4 USING THE CHILDREN'S COMMUNICATION CHECKLIST (CCC-2) AND THE TEST OF PRAGMATIC LANGUAGE TO IDENTIFY PRAGMATIC LANGUAGE IMPAIRMENT IN SPEAKERS

WITH AUTISM SPECTRUM DISORDER. J. Volden* and L. Phillips, *University of Alberta*

Background: Pragmatic language dysfunction persists despite typical structural language skills in high-functioning speakers with ASD (Landa, 2000), yet there are few standardized measures that can be used to identify it (Bishop, 1998; Adams, 2002). Young et al. (2005) found that the TOPL discriminated speakers with ASD with age-appropriate structural language skills from typically developing controls, but their performance varied and some performed as well as matched controls. Bishop (2003) found that the General Communication Composite (GCC) of the CCC-2 was also useful in identifying clinically significant communication problems. Further, Social Interaction Deviance Composite (SIDC) scores less than 0 identified those with an autism spectrum communicative profile

Objectives:This study compares the CCC-2 and the TOPL in speakers with ASD who have typical levels of structural language skill, in order to determine if one was more successful than the other at identifying pragmatic language impairment.

Methods: 15 children and adolescents with ASD (CA: 5;10 – 13;4; diagnosed with ASD by ADOS, ADI and expert clinical opinion) with CELF-IV Composite Language standard scores greater than 85, were given the TOPL and their parents completed the CCC-2.

Results: Average TOPL (84.13) and GCC (78.27) were both significantly different from average scores on the CELF-IV (105.93) ($t(14) = 6.49$, $p < .001$ for TOPL; $t(14) = 6.76$, $p < .001$ for GCC).

All 15 had SIDC scores below 0 on the CCC-2 (Accuracy = 100%), while only 7 had TOPL scores less than 80 (Accuracy = 46%).

Conclusions:

Lower standard scores on pragmatics tests than on structural tests suggests that pragmatics tests evaluate additional communication skills.

While mean score on the TOPL did not indicate pragmatic impairment in this sample, the mean score on the CCC-2's GCC indicated clinically significant communication disability. In addition, the SIDC identified all as exhibiting an autism spectrum communicative profile.

5 154.5 LANGUAGE AND LITERACY SUBTYPES IN HIGH-FUNCTIONING AUTISM SPECTRUM DISORDER. D. Jacobs* and A. Richdale, *RMIT University*

Background: One hundred and sixty-eight children (109 male and 59 female) aged between 6 years 5 months and 8 years 11 months ($M = 92.88$, $SD = 7.88$) with a diagnosis of high-functioning autism spectrum disorder **(**HFASD) ($n = 42$), specific language impairment (SLI) ($n = 42$), specific reading disorder (SRD) ($n = 42$), or who were typically developing ($n = 42$) participated.

Objectives: To examine whether or not there are language and literacy subtypes in young children with a high-functioning autism spectrum disorder.

Methods: Participants completed standardised measures of cognition, phonological processing, structural language (semantics, syntax), pragmatics, reading, and spelling. Ability groups were then formed on the basis of the children's structural language and decoding scores regardless of their diagnostic group.

Results: Children with a HFASD exhibited a wide range of language and literacy skills. Some participants demonstrated structural language and literacy outcomes comparable to typically developing children whilst others had structural language and literacy skills that paralleled those of children with SLI, SRD, or combined SLI-SRD. Additionally, a few HFASD participants presented with above average structural language and literacy ability.

Conclusions: With regard to language and literacy, HFASD comprises a heterogeneous group of individuals. Whilst pragmatic language impairment is mandatory regardless of ability level structural language deficits are not. Furthermore, decoding and reading comprehension were similarly variable. The view that a majority of children with a HFASD

have intact decoding combined with impaired reading comprehension was not supported.

6 154.6 Maternal rate of speaking predicts later language in children with ASD. J. Karaja[1], L. D. Swensen[2], G. Jaffery[1], D. Fein[1] and L. Naigles*[1], (1)*University of Connecticut*, (2)*NYS Institute for Basic Research in Developmental Disabilities*

Background: Both lexical and grammatical elements of maternal input have been found to predict subsequent child language in ASD and in typical development. Maternal clarity of speech has also been hypothesized to facilitate language development, by reducing the complexity of the acoustic signal and thereby the child's task of segmenting the speech stream. Research with typically developing children, and with children who stutter, has found that maternal slowness and clarity of speech correlates positively with child fluency and child speech perception (Ratner, 2004; Liu, Kuhl & Tsao, 2003).

Objectives: The current study investigates whether maternal rate of speaking influences language development in children with autism.

Methods: 10 boys with Autism Spectrum Disorder (ASD) were studied longitudinally between 33-45 months of age. Every four months, mother-child dyads participated in 15 minute free play sessions, which were transcribed and analyzed. Mothers' language production was coded at Visit 2 and children's language production was coded at Visit 3.

Results: Mothers' and children's speech was coded for mean speed of utterance (seconds per morpheme) and IPSyn score, a measure of grammatical complexity. Pairwise correlations revealed that children who spoke more slowly produced utterances of lower grammatical complexity (r = -.67, p = .3). However, mothers who spoke more slowly at Visit 2 had children who used utterances of *greater* grammatical complexity at Visit 3 (r = .688, p = .3). These correlations held even when children's overall cognitive abilities (Mullen scores) were partialed out.

Conclusions: These results support previous findings with other populations, that maternal clarity of speech influences child language development. Specifically, mothers who spoke more slowly had children who appeared more grammatically advanced. Thus, children with autism appear to learn from maternal speech in ways similar to typically developing children.

7 154.7 Visual fixation patterns are associated with communicative competence. C. Norbury*[1], J. Brock[2], L. Cragg[3], S. Einav[4], H. Griffiths[4] and K. Nation[4], (1)*Royal Holloway, University of London*, (2)*Macquarie University*, (3)*University of Nottingham*, (4)*University of Oxford*

Background:

Previous investigations using eye-tracking methods have reported reduced fixation to salient social cues such as eyes when participants with autistic spectrum disorders view social scenes. However, these studies have sampled relatively able participants with good language skills.

Objectives:

To explore visual fixation patterns to dynamic social stimuli in different language phenotypes within the autism spectrum.

Methods:

The eye-movements of twenty-eight teenagers with autistic spectrum disorders and 18 typically developing peers were recorded as they watched videos of same-aged peers interacting in familiar situations and environments. Within the autistic spectrum, we contrasted the viewing patterns of those with language impairments and those with age-appropriate language. The proportion of time spent viewing eyes, mouths and other aspects of the scenes was calculated across video clips. In addition, the percentage of viewers in each group showing a significant preference for viewing eye regions of the face was calculated. Finally, the association between viewing patterns and social/communicative competence was measured.

Results:

Individuals with autistic spectrum disorders and age-appropriate language abilities spent significantly less time looking at the eyes than typically developing peers. In contrast, there were no differences in viewing patterns between those with language impairments and typically-developing peers. The relationship between language ability and fixating eyes and mouths was different in the two clinical groups. A positive association between eye fixation and vocabulary knowledge was evident for those with language impairment, but the opposite pattern was seen in the more linguistically able group.

Conclusions:

We propose that attention to both the eyes and mouth is crucially important for language development and communicative competence. Small differences in fixation time to eyes may not be sufficient to disrupt social competence in daily interactions. A multiple cognitive deficit model of autistic spectrum disorders, incorporating different language phenotypes is advocated.

8 154.8 Expressive prosody in autism: Effects of prosody function and processing demands. J. Van Santen*[1], E. Tucker Prud'hommeaux[1], R. Paul[2], L. Black[1] and L. Shriberg[3], (1)*OHSU*, (2)*Yale Child Study Center, and Southern Connecticut State University*, (3)*Waisman Institute, University of Wisconsin—Madison*

Background:

Expressive prosody is often compromised in autism spectrum disorders (ASD). Less is known about which prosody functions are most affected (e.g., grammatical vs. pragmatic/affective functions) and the role of processing demands.

Objectives:

The purpose of the study was to compare performances of children with ASD vs. typical development (TD) in expressive prosody tasks varying in function (grammatical, pragmatic, affective) and processing demands (repetition vs. pictorial processing).

Methods:

Five experimental tasks were used:

(i) Lexical Stress Task (grammatical+repetition): repeating two-syllable words with initial or final stress.

(ii) Emphatic Stress Task (pragmatic+repetition) (*EST*): repeating "Bob may go home" with focus on different words.

(iii) Phrasing Task (grammatical+pictorial) (adapted from PEPS-C [Peppé & McCann, 2003]: describing a picture of, e.g., "chocolate, ice cream, and honey" vs. "chocolate-ice cream, and honey".

(iv) Focus Task (pragmatic+pictorial) (adapted from PEPS-C): correcting focus in a recording describing, e.g., a blue sheep as a black sheep or a blue cow.

(v) Pragmatic Style Task (pragmatic/affective+pictorial): talking about a pictured object using prosody appropriate to address a baby vs. an adult.

The recordings were scored using automated digital methods.

Results:

Children with ASD performed as well as children with TD on any repetition or grammatical prosody task [(i)-(iii)], but worse on those picture processing tasks that required pragmatic or pragmatic/affective prosody [(iv), (v)]. The interaction of Focus vs. EST and ASD vs. TD indicates the importance of input processing demands vs. output demands, which were identical in these two tasks.

Conclusions:

Prosody function and processing demands differentially affect children with ASD. Weakness in prosody is confined to pragmatic/affective functions of prosody. Repeat tasks, regardless of type of prosody, do not tap into these weaknesses, which may be related to echolalia in ASD. This shows the importance of studying prosody generation at deeper levels of processing.

9 154.9 Comprehension tasks reveal grammatical weakness in young children with autism. G. Jaffery*, S. Tek, D. Fein and L. Naigles, *University of Connecticut*

Background: Research on the grammatical abilities of children with autism has revealed both strengths and weaknesses; they demonstrate steady growth in MLU across development but frequently omit grammatical morphemes and use complex grammatical constructions such as Wh-questions much less frequently than typically developing children. These findings have relied on production data, though, which can be unreliable in a disorder in which children are disinclined to speak. Moreover, some have conjectured that ASD children's avoidance of Wh-questions is pragmatic rather than grammatical.

Objectives: We investigate ASD children's *comprehension* of Wh-questions, using intermodal preferential looking.

Methods: Children are tested every four months in this ongoing longitudinal study. At the study's onset, the ASD children had a mean age of 33 months and had language scores comparable to 20-month-old typical children. At Visit 4, when the children viewed the Wh-question (WHQ) video, they averaged 45.3 months of age and produced on average 34% of the words on the MacArthur CDI checklist. The typical children at the same visit averaged 33 months and produced 68.5% of the CDI checklist. The WHQ video (Seidl et al., 2003) showed 'hitting' events (e.g., an apple hitting a flower), followed by test trials showing the apple and flower on separate screens. The WHQ test audios were "What did the apple hit?/What hit the flower?"; the Name control audios were "Where's the apple/flower?" Children's eye movements were coded off-line.

Results: The ASD children showed no significant looking preferences when hearing the Wh-questions, either at Visit 4 or Visit 5. The comparison typical group demonstrated significant looking to the match at both visits.

Conclusions: Young children with autism have not yet demonstrated the ability to understand Wh-questions. These findings support the claim that even higher-functioning autistic children have specific grammatical weaknesses that are not completely attributable to pragmatic impairments.

10 154.10 Grammatical strengths in the language of young children with autism. L. Naigles*, S. Tek, G. Jaffery and D. Fein, *University of Connecticut*

Background: Research on the grammatical abilities of children with autism has revealed early and later strengths in clausal syntax in, for example, understanding SVO word order and linking verb frames and verb meanings. Fewer studies have investigated the *processes* by which ASD children acquire clausal syntax, or tried to link specific early and later grammatical abilities in the same children.
Objectives: We compare 10 ASD children's syntactic comprehension across time, using intermodal preferential looking. Understanding of SVO word order (WO) was assessed at Visit 1 and use of syntactic frames (SF) to learn verbs was assessed at Visit 4.
Methods: At Visit 1, children's mean age = 33 months, mean vocabulary = 23% of MB-CDI; at Visit 4, their mean age = 45.3 months, mean vocabulary = 34% of MB-CDI. For the WO test, children saw side-by-side static pictures of reversible events (boy pushes girl, girl pushes boy) and had to identify the correct picture to match a sentence. For the SF test, children were taught novel verbs in the transitive frame ("The duck is gorping the bunny.") while viewing a duck and a bunny engaged in simultaneous novel causal and noncausal actions. During the test trials ("Find gorping!"), the causal and non-causal actions were shown side-by-side. Children's eye movements were coded off-line.
Results: On WO, children scored 66.7% correct ($p < .5$). For SF, children mapped the novel verb onto the causal action (54.6%, $p < .5$). Performance on the two tasks was highly correlated ($r = .718$, $p < .5$).
Conclusions: These children with autism were able to use frame-based syntax to learn the meanings of novel verbs; this ability correlated with their earlier understanding of SVO word order. These findings demonstrate how earlier and later aspects of syntax are related in ASD children's grammatical development.

11 154.11 Sentence Development in Young Speakers with Autism Spectrum Disorders. M. Lewis*[1], E. Schoen[1], R. Paul[1], J. Van Santen[2] and L. Black[2], (1)*Yale University*, (2)*OHSU*

Background: Language form in high-functioning children with autism spectrum disorders (ASD) has been held to be a relative strength (Tager-Flusberg, 1995). Some recent studies suggest there may a subset of speakers with ASD who show specific grammatical deficits (Tager-Flusberg & Joseph, 2003), or more generalized weaknesses in grammatical function (Eigsti et al.,2007).

Objectives: The purpose of this study is to compare syntactical features in spontaneous language samples of children with ASD and children with typical development (TD), matched on verbal IQ.

Methods: Participants (ages 4-7) underwent extensive cognitive, behavioral, and language testing to establish research diagnoses of autism Language samples were derived from the first 50 utterances spoken during administration of the Autism Diagnostic Observation Schedule (ADOS). Language samples were transcribed and analyzed, using the SALT program (Miller & Chapman, 2008).

Results: Preliminary results indicate decreased sentence complexity among children with ASD compared to the TD group. Children with ASD used fewer conjunctions, and scored a full Brown's Stage lower than typical peers, based on MLU. Interestingly, the group with ASD made significantly fewer grammatical errors than peers with TD.

Conclusions: Despite relative sparing of language skills as evidenced by standardized testing, children with ASD show lower levels of overall grammatical development; specifically, reduced use of complex sentences, as indexed by decreased frequency of conjunction use, when compared to peers with typical development. Findings suggest young speakers with ASD produce simple, well-formed sentences, making few errors but showing little sentence elaboration. These findings have implications for understanding the language skills of children with ASD in the elementary years, suggesting that although basic grammatical rules are learned, speakers with ASD fail to move forward from these simple expressions to produce the richer, denser, more elaborated sentences that support academic and social growth.

12 154.12 Naming of artifacts and word learning in children with autism. L. Surian*, *University of Trento*

Background: children with typical development use functional, intentional and shape cues in object naming and word learning tasks (Diesendruck, Markson & Bloom, 2003; Gelman & Ebeling, 1998). Objectives: the aim of this study was to investigate such ability in children with autism. Methods: in experiment 1, 29 children with autism and a group of children with typical development were shown line drawings of objects and they were told that these objects were the product of either a deliberate action or a fortuitous event. Children were then asked to say what the objects were. Responses were classified as shape based ("a man") or substance based ("a spot of paint"). In experiment 2, 36 children with autism were shown triplets of novel objects consisting always of a 'target' object named using a novel noun ("millo"), another object with a similar overall shape and a third object with a different shape that was either (1) given no description or (2) described as bearing a functional similarity with the target object because of its potential use or its function as intended by its creator. Results: in experiment 1, children with typical development preferred shape responses on intentional trials and substance responses on accidental trials. By contrast, children with autism did not differentiate their responses in the two types of trials. In experiment 2, when asked to find another "millo", the presence of functional information increased the frequency of all children's functional match choices. However, the responses of children with autism were not affected by whether the object function was described as the intended function, rather than a merely possible one. Conclusions: these findings suggest that children with autism have difficulties in taking into account information about intentions when naming and reasoning about artifacts. We compare domain

specific and domain general accounts for these findings.

13 154.13 Discourse cohesion in high-functioning autism: A comparison of mentalistic and non-mentalistic bridging inferences. A. Nadig*[1] and S. Ozonoff[2], (1)*McGill University*, (2)*University of California at Davis*

Background:

When understanding language we use real-world knowledge to make causal, "bridging" inferences about the outcome of an event. Previous work found that individuals with autism display poor text comprehension relative to reading ability (Nationetal.,2006), and have difficulty making bridging inferences (Dennis,Lazenby&Lockyer,2001; Jolliffe&Baron-Cohen,1999; Ozonoff&Miller,1996). These studies did not control for the potentially confounding factor of social inferencing demands in their stimuli.

Objectives:

This experiment investigates whether children with high-functioning autism (HFA) show:

1) General difficulty in integrating an outcome sentence with previous discourse using real-world information

2) Specific or increased difficulty with inferences that require mentalizing

Methods:

8- to 14-year old children with HFA (n=23) and typical development (n=18), matched for language ability, word reading ability and age participated in a computer-presented experiment. They read short event scenarios consisting of a background and outcome sentence. They selected the cause of the event from three choices: 1) a bridging inference which integrated the background and outcome, 2) a local inference derived from the outcome sentence alone, 3) an implausible inference, included as a control. In half of the stimuli inferences depended on mental state attribution, the other half depended on knowledge of physical relationships. Dependent variables were accuracy (selection of the bridging inference) and response time to select an inference.

Results:

Regardless of the type of inference, the HFA group chose bridging inferences significantly less often than the TYP group, and had reliably longer response times to select an inference (adjusted for individual reading speed). Surprisingly, both groups chose bridging inferences more often in the mentalistic than non-mentalistic condition. The selection of bridging inferences was related to level of language ability ($\tau = .32$, $p < .1$).

Conclusions:

High-functioning children with autism have *general* difficulty and delays in integrating an outcome sentence with previous discourse to arrive at coherent inferences. This likely contributes to problems in text comprehension.

14 154.14 VOCABULARY AND GRAMMAR DEVELOPMENT IN TODDLERS ON THE AUTISM SPECTRUM COMPARED TO LATE TALKERS WITHOUT AUTISM. S. Ellis-Weismer*, M. Gernsbacher, E. Roos, C. Karasinski, A. Esler and S. Stronach, *University of Wisconsin-Madison*

Background: Investigation of early language development in autism has both theoretical and practical significance. This study addressed whether language delays or deficits noted in autism constitute a unique phenomenon ('distinct category account'), or whether they overlap with other language difficulties ('dimensional account'). Research focused on contrasting the distinct category vs. dimensional accounts has implications for phenotypic markers of autism as well as treatment. The current study explored the overlap in language abilities in verbal toddlers on the autism spectrum (AUT) and late talkers (LT) without autism.

Objectives:

This study examined whether autism spectrum toddlers and late talkers, matched on overall productive vocabulary, display similar use of

1) semantic categories; 2) psychological terms; and 3) word combinations and grammatical complexity.

Methods:

Two groups of toddlers (22-35 months) participated: 21 AUT and 21 LT. AUT diagnoses were determined using comprehensive diagnostic evaluations including the ADI-R and ADOS. Groups were matched on parent report of words produced (± 6 words) on the *Communicative Development Index: Words and Sentences* (CDI-WS).

Results:

Vocabulary matching resulted in significant mean age differences between the groups (AUT=30 mo, LT=25 mo). Comparison of the proportions of words within 22 semantic categories on the CDI-WS revealed equivalent usage for all categories except action words (higher for AUT). An analysis of psychological terms (e.g., "happy") revealed no significant differences for any of five categories evaluated or overall proportion of terms used. With respect to grammatical abilities, there were no significant differences in CDI complexity scores or the proportion of AUT vs. LT toddlers who were combining words.

Conclusions:

When matched on overall vocabulary level, 30-month AUT toddlers exhibited word use patterns and early grammatical abilities that were qualitatively very similar to 25-month late talkers without autism. These initial findings support the dimensional account of language delay relative to vocabulary/grammar in autism.

15 154.15 IDIOM AND JOKE COMPREHENSION IN AUTISM: PRAGMATIC EXPERIMENTS ON FINNISH SPEAKERS WITH ASD

J. Ravattinen* and J. Niemi, *University of Joensuu*

Background:

Difficulties in social and communicational skills in ASD have been described over the last few years. However, scholars in these studies have not typically been linguists. Pragmatic performance deviations are seen to lie in the core of ASD and pragmatics is part of linguistics. Thus, ASD studies are in need of linguistically-oriented analyses of pragmatics.

Objectives:

Analysis of the difficulties the HFA/As-individuals might have in figurative or humorous language.

Methods:

Series of pen-and-paper idiom and joke tasks were administered to 4 groups of HFA/As-subjects and matched controls. In order to study idiom comprehension, the subjects were asked to choose, from four alternatives, one or two sentences that, according to their judgments, meant the same as the stimulus sentence containing an unambiguous VP idiom. A judgment task was administered in order to find out what type of jokes would be categorized as "humorous" by HFA/As-subjects and another paper-and-pen decision task was administered in order to find out if they could find the correct punch-line from the list of possible alternative endings in order to make the text into a joke.

Results:

In idiom comprehension in both subject groups the number of "incorrect" responses diminishes and the number of "correct" increases with age. However, the older HFA/As-subjects remain at the level of the younger control group. The older HFA/As-subjects also have fewer idiom alternative choices as well as more literal and lexical distractor choices. The results from jokes tasks show, unexpectedly, that the HFA/As group ranked jokes more often as funny as did their controls. The punch-line task analysis is underway, but will be finalized shortly.

Conclusions:

The age related performance indicates that explicit rehabilitation methods should be developed to avoid pragmatic fossilization in function of age.

16 154.16 Grammatical Difficulties in Autism as Revealed by a Sentence-Picture Matching Task. M. Walenski*[1], S. Mostofsky[2] and M. T. Ullman[3], (1)*University of California, San Diego*, (2)*Kennedy Krieger Insititute, John Hopkins University*, (3)*Georgetown University*

Background: Although deficits of language and communication are diagnostic of autism, not all aspects of language appear to equally affected in the disorder.

Objectives: To examine syntactic processing in autism with a sentence-picture matching task – the Test of Active and Passive Sentences – that is sensitive to grammatical deficits in children with Specific Language Impairment (TAPS; van der Lely, 1996).

Methods: Participants listen to a sentence and choose the picture (one of four) that is most consistent with the meaning of the sentence. The sentences are either active ("The boy cuts the elephant"), passive ("The elephant is cut by the boy"), a shortened passive sentence ("The elephant is being cut"), or an ambiguous shortened passive sentence ("The elephant is cut", which is ambiguous between a verbal interpretation, "The elephant is being cut" and a grammatically simpler adjectival interpretation, "The elephant is in a state of having-been-cut"). We tested native-English-speaking high-functioning children with autism (n=9) and typically-developing control children (n=12).

Results: Preliminary results indicate that for the three unambiguous sentence types the children with autism performed worse than the control children (79% vs. 92%). For the ambiguous sentences, the controls were split roughly evenly between the verbal interpretation and the adjectival interpretation, while the children with autism appeared to show a stronger preference for the adjectival interpretation.

Conclusions: Both the reduction in accuracy on unambiguous sentences and the preference for a simpler grammatical structure are consistent with prior claims of syntactic and other grammatical abnormalities in autism. Additional implications will be discussed.

17 154.17 Word Reading in Hyperlexic Children with ASD. D. Saldaña*[1], M. Carreiras[2] and U. Frith[3], (1)*University of Sevilla*, (2)*University of La Laguna*, (3)*University College London*

Background: Children with Autism Spectrum Disorders (ASD) often present a hyperlexic reading profile involving outstanding word reading. It has been hypothesized that they may be accessing word representations in an unusual manner. However, data on their use of orthographic or phonological pathways is far from conclusive.

Objectives: To assess semantic, orthographic and phonological processes involved in word reading in persons with ASD and hyperlexia.

Methods: A group of English adolescents with ASD and a word reading to text comprehension discrepancy (n = 14) was matched on chronological and word reading ages to a group of typically developing readers (n = 12). Amongst the ASD participants, when verbal IQ to reading discrepancy was also taken into account, it was possible to distinguish two groups. One, labelled *true hyperlexics* (n = 7), had word reading scores above their verbal IQ, whereas the other, considered *poor comprehenders*, obtained comprehension scores below their verbal IQ. Participants completed tasks exploring access to lexical representation using orthographic, semantic and phonological pathways, sub-lexical phonological abilities (spoonerisms, non-word reading and non-word repetition), working and short term memory and rapid naming.

Results: True hyperlexics outperformed poor comprehenders and typically developing children on a task involving phonological lexical representation, and poor comprehenders on a task involving orthographic lexical representation. Their performance was not superior on the sub-lexical, memory or rapid naming tasks, and was equivalent to typically developing children on semantic access to word representations.

Conclusions: Children with hyperlexia show a combination of strong phonological and

orthographic lexical representations and typical performance on sub-lexical, working memory and rapid naming tasks. Their superior word reading does not stem from unusual access to word reading. We propose that these results are compatible with an profile of expertise in word reading acquired through extended practice.

18 154.18 The Learning of Foreign Languages by High Functioning Autistic Children. C. Besnard*, *York University - Glendon College*

Background: Today, more and more children are being diagnosed as being autistic, and because communication impairments are at the core of their disorder, speech-pathologists as well as educators tend to recommend that their language learning be limited to one language, namely the language of the community they live in.

Objectives: Given this situation, we would like to argue that high functioning autistic children as well as Asperger Syndrome children can learn foreign languages (L2), and become bilingual.
Therefore, we will show that like the population with learning disabilities who appears to benefit from L2 learning, the high functioning autistic language learners can benefit from L2 learning as it seems to have a positive impact on their linguistic, cognitive, social, psychological and cultural development. We will also argue that like with the regular population, L2 learning by high functioning autistic learners can lead to a transfer of knowledge from
L2 to L1 (their first language), and consequently can improve and strengthen their command of L1 which is an asset for this population.

Methods: Research in:
- The peculiar learning style of high functioning autistic language learners,
- Psycholinguistics applied to the learning of L2 by students with learning disabilities (Bruck 1978 and 1982, Carrasquillo et al. 1990, Crago et al.
2005, Cummins 1985, Difino et al. 2004, Ganschow et al. 1991 and 1998, Genesee 1992 and 2004, Hill et al. 1995, Saenz 2005, Scott 2000, Sparks 2001, Wire 2002),
- Foreign Language Didactics,
- 15 year first hand experience with the tutoring of an ASD student to learn French as an L2.

Results: n/a

Conclusions: Given the capacity of this population to learn L2 as well as their particular learning style, we will explore what kind of methodology and teaching strategies seem to facilitate and maximize their L2 learning.

19 154.19 An Acoustic Inspection of Vocalizations in Young Children with Autism Spectrum Disorders. M. C. Wallace, J. E. Cleary*, E. H. Buder, W. Pettit and D. K. Oller, *The University of Memphis*

Background: Few investigations have focused on the vocal quality used by children with autism spectrum disorders (ASD) during the prelinguistic stage of communication development. Previous research, using a limited range of vocal categories and not based on acoustic inspection, found that children with ASD produced significantly more syllables with atypical vocalizations than children with developmental delays (DD) (Sheinkopf et al., 2000). This finding could indicate a positive symptom for ASD thus enhancing the sensitivity of screening tools that currently rely heavily on negative symptoms. A core communication deficit in ASD is directing communicative behaviors to conversational partners, so this study also will explore relationships between the vocal quality and directedness of each vocalization.

Objectives: To reanalyze the data collected by Sheinkopf et al. (2000) by: 1) using acoustic displays and a more refined set of 20 categories to assess vocalizations produced by children with ASD and children with DD, 23-64 months of age, and 2) evaluating the relationship between vocal quality and communicative directedness.

Methods: The participants' (9 DD, 10 ASD) vocalizations produced during administration of the Early Social-Communication Scales were digitized and viewed with software designed to display videos with concurrent spectrographic

information. Measurements included two sets of codes: 1) dynamics of vocal fold vibration ("vibratory regimes"; Buder et al., in press) and 2) auditory impressions (e.g., pressed, breathy). The sets are mutually exclusive and non-redundant. Both sets incorporated inspection of acoustic displays, and the regime codes were produced with special attention to narrowband spectrograms. The video of each vocalization was observed and identified as being "directed to person" or "other".

Results: Preliminary findings suggest that children with ASD produce different phonatory regimes and vocal qualities than children with DD.

Conclusions:Implications for early diagnostic procedures and acquisition of socially appropriate voice will be discussed.

20 154.20 Language development of two to five year old children with autism and a normal intelligence. L. Roelen*, *Indigo vzw*

Background: Children with autism spectrum disorder of course have problems with communication. In children with a normal intelligence the language development may be just slightly disturbed. Especially in younger children with ASD and a normal intelligence there hasn't been a lot of publications concerning their language development.

Objectives: To investigate the language development in Flemish 2 to 5 year old children with autism and a normal intelligence.

Methods: We investigated the language development of 60 two tot five year old children with ASD and a normal intelligence, using two standardised tests for language development (R-TOS and Nijmeegse Pragmatiek Test)

Results: (preliminary:) 2 to 5 year old children with autism and a normal intelligence have a general language development slightly below their developmental age, especially the spontaneaous language and language contents score lower, on the subtests on vocabulary the results are heighest.

Conclusions: (preliminary:) The investigation confirms the problems in language development and certainly in pragmatics.

21 154.21 Language Skills in Young Children with Autism Spectrum Disorder (ASD): Are there differences between Monolingual English and Bilingual English-Spanish Toddlers?. M. Valicenti-McDermott*, M. Schouls, G. Molly, N. Tarshis, R. Seijo and L. Shulman, *Albert Einstein College of Medicine*

Background: Bilingual infants with typical development achieve language milestones at comparable ages to monolinguals and are reported to have more gestures. It is unknown whether there are differences in language skills between monolingual English and bilingual English-Spanish children with ASD. Objectives: To assess expressive and receptive language skills in monolingual English children with ASD, as compared to bilingual English-Spanish children with ASD. Methods: Retrospective chart review of 50 toddlers who underwent a multidisciplinary evaluation in a University Affiliated Center between 2002-2005 and were diagnosed with ASD. Data included demographics, maternal education, cognitive testing, autistic characteristics (Childhood Autism Rating Scale), and formal speech and language evaluation(expressive and receptive language skills and information about communicative means and functions and speech production). A Bilingual child was defined by the speech pathologist as a child who is exposed to both English and Spanish in the home, regardless of their expressive and/or receptive abilities in either language. Statistical analysis included chi square and independent t-test. Results: Sixty percent were boys, with a mean age of 27 ± 5 m.and 13(26%) children were bilingual. There were no differences in demographics, maternal education, cognitive testing and autistic features between the groups. Compared to monolinguals, bilinguals were more likely to use 2 or > gestures, including pulling (73%vs32% p=0.003) and using other's hands as an object (77%vs.35%, p=0.001), with no other differences in their expressive skills, communicative function or speech production. Parents of monolinguals

reported more frequently that their child followed 1-step commands without gesture (86% vs 17% p=0.001), with no other differences in receptive skills. Conclusions: Although language skills are deviant in young children with ASD, those who are bilingual (English-Spanish) present more gestures. This difference has been observed in children with typical development and it seems to be preserved in children with ASD.

22 154.22 Phrase speech milestone predicts autism symptoms and adaptive ability in high functioning school age children with autism spectrum disorders. L. Kenworthy*[1], D. O. Black[2], L. K. Case[2], J. Strang[1], J. L. Sokoloff[1], A. Youmatz[1], C. Anselmo[1], J. A. Silvers[2] and G. L. Wallace[2], (1)*Children's National Medical Center, George Washington University*, (2)*NIMH*

Background: Language ability is an important predictor of outcome for children with autism. This study examines the relationship between early language development and outcome in a high functioning cohort of children with autism spectrum disorders (ASDs).

Objectives: Investigate the relationship of parent reported language milestones (age of first word and age of phrase speech) to autism symptoms and adaptive behavior in school age children.

Methods: Subjects were a clinically referred sample of 88 high functioning children (mean age=8.4±3.3 years; IQ > 75 on verbal or nonverbal ability) diagnosed with an ASD based on the Autism Diagnostic Interview (ADI), Autism Diagnostic Observation Schedule (ADOS), and clinical impression. The relationships between autism symptoms (based on a composite of ADI and ADOS domain scores), adaptive behavior (Vineland Adaptive Behavior Scale (VABS)) and early language milestones were analyzed using partial correlations, controlling for age. Because nonverbal ability was related to VABS Communication, both age and nonverbal ability were partialled out of the correlations with VABS Communication.

Results: Age at first phrase speech was moderately correlated (*pr* = .26) with autism social symptoms but not communication or repetitive behavior symptoms. Age at first phrase speech was negatively correlated with adaptive behavior in all VABS domains: Communication (*pr*=-.49), Daily Living Skills (*pr*=-.30), and Socialization (*pr*=-.35). Age of first word was not correlated with any measures of symptoms or adaptive behavior.

Conclusions: In this group of high functioning children with ASD, attainment of phrase speech is a predictor of later autism symptoms and adaptive skills, while age at first word is not. This may reflect the fact that language abilities become more stable over time, as phrase speech occurs later in development than first words. Alternatively, phrase speech may be distinct from uttering single words because it is associated with communicative intent, representing early social-communicative abilities.

23 154.23 Grammar, Theory of Mind and Adaptive Functioning in Autism Spectrum Disorders: Exploring Mediation in a Multiple Regression Model. T. A. Bennett*, E. Duku, L. Vaccarella and P. Szatmari, *Offord Centre for Child Studies, McMaster University*

Background: "Theory of mind" (ToM) is considered to be an important deficit in individuals with Autism Spectrum Disorders (ASD). In a study of children with high-functioning ASD, we found that early language impairment was predictive of adolescent adaptive functioning. We are not aware of studies to date investigating ToM as a potential mediator of this relationship.

Objectives: To test whether ToM mediates the relationship between early grammar abilities and adolescent functioning (social and communication) at ages 16-18 in a longitudinal cohort of youth with high-functioning ASD (IQ > 70).

Methods: 35 children with ASD (8 Asperger's syndrome, 27 high functioning autism; M=30, F=5) were recruited at ages 4-6 as part of a larger cohort study of high functioning ASD, with psychometric testing performed every 2 years. Grammatical ability was measured

using the Test of Language Development-2 at ages 6-8; ToM at ages 13-15 years was measured using the "Reading the Mind in the Eyes Test". Outcome scores at ages 16-18 were measured using the Vineland Adaptive Behaviour Scale, Social and Communication domains. Regression analyses tested for mediation according to the Baron-Kenny model.

Results: Grammar was significantly associated with VABS Communication and Social scores ($r = 0.76$ and 0.44, $p < 0.001$), and with ToM scores ($r = 0.65$, $p < 0.001$). ToM predicted a significant amount of variation in Communication and Social scores ($r = 0.67$ and 0.40, respectively, $p < 0.1$). ToM partially mediated the association between grammar and VABS Communication scores (Sobel test = 2.7, $p < 0.4$), but not between grammar and Social scores (Sobel test = 0.77, $p < 0.44$).

Conclusions: Grammar and ToM are strongly associated over time in children with high-functioning ASD and are important predictors of adolescent adaptive functioning. ToM does not appear to mediate the relationship between early grammar and later social functioning.

24 154.24 Narrative Ability in Children with Autism Tested through the Karmiloff-Smith (1985) Stories. R. R. Jordan*, *Autism Centre for Education & Research, University of Birmingham, UK*

Background: Difficulties in personal and fictional narratives are an important aspect of autism spectrum disorders, yet there is little evidence of the precise nature of the problems with narrative in autism. In particular, it is not clear whether difficulties stem from not understanding the emotional or mental state content, in developing story schema or with the technical devices that give stories coherence and cohesion. Objectives: To compare the performance of children with autism on a narrative task to a comparison group of children with developmental delay and the 'norms' established by Karmiloff-Smith... Methods: A replication of the Karmiloff-Smith (1985) study of narrative ability, using five wordless 'story' books, .was carried out with 15 children with autism and a comparison group of 15 children with developmental delay, matched by verbal ability. The child's description of a picture from each of the 'stories' presented as a single picture, was compared with the description of the same pictures when embedded in a wordless 'story' book. Results: Overall, the children with autism did not perform significantly less well in terms of correct use of anaphoric reference, establishing a 'thematic subject', using linking devices across pictures and using devices to engage the listener. However, there were more bizarre responses and a significant difference in relation to two stories; in one this stemmed from a poorly drawn event leading to misinterpretation by the children with autism. In the other it related to the failure of the children with autism to give a causal interpretation to an emotional event. Conclusions: The results agree with other studies showing the key problem with narrative in autism as the failure to make causal statements linking the emotions of characters to events.

25 154.25 THE LANGUAGE PROFICIENCY PROFILE – 2 (LPP-2): MEASURING COMMUNICATIVE SKILLS IN AUTISM. K. Wells*[1], J. M. Bebko[1], K. McFee[1] and J. J. A. Holden[2], (1)*York University*, (2)*Queen's Univerity*

Background: The Language Proficiency Profile-2 (LPP-2) is an informant-based rating scale that was developed by Bebko and McKinnon (1993) specifically to assess the communication skills in children who are deaf and may use a combination of communication systems, somewhat similar to the situation for autism. Individuals who are deaf may communicate using a combination of systems including: spoken language, American Sign Language (ASL), signed-English (SE), an idiosyncratic signing system, or gesture. Those with autism may also be taught to communicate through a variety of alternative methods, including: speech, a signing system, PECS, gesture, etc. Traditional language measures tend to focus solely on a single modality, and therefore, will likely underestimate the true overall communication abilities of someone who

communicates through a combination of methods. The LPP-2 is now used internationally to provide a useful measure of overall communications skills in children who are deaf.

Objectives: The present study investigates the usefulness of the LPP-2 as a measure of overall communication skills in autism.

Methods: Ninety parents and caregivers of individuals with autism or PDD-NOS were administered the LPP-2, the Autism Diagnostic Interview- Revised (ADI-R), and the Pervasive Developmental Disorder Behavior Inventory (PDD-BI).

Results: Scores on LPP-2 are compared to language skills and severity of autistic symptomology as measured by the PDD-BI and ADI-R. Comparison is also made with LPP-2 norms for typical children.

Conclusions: The findings suggest that the LPP-2 may be an informative and useful new tool for better understanding the communicative impairments and overall communication skills for some individuals with autism.

26 154.26 PRAGMATIC FUNCTIONING IN NATURAL SETTING : A COMPARATIVE STUDY OF THE NEGOTIATION OF OPPOSITIONAL EPISODES IN AUTISTIC AND CONTROL CHILDREN. E. Veneziano*[1], M. H. Plumet[1], S. Cupello[1], S. Pingault[1] and C. Tardif[2], (1)*Université Paris Descartes - CNRS*, (2)*Université d'Aix-en-Provence - CNRS*

Background:
Most researchers agree that autistic children suffer from socio-pragmatic dysfunctioning. Their difficulties to use behaviors in socially meaningful ways may give rise to structural-functional incongruities affecting their "psychological" relation to their partners. This paper investigates autistic children's functioning in this domain by studying their communicative behavior in familiar naturally-occurring interactional settings, a context that still remains understudied.
Objectives:
Compare the pragmatic functioning of 9 moderately retarded autistic children (5-10 years) and of their familiar partners to that of 9 typically developing children (2-10 yrs) and of their partners, during naturally-occurring "oppositional" episodes (protests, refusals and denials).
Methods:
Autistic children, diagnosed by experienced clinicians (DSMI-IV and ADI-R), were matched to controls on a vocabulary test (TVAP). For each family, the data analysed consist in 2 sessions of 30 minutes each, videorecorded at home. Oppositional episodes, including justifications, insistence and acceptance, were systematically coded according to well defined criteria (inter-rater reliability : .85).
Results:
Compared to matched controls, less advanced autistic children (Verbal age: 3-4) produce less justifications. More advanced autistic children (Verbal age: 6-7) do not differ quantitatively from controls but their justifications are less effective in persuading their partners. Furthermore, these children do not seem to be immediately convinced by the justifications offered by their partners. Autistic children's familiar partners justify as much as controls their oppositional moves, but are not affected by the production of justifications of their children. Counter-arguing seems to be a possible cause.
Conclusions:
Findings support the existence of similarities and differences in the pragmatic functioning of autistic children and of their familiar partners compared to controls. Specific difficulties reside in the interpretation of autistic children's communicative intentions and in children's difficulties in attributing communicative intents to their partners (theory of mind).

27 154.27 Agreement across Measures of Language and Communication in Preschoolers with Core Autism. K. Hudry*[1], K. Leadbitter[2], K. Temple[3], V. Slonims[4], H. McConachie[5], C. R. Aldred[6] and T. Charman[1], (1)*UCL Institute of Child Health*, (2)*Booth Hall Children's Hospital*, (3)*University of Newcastle*, (4)*Guy's and St. Thomas' NHS Trust*, (5)*Newcastle University*, (6)*University of Manchester*

Background: Communication deficits and language delays are a core feature of autism. As such, a variety of measures have been developed and are regularly used in clinical and research settings to assess children's level of competence in these areas. Given that characteristics of autism make the job of language evaluation a challenging one, a number of different assessment approaches have been derived, including direct child assessment, and indirect methods (i.e., parent or teacher questionnaires and interviews).

Objectives: This study explores the extent of consistency/disagreement amongst scores obtained using various types of communication measure in a large sample of preschoolers with autism.

Methods: Participants were 144 children with core autism aged 2 – 5 years referred across three regions of the United Kingdom to the Preschool Autism Communication Trial (PACT; www.medicine.manchester.ac.uk/pact/). Diagnoses were confirmed through ADI-R and ADOS assessment and children were assessed with a battery of communication measures. This included receptive and expressive subscales of the Preschool Language Scales, the communication domain of the Vineland Adaptive Behaviour Scales (parent survey and teacher rating forms), and receptive and expressive vocabulary counts from the MacArthur-Bates Communication Development Inventory; Words and Gestures.

Results: Appropriate scores were derived so as to permit comparison of scores across the various measures. Preliminary exploration on a subset of cases indicated high variability of scores for individual children with broad agreement across the various measures. Effects of type of measure (i.e., direct vs. indirect assessment) and domain of communication (i.e., receptive vs. expressive) will be evaluated for the whole sample.

Conclusions:These results will describe a profile of language abilities in a relatively homogeneous group of preschoolers with core autism. It will also speak to the relative contribution of different informants and types of instruments in the assessment of communication in this group.

28 154.28 METAPHOR IDENTIFICATION IN CHILDREN WITH ASPERGER SYNDROME AND IN TYPICAL CHILDREN IN FRENCH LANGUAGE

S. De Martino*, *HOPITAL SAINTE MARGUERITE*

Background: The Asperger Syndrome is a pervasive developmental disorder, characterized by impairments in communicative and pragmatic competences. In particular, difficulty understanding metaphor has been observed. This study concerns about difficulties on metaphor identification in children with Asperger Syndrome.

Objectives: 1/ Create an metaphor identification task and compare the performances in children with Asperger Syndrome and typical children. 2/ Constitute a data basis with the results of typical children. 3/ Objective the deficit on metaphor identification in children with Asperger Syndrome by using a methodological tool.

Methods: 101 young typical children participated to this study in order to constitute a referred data basis. The children with Asperger Syndrome were recruited from « Centre de Ressources Autisme » of Child Psychiatric Unit of Hospital Ste Marguerite in Marseille (France). They are asked on metaphoric sentences identification task.

Results: The results in typical children show that the 6,5 to 7,5 years old typical children identify 39,4 % of methaphoric sentences, the 8 years old children identify less than 50 % of metaphoric sentences. The 9 years old typical children perform over 50 %, but they don't reach 100 % on metaphor identification. Preliminary findings reveal a deficit on metaphor identification in Asperger Syndrome children.

Conclusions: We hypothese that the children with Asperger Syndrome present a particular process in metaphor identification and the results were discussed towards the theory of Weak Central Coherence.

29 154.29 Language Development and Sensory Processing Issues In Young Children with Autism: The Role of Social Withdrawal. V. P. Reinhardt* and E. Kelley, *Queen's University*

Background:
Autism is a neurodevelopmental disorder characterized by impairments in the domains of communication, social interaction and behavior (Volkmar, Chawarska & Klin, 2005). Children with autism have marked difficulties with communication and some acquire little to no language (Volkmar et al). The existence of atypical sensory processing in Autism Spectrum Disorders (ASD) is well documented, (O'Neill & Jones, 1997), yet little empirical research has examined the effect of sensory processing issues (SPI) on language development.
Objectives:
This study investigates the relationship between SPI, language development and social withdrawal in young children with ASD.
Methods:
Twenty participants with ASD with mental ages between two and six years and a control group of 20 typically developing children matched on nonverbal mental age and sex directly to participants with ASD completed the *Mullen Scales of Early Learning* (Mullen, 1995) and *Peabody Picture Vocabulary Test Fourth Edition* (Dunn & Dunn, 2007). Caregivers completed the *Sensory Profile* (Dunn, 1999) questionnaire, *Vineland Adaptive Behaviour Scales- Second Edition* (Sparrow, Cicchetti, & Balla, 2005) and the Qualitative Abnormalities in Reciprocal Communication Subscale of the *ADI-R* (Rutter, Le Couteur & Lord, 2005) as a measure of social withdrawal. ASD diagnoses were confirmed using the *Autism Diagnostic Observation Schedule-Generic* (Lord et al., 2000)
Results:Data collection is approaching completion. A negative relationship between SPI and language development is expected such that individuals with more SPI will exhibit lower language levels. I hypothesize that social withdrawal will mediate the relationship between SPI and language development, such that those children with more SPI will be more socially withdrawn and hence display lower levels of language development.
Conclusions:
It is hypothesized that SPI in some individuals with ASD lead social stimuli to be perceived as aversive, leading to social withdrawal. This social withdrawal, in turn results in lower language levels of language development.

30 154.30 Narratives of Personal Events in Children with Autism and Developmental Language Disorders. S. Goldman*, *Albert Einstein College of Medicine*

Background:

Narrative is a complex language activity involving cognitive and social skills. Talking about personal experiences poses unique challenges for verbal children with autism and may affect their self-awareness and the development of autobiographical memories. Children have a natural drive to share events and learn to construct narratives during joint linguistic interactions. They first learn to talk about scripted events like going to a restaurant or celebrating a birthday and are taught to follow a conventional format including core elements such as beginning, middle, and end. Preschool children move to personal narratives with the development of pragmatics and the understanding of people's feelings.

Objectives:

The aim of this study is to examine the interactions of language and social deficits in autism through narratives of life events that ranged in emotional value and familiarity.

Methods:

Eight personal events were elicited among 3 groups of schoolage children: 14 high-functioning with Autism Spectrum Disorders (HFA), 12 non-autistic with developmental language disorders (DLD), and 12 typically developing (TD) matched for chronological age and non-verbal IQ. Narratives were transcribed and analyzed for (1) presence of conventional narrative elements and (2) narrative style (e.g., coherence).

Results:

The results showed that all children used conventional narrative elements. Compared

to DLD and TD children, HFA children needed more prompting to recall emotional, unique or remote events. Overall, their stories included significantly less high-point and specific persons and tended to be less coherent and goal oriented.

Conclusions:

Narrative analysis of personal events provided an opportunity for identifying autism specific issues related to verbal communication and social impairments. The results represent a step towards understanding autobiographical memory in HFA children and the use of emotion as a cue during the recall of events. The findings are interpreted in relation to the social role of narrative and shed light on novel remediation techniques.

31 154.31 Automated measurement of expressive prosody in neurodevelopmental disorders. E. T. Prud'hommeaux*[1], J. Van Santen[1], R. Paul[2] and L. Black[1], (1)*OHSU*, (2)*Yale Child Study Center and Southern Connecticut State University*

Background: Autism spectrum disorders (ASD) are often associated with impaired expressive prosody. Existing methods for evaluating prosodic performance rely on time-consuming, subjective human judgments rather than automated methods. Objectives: The purpose of the study was to establish the validity of our automated digital measures of prosody by comparing those measures with human judgments. Methods: Responses for the following four tasks were scored using automated methods: (i) Lexical Stress (repeat a bisyllabic word with initial or final stress). (ii) Phrasing (describe a picture, indicating the number of pictured items, e.g., "chocolate, cookies, and jam" vs. "chocolate-cookies and jam"; adapted from PEPS-C (Peppé & McCann 2003)). (iii) Pragmatic Style (talk about a picture using prosody appropriate to address a baby vs. an adult). (iv) Focus (correct an inaccurate description of a picture, e.g., if the recording describes a blue cow as green, the subject responds "BLUE cow"; adapted from PEPS-C). The methods capture features of the melodic and temporal patterns that distinguish between contrasting speech responses. Four judges listened to forty utterance pairs for each task, with each pair from the same speaker with the same content but different target prosody. The judges were to identify the intended meaning of the two utterances (e.g., of two recordings, which one was meant to be "BLUE cow" rather than "blue COW"). Results: For all four tasks, the objective measure correlated with the weighted mean rating as well as or better than some of the judges correlated with each other. Conclusions: The automated digital measures were shown to be comparable in reliability to subjective judgment. Using these time-saving automated measures may eventually differentiate between the diagnostic groups more accurately for some tasks than human judgment-based measures and potentially lead to new speech-based markers for ASD.

32 154.32 Understanding Pronominal Reference in Adults with High-Functioning Autism. A. Mizuno*[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,' alternate to whom they refer according to the context. To comprehend and operate these pronominal shifts in conversation, the constant updating of the center of reference, or perspective-taking skill, is required. Atypical usage of pronouns is characteristic of the language deficit in autism but exclusively during childhood (Cantwell et al., 1989; Lee et al., 1994). However, the underlying processing difference that resulted in pronominal reversal in childhood may still be detectible in adults with autism.

Objectives: This study had two objectives: (1) to investigate the atypical preference towards proper names over pronouns and the impediment of pronoun shift as a function of linguistic perspective-taking, (2) and to confirm the intact visuo-spatial perspective-taking in adults with autism.

Methods: Participants were 14 adults with high-functioning autism (mean age 26.43, full-scale IQ 105.64) and 13 age- and IQ-matched controls. They performed computerized role-

taking tasks. The visual stimuli presented a simple object and a question regarding the object from either the participant's or experimenter's perspective.

Results: The results showed that adults with autism performed the task as well as the matched control participants based on the error rates; however, the autism group took a significantly longer time to accomplish the task when using a pronominal expression to refer the subject or experimenter rather than their proper names. The autism group also showed a slower reaction time than the control group, when the center of reference was shifted between the experimenter and the participant in the trial, requiring a pronoun reversal. It is also confirmed that there was no performance difference in the visuo-spatial perspective-taking tasks between groups.

Conclusions: These results suggest that, whereas adults with autism do not have obvious difficulty with pronominal expressions, their mental processing may be atypical, probably associated with difficulty with perspective-taking.

Poster Presentations Program

155 Neuropathology Posters

33 155.1 Brain Derived Neurotrophic Factor (BDNF) in Children with PDDs and their Parents. K. Francis*[1], A. Dougali[1], K. Dimas[1], K. Sideri[1], A. Nikolaou[2] and E. Lykouras[1], (1)*Athens University*, (2)*Penteli General Hospital for Children*

Background: Brain Derived Neurotrophic Factor (BDNF) is a protein widely expressed in the developing brain which is known to regulate neuronal cell survival, differentiation, and plasticity. BDNF has been implicated in the study of Autism among other various disorders, such as Depression and Schizophrenia. Albeit some contradictory findings in various age groups, a BDNF excess theory has been put forward.

Objectives: In the present study we intend to compare BDNF concentration in the serum both of children with PDDs aged 30-42 months and their parents with that in normal controls.

Methods: The diagnosis of the children is based on ADI-R and ADOS-G. Subjects were selected if they were of normal intelligence by the use of Leiter-R and they had no history or signs of any birth complications, seizures or a known cause of Autism such as Fragile-X or Tuberous Sclerosis. Since BDNF concentrations are altered in the presence of atopy, total IgE is also measured and skin prick tests are carried out for 10 common allergens. Parents are assessed for depression symptoms using the Beck Depression Inventory and for feautures of the Broader Autism Phenotype using the Broader Phenotype Autism Symptom Scale (BPASS). The presence of any chronic disorder, apart from Depression, or the current use of medications represents an exclusion criterion. Controls are matched for age and sex children in preparation for an orthopedic surgery and age and sex matched adult blood taken from a blood bank, with a total IgE less than 120 kU/m.

Results: The findings of the first 25 families will be presented.

Conclusions: To be discussed at IMFAR 2008 conference.

34 155.2 Can serotonin brain changes in Down syndrome provide insights into the etiology of Autism?. E. Azmitia*[1], Y. Rodriguez[1], X. P. Hou[1], P. Whitaker-Azmitia[2] and J. Wegiel[1], (1)*New York University*, (2)*State University of New York*

Background: Serum serotonin levels in children are increased in Autism but decreased in Down syndrome. Serotonin functions as a developmental trophic factor in the mammalian brain with high levels promoting accelerated maturation and low levels resulting in delayed maturation. The sizes of neurons in the brains of autism children are smaller, but the sizes in Down syndrome are larger.

Objectives: Following the serotonin axons in the postmortem brains of Down syndrome adults compared to undiagnosed controls may provide insights into how peripheral serotonin levels may impact the CNS serotonin system.

Methods: Brains from DS (28-61 yrs) and control (33-61 yrs) were obtained from IBR using the Hemispheric PEG protocol. The brains were fixed in 10% formalin for at least 30 days. Slabs through the temporal gyrus were dehydrated in ethyl alcohol and embedded with Polyethylene glycol. Serial 50-um-thick sections are cut and stored in 70% ethyl alcohol. Serotonin axons were visualized using an Anti 5-HT-transporter Rabbit Polyclonal Antibody.

Results: In control brains, 5-HTT-immunoreactive axons were seen in all brain regions examined. Highest levels occurred in hippocampus, entorhinal cortex and in layers III-IV of neocortex. Fibers were seen in fornix, white matter and perforant path. In the DS brains, an increased 5-HTT-IR expression was seen at all ages. The serotonin axons showed enlarged varicosities and clear evidence of pathology. Large dense aggregates began to form by age 28 and continued to increase in size with age. 5-HTT-IR aggregates formed pathological zones identified in surface plots. Neuronal sizes in layer III neurons showed increase in DS brains.

Conclusions: Lower serotonin serum levels are associated with larger neurons and increased serotonin aggregates in DS. Since serotonin serum levels are high in Autism, and neurons are smaller, we expect that serotonin innervation will be reduced in brains from autism patients. Funded by Autism Speaks

35 155.3 Embedded Figures Performance in the Broader Autism Phenotype. E. Grinter*[1], M. Maybery[1], D. Badcock[1], E. Pelliano[2] and J. Badcock[3], (1)*University of Western Australia*, (2)*University of Bristol*, (3)*Centre for Clinical Research in Neuropsychiatry/Graylands Hospital*

Background: Individuals with autism demonstrate superior capabilities on the Block Design subscale of the Wechsler Intelligence Scales and on the Embedded Figures Test (EFT). Recent research has demonstrated that these abilities extend to individuals in the general population who self-report autistic-like traits using the Autism Spectrum Quotient (AQ). **Objectives:** The current research examined visual processing in such individuals with the broader autism phenotype in an attempt to determine whether reduced global processing in the ventral stream can explain enhanced performance on visuospatial cognitive tasks such as the EFT. **Methods:** In conjunction with the EFT, psychophysical tests of local and global visual functioning in the ventral stream were administered. A pulsed-pedestal task was used to investigate parvocellular functioning at the V1 level, and a Glass pattern task was used to assess global processing ability in V4. **Results:** We found that people who scored high on the AQ were faster at identifying simple shapes within a complex figure, poorer at global form processing, but no different from those who scored low on the AQ on the pulsed-pedestal task assessing lower-level input to the ventral stream. In addition, higher Glass pattern thresholds were correlated with faster EFT responses. **Conclusions:** The results indicated that individuals with the broader autism phenotype experience difficulties with global integration of visual information in the visual form pathway. Results are discussed with reference to the notion of an 'autism spectrum' and the Weak Central Coherence theory of autism.

36 155.4 Saccadic Adaptation in Autism. A. M. D'Cruz*[1], C. V. Nowinski[1], M. Kay[1], A. Seidenfeld[1], L. H. Rubin[1], M. W. Mosconi[1], C. Scudder[2], B. Luna[3], N. J. Minshew[3] and J. A. Sweeney[1], (1)*University of Illinois at Chicago*, (2)*University of Oregon*, (3)*University of Pittsburgh School of Medicine*

Background: Post-mortem and structural MRI studies have identified cerebellar alterations in autism. Functional impairments associated with these alterations have not been identified. Saccadic adaptation occurs when the oculomotor system adjusts for systematic errors in the accuracy of saccadic eye movements. This process is heavily dependent on cerebellar networks, in particular the vermis. Thus, studies of saccadic adaptation may be useful for assessing the functional integrity of the cerebellum in autism.

Objectives: To examine saccadic adaptation in individuals with autism.

Methods: Fifty-six individuals with autism and 53 age- and IQ-matched healthy controls performed an intrasaccadic target step task known to elicit saccadic adaptation. In this task, targets are displaced to a new location during saccades, and subjects learn to make saccades to where the target will be displaced rather than to the location of the target that elicited the saccade.

Results: Participants in both groups demonstrated similar rates of saccade adaptation over trials. However, individuals with autism showed a pronounced lateral asymmetry of saccade adaptation. During adaptation, the autism group's saccades were hypometric to the left hemifield (e.g., closer to displaced target) but hypermetric to the right hemifield. Healthy controls did not show this hemifield difference. Additionally, individuals with autism exhibited greater variability in saccade accuracy across trials, indicating failure of the variability-reducing function of the vermis in saccade control.

Conclusions: The alterations in adaptational processes in our autism subjects are similar to those seen in human and animal studies of chronic unilateral cerebellar vermal lesions, and thus indicate a lateralized disturbance of vermal function in autism. Data are consistent with a previous report from our lab (Takarae et al., 2004) suggesting lateralized dysfunction of visual sensorimotor brain systems in autism.

37 155.5 INHIBITION OF SYNAPSE FORMATION BY PCB METABOLITES ACCUMULATED IN THE HUMAN BRAIN; A POSSIBLE ENVIRONMENTAL CAUSE OF AUTISM SPECTRUM DISORDER. Y. Kuroda* and J. Kimura-Kuroda, *Tokyo Metropolitan Institute for Neuroscience*

Background: Deficits of function in autism spectrum disorder are explained by abnormal neural connectivity as a consequence of alternations in synapse formation during development. Thyroid hormones (THs) are essential for functional brain development through TH-dependent gene expressions which are disrupted by polychlorinated biphenyls (PCBs) at pM order concentrations (Miyazaki et al.J.B.C.279:18195,2004). PCBs and their metabolites hydroxy-PCBs (OH-PCBs), which have similar chemical structure to THs, have accumulated in almost all human blood examined, even in their brain by global environmental contamination. 4- OH-PCB 187 is found as the major OH-PCB in human cerebrospinal fluid (Takasuga et al.Org.Halogen Comp.66:2529,2004). These toxic chemicals pass easily through placenta to fetal brain where the blood-brain barrier has not yet developed. We reported two other OH-PCB congeners inhibited TH-dependent dendrite arborization of Purkinje cells in culture (Kimura-Kuroda et al.Dev.Brain Res.154:259,2005). Monkey experiments showed maternal PCBs exposure caused some difficulties in the development of social communications of their offspring (Nakagami et al., 2007). Objectives: Effects of OH-PCB congeners on synapse formation and dendrite extension were investigated using cultured Purkinje cells of fetal mice. Methods: Dissociated cerebellar culture was prepared as previously described (Kimura-Kuroda et al.,Dev.Brain Res.137:55,2002).After OH-PCB treatments, Purkinje cells and synapses were immunostained , observed by confocal laser microscope and quantified using CCD - MetaMorph imaging system. Results: Addition of 4-OH-PCB 187 significantly inhibited synapse formation on Purkinje cells at pM order concentrations. 4-OH-PCB 187 also caused abnormal dendrite extension in the Purkinje cells. Conclusions: These data further support the hypothesis that interaction with genetic backgrounds, PCBs (and probably other neurotoxic chemicals) contaminated in perinatal brain cause abnormal synaptic connections during development, result in heterogeneous symptoms of autism spectrum disorders and/or other comorbid disorders like LD, ADHD, depending on spatio-temporal difference in sensitive synaptogenesis and in chemical exposure doses (Kuroda, Environ. Sci.,10:23,2003).

38 155.6 Quantitative assessments of neuroadaptation in autism. M. Tommerdahl*, V. Tannan, J. K. Holden, Z. Zhang and G. Baranek, *University of North Carolina*

Background:

Adults with autism exhibit inhibitory deficits that are often manifested in behavioral excesses, such as repetitive behaviors, and/or sensory hyper-responsiveness. If such behaviors are the result of a generalized deficiency in inhibitory neurotransmission, then it stands to reason that deficits involving localized cortical-cortical interactions – such as in sensory discrimination tasks – could be detected and quantified

Objectives:

This study exemplifies newly developed methods for quantifying sensory testing metrics. Our novel sensory discrimination tests may provide (a) an effective means for biobehavioral assessment of deficits specific to autism and (b) efficient and sensitive measures of change following treatment.

Methods:

The sensory discriminative capacity of 10 subjects with autism and 10 controls was compared both before and after short duration conditioning stimuli and in the presence/absence of synchronizing stimuli. Specifically, vibrotactile amplitude discriminative capacity was obtained both in the presence and absence of 1 sec conditioning stimuli that were delivered 1 sec prior to the comparison stimuli. Additionally, temporal order judgment was obtained in the presence and absence of synchronizing tactile stimuli.

Results:

Although conditioning stimuli had a pronounced effect on the amplitude discriminative capacity of the control subjects, the conditioning stimuli had little or no impact on the sensory discriminative capacity of the subjects with autism. Similarly, while synchronizing stimuli had a significant effect on sensory perception in the control subjects, it had little impact on the sensory percepts of individuals with autism.

Conclusions:

The lack of impact of the conditioning stimuli on the responses of the subjects with autism was interpreted to be consistent with the reduced GABAergic mediated inhibition described in previous reports. One significant aspect of this study is that the methods could prove to be a useful and efficient way to detect specific neural deficits in autism and perhaps monitor the efficacy of pharmacological or behavioral treatments.

39 155.7 DECREASED GABA-B RECEPTOR DENSITY IN THE ANTERIOR AND POSTERIOR CINGULATE CORTICES IN AUTISM.

A. Oblak*, T. Gibbs, M. Bauman, T. Kemper and G. Blatt, *Boston University School of Medicine*

Background: Neuropathology and genetic studies have implicated abnormalities in GABA as a potential substrate for autistic behavior. Prior autoradiographic studies have demonstrated widespread, significant changes in $GABA_A$ receptors. Comparable studies on $GABA_B$ receptors are lacking in the autistic brain. $GABA_B$ receptors are normally distributed throughout the brain both pre- and postsynaptically. Presynaptic $GABA_B$ receptors suppress neurotransmitter release by inhibiting calcium channels. These receptors have been detected at extrasynaptic sites and occasionally at glutamatergic or GABAergic terminals. Postsynaptically, the receptors are found on dendritic shafts and spines of cortical pyramidal neurons and interneurons, respectively. The cingulate cortex has been implicated in mediating socio-emotional behavior, a core deficit in autism.

Objectives: To determine the density and laminar distribution of $GABA_B$ receptors in the anterior (ACC) and posterior cingulate (PCC) cortices in adult autistic and control cases.

Methods: Radioligand binding experiments were completed in the ACC and PCC for $GABA_B$ receptors using ^{3}H-CGP54626 in adult autistic (ACC, n=7; PCC, n=6) and control (ACC, n= 9; PCC, n=7) brains controlled for age and post-mortem interval. Optical densities were measured in the superficial (I-III) and deep (V-VI) layers using the Inquiry program. Student t-tests were used to compare the layers by group.

Results: Overall, there was a significant reduction in the density of $GABA_B$ receptors in

the autistic brains in the ACC (p=0.2) and PCC (p=0.008). Specifically, a significant reduction in the density of $GABA_B$ receptors was found in the superficial layers of the ACC (p=0.001) and PCC (p=0.007) without significant difference in the deep layers of either the ACC or PCC.

Conclusions: Decreased density in $GABA_B$ receptors provides additional quantitative evidence for the involvement of the GABA system in the neuropathology of the ACC and PCC in autism and may in part underlie some of the social-emotional behavioral alterations observed in this disorder.

40 155.8 DECREASED mGLUR1 RECEPTORS IN THE DENTATE NUCLEUS AND AMPA RECEPTORS IN THE POSTEROLATERAL CEREBELLAR CORTEX IN AUTISM. G. Blatt*, S. Thevarkunnel and T. Gibbs, *Boston University School of Medicine*

Background: Purkinje cells in the lateral hemisphere of the cerebellum send robust projections to the dentate nuclei that in turn project to the cerebral cortex. There is strong emerging evidence that this pathway modulates cognitive activity in the cortex and, that the lateral hemisphere sustains a significant decrease in Purkinje cells in many cases of autism. Inputs to the cerebellar cortex are largely glutamatergic and the preservation of the balance of key GABA and glutamate receptor subtypes is critical to the normal functioning of the cerebellum.

Objectives: To determine the density and distribution of AMPAR, NMDAR, and mGluR1 receptors in the posterolateral cerebellar cortex and dentate nucleus in adult autistic and control cases.

Methods: Radioligand binding experiments were performed in the posterolateral cerebellar cortex (granule cell, Purkinje cell and molecular layers) and dentate nucleus using ^{3}H-AMPA for AMPAR, ^{3}H-MK-801 for NMDAR and ^{3}H-quisqualate for mGluR1 in adult autistic and normal cases. Optical densities were measured and student t-tests were used to compare density by layer and group.

Results: In the autism group, ^{3}H-AMPA binding was significantly decreased in the granule cell layer (p = 0.4), there was a trend for a decrease in the molecular layer (p = 0.7), and ^{3}H-quisqualate binding was significantly reduced in the dentate (p = 0.3). All other measures were in the normal range including ^{3}H-MK-801 in both areas.

Conclusions: In autism cases, decreased binding of AMPA in the granule cell layer suggests an alteration in afferents from precerebellar nuclei and/or altered glutamate release from mossy fiber terminals at the glomeruli. The trend for a decrease in the molecular layer suggests that the parallel fiber input to the remaining Purkinje cells may also be affected. Decreased mGluR1 binding in the dentate in autism cases may reflect alterations in mossy fiber/climbing fiber collaterals.

41 155.9 Detection of leading developmental defects in brains of autistic subjects. J. Wegiel*[1], E. London[2], I. L. Cohen[1], M. Flory[1], T. Wisniewski[1], H. Imaki[1], I. Kuchna[1], J. Wegiel[1], S. Y. Ma[1], K. Nowicki[1], K. C. Wang[1] and W. T. Brown[1], (1)*New York State Institute for Basic Research in Developmental Disabilities*, (2)*NYS Insitute for Basic Research in Developmental Disabilities*

Background: In autism, a plethora of genetic and non-genetic factors can result in different patterns of neuropathological structural equivalents. A majority of these structural modifications are detectable only with stereological methods. We hypothesized that reduced volumes of the neuronal body and nucleus are the most consistent markers of developmental pathology detectable in autism.

Objectives: This project focuses on establishing protocols for detection of markers of developmental abnormalities of the neuron, neuronal networks within brain structures, and neuronal circuits integrating brain structures in morpho-functional units.

Methods: We examined brains of 14 subjects with autism and 14 controls by using routine neuropathological methods, electron microscopy, and morphometry.

Results: We observed a broad spectrum of neuropathological changes. However, the most consistent was reduced size of neurons. In 4-7 year old autistic children, Purkinje cells were smaller by 38%. Neurons in the dentate nucleus were reduced by 26%; in amygdala by 24%; in nucleus accumbens by 41%; in caudate by 20%; and in putamen by 27%. Neurons in the nucleus of the facial nerve and nucleus olivaris did not show a significant difference from controls. In many brain subdivisions, a partial or complete correction of the size of neurons was observed in late childhood or adulthood.

Conclusions: We found evidence of disproportional development of the cell nucleus and cell body, and dramatic delay of growth of both neurons and neuronal networks. The increase of neuronal volume observed in late childhood may contribute to behavioral improvement in some patients. This study will help to identify the potential target of treatment for developmental deficits in autism.

The Harvard Brain Tissue Resource Center (R24-MH 068855), and Brain and Tissue Bank at the University of Maryland, Baltimore provided tissue. Autism Tissue Program coordinated tissue acquisition.

42 155.10 Neuropathologic changes in subjects with chromosome 15 duplication and autism. W. T. Brown*[1], T. Wisniewski[1], I. L. Cohen[2], E. London[2], M. Flory[1], H. Imaki[1], I. Kuchna[1], J. Wegiel[1], S. Y. Ma[1], K. Nowicki[1], K. C. Wang[1] and J. Wegiel[1], (1)*New York State Institute for Basic Research in Developmental Disabilities*, (2)*NYS Institute for Basic Research in Developmental Disabilities*

Background: Duplications of the proximal long arm of chromosome 15 cause autistic features, mental retardation, seizures, functional deterioration with age and increased risk of sudden death. The pattern of neuropathological changes caused by this genetic defect is not known.

Objectives: Detection of (a) developmental changes contributing to mental retardation, (b) markers of neuronal degeneration contributing to clinical deterioration, and (c) pathology contributing to sudden death.

Methods: Brains of four subjects (11, 15, 20, and 25 yrs) with chromosome 15 duplications, and four age-matched controls were examined by light and electron microscopy.

Results: The most consistent findings were a reduced size of the brain, and reduced volume of neurons and neuronal nuclei in the amygdala, accumbens, entorhinal cortex and Purkinje cells, indicating a delay in neuronal development. Microdysgenesis in the hippocampus represented by hyperconvolution and duplication of the granule cell layer in the dentate gyrus observed in two subjects may have contributed to seizures and sudden death. Enhanced accumulation of amyloid beta protein in phagosomes/dense bodies in all four subjects was a marker of modified APP processing, trafficking and deposition. Amyloid beta positive inclusions in dendrites in the CA1 sector were another marker of neuronal deterioration. Osmophilic inclusions in the mitochondrial matrix suggested mitochondrial degeneration. Chaslin's gliosis observed in one subject may reflect epilepsy-related brain damage.

Conclusions: In subjects with chromosome 15 duplications, reduced size of the brain and delayed growth of neurons appear to be the main contributors to developmental deficits, whereas behavioral worsening could be the result of early neurodegeneration. Sponsors: Autism Speaks and the NYS Office of Mental Retardation and Developmental Disabilities. The Harvard Brain Tissue Resource Center (R24-MH 068855), and Brain and Tissue Bank at the University of Maryland, Baltimore provided tissue. Autism Tissue Program coordinated tissue acquisition.

43 155.11 Complement activation in brain of patients with autism. D. Vargas*[1], A. W. Zimmerman[2] and C. A. Pardo[3], (1)*Johns Hopkins University School of Medicine*, (2)*Kennedy Krieger Institute*, (3)*Jonhs Hopkins University School of Medicine*

Background:

Activation of the complement system is an important component of immune responses during inflammation. Complement activation is also involved in critical neurodevelopmental processes including synaptic elimination (Stevens et. al., Cell 2007). The presence of activation of neuroimmune pathways in brain tissues of patients with autism suggests complement activation may play pathogenic roles in autism.

Objectives: To determine whether complement activation is part of the immune mechanisms associated with neuropathological changes in autism

Methods: Immunopathological studies were performed in brain tissues from 11 patients previously diagnosed with autism and age-matched controls obtained from the Autism Tissue Project. Frontal, anterior cingulated and cerebellum tissue samples were used for immunostaining with specific antibodies that recognize proteins of the complement system including a membrane complex attack marker (C9neo). Co-localization studies with neuronal and neuroglial markers were also used to establish the localization and pattern of immunostaining.

Results: Immunoreactivity for the membrane complex attack (C9neo) was noted in 4 of 11 samples from cerebellum of patients with autism. Immunostaining with C9 neo was seen predominantly in neurons of the Purkinje cell layer and perineuronal compartment. Immunostaining appeared to be localized in Purkinje neurons and microglia processes within the perineuronal compartment. Other proteins associated with complement such as C1q was noted but the magnitude and patterns of staining was variable.

Conclusions: Activation of the complement system occurs in a subset of patients with autism and the pattern of distribution coincides with the involvement of cerebellum, an area of the brain affected in patients with autism as shown by neuropathological and neuroimaging studies. The presence of complement activation may be associated with pathogenic processes leading to neuronal degeneration and neuroinflammation.

44 155.12 Intraventricular Infusions of Propionic and Butyric Acid Induce Behavioural, Neuropathological and Gene Expression Changes in Rats- Possible Relevance to Autism Spectrum Disorders. B. B. Nankova[1], L. J. Tichenoff[2], A. R. Taylor[2], Y. Mohammad-Asef[2], E. F. LaGamma[1] and D. F. MacFabe*[2], (1)*New York Medical College/Westchester Medical Centre, Valhalla NY, USA*, (2)*University of Western Ontario*

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 a possible environmental trigger 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 individually placed into an automated open field (Versamax) and a variety of locomotor 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. Both SCFA produced increased innate neuroinflammation(GFAP,IL-6) but only PPA produced activated microglia (CD68, IbA1). The alignment of gene content identified sets of genes unique for BA (274) and PPA (309).

Comparison analyses of RNA identified a large number of genes (769) common for both groups, involved in canonical pathways/processes including cell development and differentiation, cytoskeleton organization and biogenesis, cell adhesion, inflammatory response, synaptic plasticity, cell-cell communication, neuroprotection and glutathione metabolism.
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.

45 155.13 Abnormalities in cholesterol, ceramides and markers of oxidative stress are revealed by lipidomic analysis of brain tissues in autism. C. A. Pardo*[1], D. Wheeler[2], D. Vargas[3], N. Haughey[3] and A. W. Zimmerman[4], (1)*Jonhs Hopkins University School of Medicine*, (2)*Medical Scientist Training Program, University of Pittsburgh School of Medicine*, (3)*Johns Hopkins University School of Medicine*, (4)*Kennedy Krieger Institute*

Background:
Neuropathological and imaging studies in autism have shown abnormalities in neuronal-cortical organization as well as neuroinflammation. Because lipidomic analysis of tissues may provide evidence of abnormalities in lipid composition as well as oxidative stress as result of structural and neuroimmune reactions.
Objectives:
To determine the presence of abnormal patterns of lipid composition and oxidative stress in brain tissues obtained from patients with autism as compared with neurologically normal controls.
Methods:
Global lipid levels were obtained using a Sciex API 3,000 triple stage quadrupole tandem mass spectrometer (ESI/MS/MS) from fresh frozen brain tissues in patients with autism and controls obtained from the Autism Tissue Project. Brain samples from the frontal and occipital lobes (cerebral cortex, subcortical white matter, deep white matter) and cerebellum (folia and deep white matter) were available from 7 patients with autism and age-matched controls (n=9).
Results:
When brain sections of autistic patients were directly compared with normal controls the most significant changes were seen in the deep white matter of the frontal lobe. In this brain region, several species of ceramides (C16:0, C18:0 and C22:0), 4-hydroxynonenal (lysine and histidine), Vitamin E, and cholesterol (monomer and dimmer) were found to be elevated in autistic patients compared to controls. Interestingly, analysis of brain regions when we eliminated interpatient variation by using the occipital lobe of patients with autism as an internal control uncovered subtler changes in lipid levels such as a frontal lobe increases in cholesterol esters (palmatate and linoleate) within the deep white matter and increases of short chain sphingomyelin species (C18, C20, C22) in the cortex.
Conclusions:
Brain lipid alterations in autism may allude to three pathogenic mechanisms 1) increase oxidative stress and physiological compensation 2) deregulation of sterol metabolism and 3)possible alteration in packing density within the frontal lobe.

46 155.14 Computational Models of Dopamine Dysfunction in Autism Spectrum Disorders. T. Kriete* and D. C. Noelle, *University of California Merced*

Background: Despite the diverse behavioral and neurobiological profile exhibited by individuals with autism, dopamine, a neurochemical with widespread influence throughout cortex, is conjectured to play a central role in many aspects of the autism phenotype. Abnormal neurogenesis, increased seizure prevalence, motor problems, stereotypies, and difficulties learning to follow eye gaze are all associated with autism, and, importantly, are also influenced by dopamine. Initial computational modeling results demonstrate how dopamine dysfunction may explain aspects of executive dysfunction, overselectivity, and weak central coherence (WCC). In these models, the prefrontal cortex (PFC) supports top down attentional modulation based on current goals and task constraints. Dopamine interacts with the PFC supporting both a mechanism capable of

toggling maintenance currents within the PFC, effectively switching the attentional target, and a teaching signal allowing the system to learn the proper timing of attentional updating. Dopamine dysfunction is postulated to result in overly perseverative attention, leading to excessively restricted access to parts of an object or situation, possibly accounting for many behavioral aspects of the disorder.
Objectives: To demonstrate the viability of viewing dopamine dysfunction as central to the disorder, unifying many formally disparate areas of theorizing in autism.
Methods: Computational models, inspired and constrained by actual neuroscientific findings, are employed to investigate aspects of overselectivity, executive dysfunction, and WCC. Each model was manipulated to investigate our hypothesis of overly perseverative top-down attentional influence of the PFC, driven by perturbed dopamine / PFC interactions, on behavior.
Results: Initial modeling results capture performance of both people with autism and controls on tasks of overselectivity, executive functioning, and WCC.
Conclusions: Dopamine's widespread influence and strong ties to the autism phenotype make it an intriguing candidate for a neural underpinning of autism. Our initial modeling results provide additional support, warranting further investigation into dopamine's role in autistic behavior.

Poster Presentations Program

156 Cognition Posters 3

47 156.1 The Framework for Disturbed Affective Consciousness in Autism. N. Khetrapal*, *University of Allahabad*

Background:The current article explores the implication of the interaction of emotion and consciousness for autism.

Objectives:The framework that is proposed for the disorder explains that the compromised functional integrity of the amygdala is the root cause of disturbed
affective consciousness.
Methods:Various papers on consciousness, attention, emotions and autism were reviewed to develop the theoretical framework.

Results: Amygdala with its connections to various cortical and subcortical problems helps bring a detected fearful facial expression at the attentional periphery to the focus of attention and awareness for enhanced processing.
Conclusions:The conscious life of autistics with respect to affective objects can thus be very different from that of
normal people leading them to perceive the world differently. They process fearful stimuli the way normal controls perceive common objects by activating areas responsible for feature based analysis rather than the amygdala and other connected areas. Conscious perception of such stimuli is important for appropriate development of emotion concepts,
something that the autistics lack thus leading to impairment in the awareness of one's own emotions especially within the negative spectrum with a prominent position for fearful stimuli. Thus the interaction of emotion with consciousness is ripe for investigation and can help to throw light on the mental life of autistics.

48 156.2 Implicit Sequence Learning in Persons with ASD. B. G. Travers*, M. Klinger, L. Klinger and J. Mussey, *University of Alabama*

Background:

Recent studies have found impairments in implicit concept learning in persons with autism spectrum disorder (ASD). However, it is unclear whether persons with ASD also show impairments in implicit motor learning. The serial reaction time (SRT) task is the most common measure of implicit motor learning. Previous research with the SRT in persons with ASD has yielded contradictory findings. One study showed implicit motor learning impairments (Mostofsky et al., 2000), but two studies did not show impairments (Gordon & Stark, 2007; Müller et al., 2000).

Objectives:

The present study sought to test whether persons with ASD show impairments in the

SRT task. This study aimed to decrease the role of explicit learning processes in the SRT task so that it more strongly tapped implicit learning processes.

Methods:
Fourteen high-functioning adolescents and young adults with ASD and 15 age and verbal-ability matched controls completed a SRT task. Participants responded with a keypress indicating the location of a racecar on the computer. Unknown to participants, the location of the racecar followed a repeating 12-step sequence. Participants completed four blocks of 120 sequenced trials followed by a block of 120 random location trials and another sequenced block.

Results:

For this task, learning is seen as the difference in reaction time to the final blocks of sequenced trials compared to the block of random trials. Both groups of participants responded faster to the sequenced trials than the random trials (control group difference=+35.3ms; ASD difference=+43.24ms). Differences between groups were not significant.

Conclusions:

It appears that persons with ASD demonstrated implicit motor learning equivalent to a matched control group. This result suggests that not all implicit learning is impaired in persons with ASD. Differences may exist between implicit learning of concepts and motor actions.

49 156.3 AUTISM AND MORAL REASONING. J. Lawson*, *Oxford Brookes University*

Background: Autism research on the cognitive level has been dominated by three main models: Executive Dysfunction, Central Coherence and Theory of Mind/Empathising-Systemising. However, none of these models seem able to fully explain all of the behavioural features of the condition. More recently a theory has been developed to address this problem and move towards a synthesis of the main models by drawing on a distinction made within philosophy between *open* and *closed* systems.

Objectives: This new theory posits that a) biases towards open and closed systems can be used to conceptualise autism b) such biases exist in the general population c) these biases shape general cognition. To examine these ideas a new test was designed, the Moral Orientation Questionnaire (MOQ), to focus on one specific area of cognition; moral reasoning. The test comprised twenty moral dilemmas. Each was accompanied by a choice of two courses of action – one based on open system reasoning and one on closed. The test also featured two kinds of dilemma: a) the participant was the key character in the dilemma and b) a third party was the key character in the dilemma.

Methods: The MOQ was applied to three groups: males with Asperger syndrome (n25); males without Asperger syndrome (n49), and females without Asperger syndrome (n46). Total open system and closed system choices were calculated for each participant and group averages were compared.

Results: Significant differences were found between all three groups. These are discussed in terms of the current theory, the extreme male brain theory and the previous three cognitive models. Implications regarding general moral reasoning are raised.

Conclusions: The distinction between open and closed systems seems to be useful in conceptualising not only the autism spectrum but also cognitive sex differences in the general population.

50 156.4 Value of Draw-A-Person test as a fast screening of intelligence in autistic children. N. E. Granana*, E. B. Fernandez, M. M. Gimenez and R. F. Allegri, *Hospital Zubizarreta*

Background: Children with Pervasive Developmental Disorders (PDD) may be difficult to evaluate with an intelligence quotient (IQ). It would be useful a fast tool to make a screening of cognitive development at first interview,
Objectives: We analyzed the correlation between Draw-A-Person test (DAP) and

Wechsler Scales on the determination of IQ in a population of 50 children and adolescents with PDD,
Methods: we evaluated 50 patients between 3.11 and 13 years of age, determining IQ with Goodenough`s DAP test and Wechsler scales (WPPSI and WISC) . We established the correlation between both tests and also Vineland ç and Visuomotor integration tests to compare with adaptative and visuoconstructive quotients,
Results: we found out a significant correlation with a $p<0.001$ between IQ from Wechsler and DAP tests. There was no significant correlation with Vineland adaptative quotient nor visuomotor integration quotient,
Conclusions: DAP test let us predict the IQ from children with PDD. It may be used as a fast screening at the first consultation of patients with PDD.

51 156.5 SOCIAL COGNITIVE CORRELATES OF PROSOCIAL BEHAVIOR IN YOUNG CHILDREN WITH AND WITHOUT ASD. L. J. OConnell*[1], K. A. Dunfield[1], V. Reindhardt[1], L. Goodman[2], E. Kelley[2] and V. Kuhlmeier[1], (1)*Queens University*, (2)*Queen's University*

Background: Recent research has identified a positive relationship between early social-cognitive skills (e.g., joint-attention (JA), imitation, intentional understanding) and the production of cooperative behavior in children with autism (Colombi et al., 2006). Delays in social-cognitive skills in children with autism spectrum disorders (ASD) are well documented, leaving these individuals at a potential disadvantage at developing a wider range of prosocial behaviors that extend beyond cooperation. This study seeks to explore the relationship between the development of early social-cognitive skills and several prosocial behaviors in both children with ASD and typically developing (TD) children.

Objectives: The current study seeks to extend previous findings by 1) exploring the relationship between social-cognitive skills and a broader range of prosocial behaviors and 2) examining this relationship in *both* TD children and children with ASD.

Methods: Children with ASD (N=15, mental age of at least 12 months) TD children (N=15, 18- to -24 months old) were examined. Participants engaged in a play-based activity designed to examine: their ability to initiate JA as well as to imitate bodily movements/expressions and actions on objects, their intentional understanding, and their engagement in several prosocial behaviours (e.g., helping, sharing, and comforting). Children's developmental level was assessed using the *Mullen Scales of Early Learning* and diagnosis of an ASD was confirmed with the *ADOS.*

Results: Presently, data collection is nearing completion. We anticipate that children with ASD will be delayed on all measures as compared to TD children. We also expect that both groups' JA, imitation, and intentional understanding skills will be correlated with their tendency to display prosocial behaviours.

Conclusions: Charting the developmental course of social cognitive difficulties and their relationship with the acquisition of prosocial skills in the ASD population will facilitate effective early interventions and education programs.

52 156.6 Inferior Performance on Embedded Figures Tasks by High Functioning Children and Adults with Autism Consistent with Reduced Local Connectivity & Slower Search Strategy. N. J. Minshew*[1], D. L. Williams[2], H. Z. Gastgeb[3] and K. E. Bodner[3], (1)*University of Pittsburgh School of Medicine*, (2)*Duquesne University*, (3)*University of Pittsburgh*

Background: Enhanced local processing is considered a characteristic feature of autism and has been associated with superior performance on embedded figures tests. Some recent studies of higher functioning children have not documented this superiority.

Objectives: To assess the impact of age and higher IQ on Embedded Figures performance in autism

Methods: The child groups (ages 8-15 years) consisted of 65 children with HFA (mean age 11.8) and 43 age and IQ-matched typical controls (mean age 11.6). The adult groups included 45 with HFA (16-49 years; mean 23.4) and 53 age and IQ-matched normal controls (16-54 years; mean age 23.8). The child HFA group had a mean Verbal IQ of 102.9 (range 82-129), mean Performance IQ 109.1 (range 87-139); the controls mean VIQ was 106.3 (range 84-125), mean PIQ 107.7 (range 88-129). Mean VIQ of the HFA adults was 104.4 (range 83-133); mean PIQ was 105.5 (range 75-132). Mean VIQ of the adult controls was 107.5 (range 84-126); mean PIQ was 109.0 (range 91-127). The age-appropriate version of the Embedded Figures Test (EFT) was administered using standard procedures.

Results: The mean number correct score for the HFA children (7.1) was marginally lower than that of controls (8.3), p = .6; the difference in mean scores and response times was reliably different when PIQ was covaried with slower responses for the HFA child group. The mean number correct score for the HFA adults (8.4) was reliably lower than that of the controls (10.2), p = .002; response time was also reliably greater for the HFA adults.

Conclusions: HFA children exhibited no superiority on CEFT and a trend toward taking longer to make fewer correct responses. HFA adults were inferior to peers on the Embedded Figures Test, taking longer and making fewer correct responses.

53 156.7 Overly Focused Attention in Adults with Autism. I. E. Drmic*[1], S. E. Bryson[2] and R. M. Klein[3], (1)*Hospital for Sick Children*, (2)*IWK Health Centre*, (3)*Dalhousie University*

Background: Evidence suggests that the attentional spotlight is overly narrow in autism (e.g., Townsend & Courchesne, 1994). However, it remains unclear whether the problem is strictly one of a narrow beam, or inflexibility in changing its size. Objectives: Examine size and flexibility of the attentional spotlight, and test for corroborating evidence of spatial inattention in autism spectrum disorder (ASD). Methods: High-functioning adults (n = 29) with autism/ASD and matched controls (n = 29) were compared on two tasks. Experiment 1: Size of the attentional spotlight was examined by determining whether individuals with ASD make same-different judgments more quickly and accurately when stimuli are presented closer in space versus farther apart. Switching the size of the attentional beam was assessed by examining the impact on performance of the distance between stimuli on the previous trial. Experiment 2: Spatial inattention/neglect was examined using the greyscales task. Participants were required to judge which of two left-right mirror-reversed brightness gradients was darker. Results: Experiment 1: In ASD, reaction times (RTs) were fastest when stimuli were close together (p's < .1), and this was even more evident when attention was narrowed in the previous trial (p's < .003). In addition, when attention was broadened in the previous trial and remained broad on the current trial, the ASD group made more errors (p = .004). In Controls, RTs and error rates did not differ across conditions. Experiment 2: The ASD group was biased more to the right side of space than controls (p < .5). Conclusions: Our findings implicate both overly narrow and inflexible attention in ASD: the beam appears to be set too "small", and, once narrowed, attention becomes overly focused, making it difficult to broaden the beam. Evidence suggests further that attention is overly focused to the right side of visual space in ASD.

54 156.8 Music based intervention in autism: a framework. S. Baijal and N. Khetrapal*, *University of Allahabad*

Background: Autism involves problems in communication and social interaction that results in impairments in linguistic abilities. Objectives: Although several music therapy interventions have been useful with these individuals, the mechanisms remain to be unclear. Methods: The present paper examines the effects of music therapy on autistics and the relationship between music and cognition. Results: A framework explaining processes underlying beneficial effects of music has been proposed that comprises of two components – mood-based effects and language-based effects. The positive mood induced by music

has been elucidated in several studies which has direct impact on automatic processes impaired in autism. Moreover, the mood effects of music also modulate the neurochemical functioning such as in the dopaminergic system which is dysfunctional in the disorder. Language-based effects of music have been investigated to observe similarities in the temporal dynamics of language and music as well as the general cognitive principles involved in syntactic processing of language and harmonic processing of music. This exemplifies the close correspondence between music and language. Neuroimaging techniques have allowed documentation of plastic changes due to learning from prolonged exposure to music. Conclusions: The behavioral plasticity observed with music-based interventions occurs due to the combined effects of efficient functioning of the automatic processes and language subsystems. Further systematic testing of these components is required to confirm and expand the preliminary proposed framework.

55 156.9 Dual Attention Abnormalities in Children with Autism. E. Obukhova*[1], T. A. Stroganova[2] and V. V. Grachev[3], (1)*Moscow State University of Psychology and Education*, (2)*Psychological Institute of the Russian Academy of Education*, (3)*Scientific Center of Mental Health of the Russian Academy of Medical Sciences*

Background: Although autism and attention deficit/hyperactivity disorder (ADHD) represent different nosological diagnoses they partly include similar symptoms like hyperactivity, impulsivity that are hypothetically linked to impairments in executive attention control. The specificity of the executive control disturbances in ADHD and higher functioning autism (HFA) is poorly understood.

Objectives: To determine the sort and degree of deficiency in executive attention profile in ADHD, HFA comparing to typically developing boys (TDB). Methods: 15 boys with HFA aged 6-7 years were compared with 15 IQ-matched TDB and 15 IQ-matched boys with ADHD. To delineate more specifically the efficiency of different executive attention operations (control of interference; dividing attention between visual and auditory sensory modalities; set-shifting) we have developed the child test of executive attention (TEA). Repeated measures ANOVA was used for analysis of reaction time, percentage accuracy and false alarms.

Results: Unlike the ADHD who demonstrated the specific difficulty in controlling attention under the tasks tapping control of interference, children with HFA performed worse than ADHD and TDB in all tasks requiring continuous visual attention with no particular deficit in executive attention tasks. This suggest the decreased efficiency of alerting system in autism, which is involved in maintaining readiness to react. The second feature of HFA, which strikingly differentiate them from both TDB and ADHD, was the abnormally poor reaction (in terms of RT and percent accuracy) to auditory target but not to visual target when they were presented in alternating fashion (dual attention task). Their reaction to isolated sound presentation did not differentiate them from two other groups.

Conclusions:Children with autism and ADHD showed different profile of attention impairment. The disturbed tonic alerting system and unresponsivness to sound due to attention switching abnormalities may be specific to autism and unrelated to deficits in frontal functions.

56 156.10 Peaks of ability as a subtyping tool for autism. L. Mottron*, I. Soulieres, A. A. Meilleur and M. Dawson, *Université de Montréal*

Background:The autistic spectrum is subtyped in DSM-IV by the presence or absence of certain signs (e.g. speech delay). However, DSM-IV fails in operationalizing the autism vs Asperger syndrome distinction (Szatmari, 2000). Differences in cognitive profile between Asperger syndrome and autism are reported (Ghaziuddin & Mountain-Kimchi, 2004), but not included in diagnostic criteria. Despite clinical recognition of contrasted phenotypes, autism and Asperger syndrome are considered as arbitrary segments within an autistic

spectrum continuum (Macintosh & Dyssanayake, 2004).

Objectives:The aim of the present study was to investigate how Wechsler intelligence scales subtest peaks can predict the presence or absence of DSM-IV phenotypic markers relevant for the autism vs. Asperger distinction.

Methods:Subjects were 250 participants ADI-R and ADOS-G positive for autism, from the Riviere-des-Prairies Hospital (Montreal) database. Participants without ADI-defined speech delay or atypicalities (echolalia, stereotyped language, pronoun reversal) were re-coded as Asperger. Participants with identified neurological or genetic syndromes (apart from idiopathic epilepsy) were excluded. Wechsler peaks were individually computed as a 1.5 SD difference between scaled scores and Wechsler full scale IQ baseline.

Results:Initial small sample results indicate the possibility of peaks which predict a "0" score for 5 ADI items (one word delay, two word delay, echolalia, stereotyped language, pronoun reversal) and peaks which predict scores higher than 1 at these ADI items. Results from a larger data set will be reported.

Conclusions: A combination of cognitive and behavioral dimensions may be a valid candidate for the subtyping of the autistic spectrum according to DSM-IV rules.

57 156.11 COGNITIVE PROFILES IN THE AUTISTIC CHILDREN. A. M. Girardot*, *HOPITAL SAINTE MARGUERITE MARSEILLE*

Background:

Researches on the cognitive profiles of the children with autism demonstrated superior skills in the field of the spatial abstraction and of the reasoning by visual analogy (Mottron).

Objectives:

The purpose of our study is 1/ to observe the possible duplication of the results of Mottron while widening it to a younger population, 2/ to compare the cognitive skills at different ages, 3/ to discuss on the skills of the autistic children according to their age and their cognitive deficit. Methods:Two groups participated this study : Group 1 : from 3 to 6 years olded children/Group 2 : from 6 to 16 years olded children.
Each of these two groups is subdivided into two subgroups: a group with a global cognitive delay and a group without global cognitive delay. The cognitive skills were tested whith the WPPSI III and the WISC III, IV.

Results:

The first results confirm those of Mottron who demonstrates a peak of skill in cube only in from 6 to 16 years olded high-level autistic children.
On the other hand we observe in the younger autistic children a peak of skill in the task in puzzles but not in the task of the cubes.
This skill represents a peak of performance in the young autistic children with or without mental deficiency.

Conclusions:

These results demonstrate a specific cognitive profile in autism based on the spatial structuralization and the visual analysis.

58 156.12 THE ACCESSIBILITY OF SPECIFIC AND GENERAL AUTOBIOGRAPHICAL MEMORY (ABM) IN ADULTS WITH AUTISM SPECTRUM DISORDERS (ASD): THE ROLE OF GOAL PURSUIT. L. Crane*, L. Goddard and L. Pring, *Goldsmiths, University of London*

Background: ABM is stored hierarchically, at both general and specific levels of representation. Furthermore, it has been proposed that the self is the structure around which ABMs are organised (Conway & Pleydell-Pearce, 2000). Deficits in ABM retrieval have been consistently reported in ASD (Crane & Goddard, in press). Considering that ASD is associated with difficulty in processing self-referential information (Toichi et al., 2002), this may therefore be one factor underlying the memory difficulties in ASD.

Objectives: Research demonstrating an ABM deficit in ASD has focused on memories for specific events. Therefore, the first aim of this

study was to examine ABM in ASD at both general and specific levels of representation. The second aim was to examine whether the ABM difficulties in ASD relate to difficulties in using the self as an effective memory cue, focusing on the role of personal goals in memory retrieval.

Methods: 24 adults with ASD and 24 age, gender and IQ matched controls participated in this study. Participants identified a series of goals that they were currently pursuing, and then these goals (and a series of randomly selected non-goals) were used as memory cues in a specific event-memory task. A computer-based task was used to investigate access to general event memory.

Results: The ASD group took significantly longer to access both general and specific ABMs and retrieved fewer specific ABMs, relative to controls. However, contrary to predictions, the ASD and control groups displayed similar patterns of results regarding the use of personal goals as memory cues.

Conclusions: Difficulties in accessing ABMs were found for both general and specific memories in ASD. However the results also suggest that the ASD group were able to use the self to structure memory recall. These results are discussed with respect to theoretical models of ABM (e.g. Conway & Pleydell-Pearce, 2000).

59 156.13 Lower Levels of Prejudice in Adults with Autism Spectrum Conditions. J. Kirchner*[1], K. Schnabel[2], F. Schmitz[3], S. Preißler[1], I. Wolf[1], S. Schneider[1], H. R. Heekeren[1] and I. Dziobek[1], (1)*Max-Planck-Institute for Human Development*, (2)*Humboldt University of Berlin*, (3)*Albert-Ludwig University of Freiburg*

Background: Autism spectrum conditions (ASC) are characterized by impairments in Theory of Mind (ToM) and imitation, both of which are crucial for social learning. According to theoretical threads going back to Aranson (2004), social learning is an important mechanism underlying the development of prejudice. Cognitive rigidity is another factor thought to play a role.

Objectives: The study investigates our hypothesis that people with ASC have lower levels of prejudice than neurotypical controls, due to their deficit in social learning.

Methods: We compared a group of 20 German adults with ASC with a group of 20 neurotypical controls matched in nationality, age, gender and IQ on measures of prejudice. As explicit measure we used the group-focused enmity questionnaire (GFE, Heitmeyer, 2007, Zick et al., in press). A prejudice Implicit Association Test (IAT, Schmitz & Klauer, 2007) was used to assess prejudice more objectively. To account for the effects of cognitive rigidity, the German version of the "Personal need for structure" scale was administered (Machunsky et al, 2006).

Results: The group with ASC scored significantly higher on cognitive rigidity. Covariance analyses yielded significantly lower scores on the GFE in the group with ASC when controlling for cognitive rigidity. Moreover, we found significantly lower scores on the IAT in the group with ASC. Finally, there was a significant negative correlation ($r = -.69$) between the IAT and the Autism Spectrum Quotient (Baron-Cohen et al., 2001). No associations were found between the measures of prejudice and ToM abilities.

Conclusions: Both, explicit and implicit measures of prejudice revealed differences between the ASC and the control group in the anticipated direction. Moreover, higher degrees of autistic symptomatology were associated with a lower tendency for prejudice. However, levels of prejudice were not dependent on inferring others mental states.

60 156.14 Face and gaze processing in the broader autism phenotype: independent differences in ASD relatives. M. N. Coutanche*, S. Wallace, K. B. White, S. Foley, A. Bailey and I. M.G.S.A.C., *University of Oxford*

Background: Our previous research in adults with an Autism Spectrum Disorder (ASD) suggests that ASD face processing differences fall into two categories: face perception and making judgements about eye stimuli. Previous studies have also reported deficits on

'higher level' face tasks that are believed to tap Theory of Mind. Relatives of individuals with ASD frequently show a 'broader autism phenotype', but the exact pattern of their face processing differences is still unclear.

Objectives: This study aimed to examine the relationship between performance on face and eye-gaze tasks in the broader autism phenotype, including a Theory of Mind face test, and so investigate whether these tasks are tapping separate skills.

Methods: Sixty-seven UK parents and siblings without an ASD were tested as part of the IMGSAC study. All participants were assessed on the Benton Facial Recognition Test (BFRT), a task of discriminating pairs of faces or houses, the 'Reading the Mind in the Eyes' Test, and judging eye-gaze direction at brief exposure durations.

Results: Performance on the Reading the Mind in the Eyes Test was significantly positively correlated with accuracy at detecting the direction of briefly presented averted eyes in faces. BFRT scores were positively correlated with sensitivity to face differences in the faces/houses task. These correlations remained strong after controlling for both verbal and performance IQ, and despite high correlations within these pairs of tasks, there were no correlations between the pairs.

Conclusions: The Reading the Mind in the Eyes Test paired with the eye-gaze task, and the BFRT paired with the facial discrimination task, appear to tap individual variation in two separate mechanisms: Face discrimination and a separate eye-gaze system. Our future research will explore the relationship between severity of the broader autism phenotype and performance on tasks that assess these two face processing mechanisms.

61 156.15 Self-Awareness, Self-Monitoring, and the Enactment Effect in Autism Spectrum Disorder: Evidence From a Self-Other Source Memory Task. S. Lind* and D. Bowler, *City University, London*

Background:

By 6 years of age, typically developing children demonstrate superior recall/recognition of self-performed, as opposed to other-performed, actions (Baker-Ward et al., 1989; Roberts & Blades, 1998). This performance advantage, associated with being a participating agent rather than an observer, is known as the "enactment effect" (Engelkamp, 1998) and is thought to be related to developments in self-awareness and/or action monitoring. It has been argued that ASD involves primary impairments in both of these areas. If individuals with ASD have difficulty in monitoring their own actions (Russell, 1997) they may fail to encode motor information into their memory traces, thereby eliminating the enactment effect. Furthermore, if individuals with ASD have insufficiently developed representations of self (Frith & Happé, 1999; Hobson, 1993) they may be less able to encode information in relation to this structure. Both of these accounts predict that individuals with ASD will be less subject to the enactment effect in memory tasks.

Objectives:

To test the prediction that individuals with ASD show a reduction in the enactment effect, in order to assess the claims that individuals with ASD show impaired self-awareness and action monitoring abilities.

Methods:

Thirty-six children with ASD and 36 comparison children, matched on age and verbal ability, completed a self-other source monitoring task. The procedure involved participant and experimenter taking turns to pick up and name a series of picture cards. Both item recognition and source memory were assessed.

Results:

Contrary to predictions, both the ASD and comparison groups demonstrated the enactment effect in both item and source memory.

Conclusions:

These results appear to speak against the theory that ASD involves an impairment in self-monitoring and/or self-awareness. However, it is possible that the enactment effect is due to alternative underlying factors.

62 156.16 The Role of Language in Mentalizing. B. Forgeot d'Arc*[1] and F. Ramus[2], (1)*Centre National de la Recherche Scientifique/Assistance Publique des Hôpitaux de Paris*, (2)*Centre National de la Recherche Scientifique*

Background: Theory of Mind deficit is one of the most influent theoretical explanations of autistic symptoms. Poor performances in false belief tasks (FBT) have been widely observed in subjects with autistic spectrum disorders (ASD), and are one essential argument for this account. However, the paradox of high-functioning subjects with ASD passing FBT has led to a dual-processing explanation of belief representation including two hypotheses:
(1) An intuitive processing of beliefs in normal subjects and
(2) A deficit of this intuitive processing in autistics, with compensatory verbal reasoning in high-functioning subjects (Happé 1995).
However, contrary to (1), other authors (Newton & de Villiers 2007) argue that verbal reasoning may be essential in representing beliefs in all subjects.
Objectives: In order to test (1), we aimed to set apart the roles of intuitions and reasoning in representing beliefs in normal adults.
Methods: We used verbal shadowing to inhibit reasoning, during a series of forced choice non verbal false belief tasks based on animated cartoons, in 20 healthy adults.
Results: Data obtained on normal subjects indicate that performance is only partly dependant on verbal reasoning.
Conclusions: Consistent with the first hypothesis of the dual-processing explanation of belief representation, normal adults remain able to process mental states despite heavy verbal interference to their reasoning. Data on adults with Asperger syndrome are currently being collected to test the second hypothesis: the compensatory role of verbal reasoning in high-functioning subjects with ASD.

63 156.17 Low-level Auditory Processing of Simple and Complex Sounds in Autism. A. C. Bonnel*[1], S. McAdams[1], B. K. Smith[1], A. Bertone[1], J. A. Burack[1], V. Ciocca[2] and L. Mottron[3], (1)*McGill University*, (2)*University of British Columbia*, (3)*Université de Montréal*

Background: Enhanced and diminished patterns of performance across visual and auditory domains are now a consensual characteristic of the autistic cognitive phenotype (e.g., Mottron et al, 2006). The results of a study by Bertone et al. (2005) suggest that patterns of performance in low-level visual processing tasks may depend on the level of neural complexity required to process stimuli. There are preliminary indications that a dissociation between enhanced and diminished performance linked to the neural complexity required to process acoustic stimuli may exist in the auditory modality as well (Samson et al., 2006).
Objectives: The purpose of the current study is to assess the neural complexity hypothesis in the auditory modality.

Methods: To test this hypothesis, four discrimination experiments were designed targeting pitch, spectral envelope, vocal timbre, and loudness. A range of pure- and complex-tone stimuli, with or without frequency or amplitude modulation, varied along spectral and temporal dimensions.
An adaptive procedure was used to assess the auditory discrimination thresholds of groups of high-functioning participants with autism (HFA), Asperger syndrome (ASP), and typically developing individuals (TDs). Participants were matched in full scale IQ, chronological age and sex. Our research question was whether increasing the level of spectral and/or temporal complexity would have a detrimental impact on the ability of HFA- and ASP participants to discriminate between acoustic stimuli.

Results: Preliminary results suggest that auditory discrimination performance of the autism spectrum disorders groups is not as dependent on levels of spectro-temporal complexity as originally predicted.

Conclusions: The results will be interpreted in the context of current perceptually based models of enhanced and diminished perceptual functioning in autism.

64 156.18 Self-Awareness of Autistic Symptoms, Empathy, and Systemizing in High-Functioning Children and Adolescents with an Autism Spectrum Disorder. J. H. Filliter* and S. A. Johnson, *Dalhousie University*

Background: Studies of theory of mind in Autism Spectrum Disorders (ASD) typically focus on the ability to perceive and understand others' mental states. It has been proposed that the mechanisms that underlie understanding of others' mental states are similar to those involved in attributing mental states to the self.

Objectives: We investigated self-awareness of autistic symptoms and empathic and systemizing characteristics in high-functioning individuals with ASD.

Methods: We compared parent and self-report scores on the Autism Spectrum, Empathizing, and Systemizing Quotients (AQ, EQ, & SQ). Participants were 15 individuals with an ASD and 16 age- and IQ-matched controls, ages 9 to 19 years.

Results: Parents of ASD participants reported significantly more autistic features (higher AQs) and lower empathy (lower EQs) than parents of controls. No differences were found for parental SQ ratings. Comparisons of parent- and self-report scores revealed that ASD participants reported fewer autism symptoms and higher empathy levels relative to their parent, but there was no difference on the SQ. In contrast, parent- and self-reports for the control group did not differ for the AQ and SQ measures, but parents reported more empathizing than participants. Correlational analyses showed significant positive correlations between parent and self-report AQs for both groups (ASD, r=0.63; controls, r=0.57, both p<0.5). Thus, despite different overall ratings for the ASD group, higher parental ratings were associated with higher self ratings. Parent- and self-report EQs were positively correlated for controls, but not ASD participants (r=0.66, p<0.1 and r=0.37, n.s., respectively). Analyses of AQ and EQ subscales also revealed group differences; these findings will be discussed.

Conclusions: These results suggest that individuals with autism may differ from typically-developing peers with respect to insight into specific domains of their own functioning. Findings will be discussed in the context of current research on theory of mind.

65 156.19 Visuospatial Processing Style and Social Functioning in Down Syndrome With and Without Symptoms of Autism. E. Kuschner*, L. Bennetto, S. Hyman and A. Diehl, *University of Rochester*

Background: Enhanced detail-focused visuospatial processing in autism (Mottron et al., 2003) may influence other areas of development, including social functioning (Joseph et al., 2002). Children with Down syndrome show a contrasting profile: visuospatial processing is generally globally-focused (Bihrle et al., 1989), and social functioning is enhanced compared to mental age (Laws & Bishop, 2004).

Objectives: To elucidate the relationship between visuospatial processing style and social functioning by comparing profiles of children with Down syndrome with and without features of autism.

Methods: The Leiter International Performance Scale-Revised (Leiter-R) was administered to 36 children with Down syndrome (4-13 years). The Autism Diagnostic Interview-Revised (ADI-R) was completed with the parent(s). ADI-R diagnostic algorithms were positive in 12 children and negative in 24. Groups were similar in age, gender, IQ, expressive, and receptive language ability (all *p*'s>.10). Detail-focused processing style was operationalized via Leiter-R Figure Ground subtest deviation scores, which measure disembedding. Social functioning was measured with ADI-R social domain scores.

Results: Figure Ground deviation scores were correlated with social domain scores for the ADI-positive group, r=.79, *p*<.002, with greater detail-focused processing related to more autism-like social behaviors. Detail-

focused processing was not significantly related to social domain scores for the ADI-negative group, r=-.23, *p*=.27. These correlations do not appear to be due to restricted ranges, and were significantly different, Z=3.28, *p*=.0007. Furthermore, deviation scores were not significantly related to overall IQ, receptive, or expressive language (groups separately or combined).

Conclusions: Findings suggest that visuospatial processing style may be developmentally related to social functioning when autism symptoms are present in Down syndrome. These domains may not have the same implications in children with only Down syndrome. This relationship will be examined in children with autism (without Down syndrome) and typical controls to further explore how visuospatial processing impacts social interaction.

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66 156.20 Intention Recognition in Autism Spectrum Disorders (ASD) using animacy displays derived from human action scenarios. P. McAleer*[1], M. D. Rutherford[2], J. W. Kay[1] and F. E. Pollick[1], (1)*University of Glasgow*, (2)*McMaster University*

Background:

Research investigating autism-related deficits in understanding the intent of others has made use of simple animacy displays, similar to those of Heider and Simmel (1944), depicting dynamic geometric shapes. Previously it has been reported that ASD populations are relatively poor at judging the intentions portrayed in these displays (Abell et al, 2000; Castelli et al 2000, 2002; Rutherford et al., 2006). These findings have been related to the reduced social abilities found in ASD populations.

Objectives:

We aim to provide a description of deficits in social understanding associated with ASD by having people with and without ASD judge intentions in real-world video displays and corresponding animacy displays.

Methods:

Typically animacy displays are synthetically created, resulting in displays which may have little relation to actual human movement. Instead, we use a subtractive technique where video recordings of human interactions are reduced into geometric shapes mimicking the motion of the original actors. Displays were created depicting 6 intentions shown from 2 viewpoints: Chasing, Fighting, Flirting, Following, Guarding and Playing (Blythe et al, 1999) viewed from both the Overhead and Side-View. 14 people with ASD, diagnosed using ADOS and ADI-R, were compared to an age and IQ matched control population. Each participant saw all combinations of animacy and video displays once and indicated the intention displayed via a 6AFC task.

Results:

Preliminary results suggest no overall differences between the ASD and control populations. Both groups were able to recognise the displayed intentions at levels above chance. The viewpoint from which the displays were viewed had no effect on ability to recognise intentions. Recognition was better in video displays than animacy displays.

Conclusions:

The ability of people with ASD to recognise social intentions may not be as reduced as thought, and in certain situations is equivalent to controls.

67 156.21 Memory as a Discrimination Problem: Comparison of Retrieval between Participants with Asperger's Syndrome and Neurotypical Individuals. M. Poirier*, S. Lind, J. Martin, S. Gaigg and D. Bowler, *City University*

Background: It is now relatively well established that memory functioning in individuals with Asperger's syndrome shows subtle and sometimes complex differences to what is observed in neurotypical controls.

Objectives: This study aimed to compare certain aspects of memory retrieval in individuals with Asperger's syndrome and in matched neurotypical participants.

Methods: In the task called upon, participants first learned what the two favourite foods of each of three animals were. One food was unique to each animal while the second was either also unique or shared between 2 of the 3 animals. During the learning phase of the task, the number of trials necessary to reach 75% correct performance was measured as well as response times. Then a test phase examined the speed at which the correct animal could be identified depending on the cue provided. The conditions included presenting one unique cue, one shared cue, one unique plus one shared cue, or two unique cues.

Results: Preliminary results indicate that 1) more Asperger's participants fail to reach criterion performance on the task; 2) the number of training blocs necessary to reach criterion is higher for the Asperger's participants; 3) the pattern of performance in the learning and test phases is similar for controls and individuals with Asperger's; 4) however, interestingly, in the actual post-training performance, individuals with Asperger's outperform controls, i.e. they are faster to respond and their accuracy is comparable.

Conclusions: Once the bindings between cues and targets had been learned, individual's with Asperger's syndrome outperformed controls – however, developing these bindings was more demanding for the participants with Asperger's.

68 156.22 Visual attention in infants at-risk for autism. M. Elsabbagh*[1], A. Volein[1], H. Garwood[1], L. Tucker[1], G. Csibra[1], S. Baron-Cohen[2], P. F. Bolton[3], T. Charman[4], G. Baird[5] and M. Johnson[1], (1)*Centre for Brain and Cognitive Development*, (2)*University of Cambridge*, (3)*Institute of Psychiatry*, (4)*University College London*, (5)*Guy's Hospital*

Background: Recent studies of infant siblings of children diagnosed with autism have allowed for a prospective approach to examine the emergence of symptoms and revealed behavioural differences in the broader autism phenotype within the early years. In the current study we focused on a set of functions associated with visual attention, previously reported to be atypical in autism.

Objectives:The aim was to assess whether visual attention functions differ in infants at-risk relative to a matched control group.

Methods: We compared performance of a group of 40 6-10-month-old infant siblings of children with autism (sib-ASD) to a control group with no family history of autism on the "gap-overlap task", which measures the cost of disengaging from a central stimulus in order to fixate a peripheral stimulus. Two measures were derived on the basis of infants' saccadic reaction times. The first is the Disengagement effect, which measures the efficiency of disengaging from a central stimulus to orient to a peripheral one. The second was a Facilitation effect, which arises when the infant is cued by a temporal gap preceding the onset of the peripheral stimulus, and would orient faster after its onset.

Results: The sib-ASD group showed longer Disengagement latency as well as less Facilitation relative to the control group.

Conclusions: These differences indicate that certain characteristics of the broader autism phenotype are present in infancy and may relate to differences in scanning both social and non-social stimuli.

69 156.23 Autobiographical Memory Retrieval in Young Adults with Asperger's Syndrome / High Functioning Autism. T. L. Beattie* and F. Szeligo, *University of New Brunswick*

Background: Autobiographical memory is a complex memory system linked to the development of self-identity and the formation of personal goals over time (Conway and Pleydell-Pearce, 2000). Impairments in episodic memory have been well documented in AS/HFA; however, less is known about autobiographical memory recall in this population. Conway and Pleydell-Pearce (2000) proposed a cognitive-motivational model of autobiographical memory that suggests a primary role of executive functioning (e.g., planning and goal-directed behaviour). Executive deficits have been well documented in autism; however, the impact of

these deficits on autobiographical memory is not well understood.

Objectives: The purpose of this study was to examine autobiographical memory retrieval in adults with AS/HFA and a matched control group without this diagnosis. This study examined differences in autobiographical memory recall between these groups and investigated possible factors (specifically, executive functioning) that contribute to these differences.

Methods: Participants: 11 adults with AS/HFA and 11 matched controls. Primary measures: the Autobiographical Interview (Levine, et al., 2002), which assesses recall of autobiographical memories across major life periods and the DKEFS Tower Test. Participants also completed standardized measures of IQ, verbal memory, personal semantic memory, and mood functioning.

Results: Compared to controls, the AS/HFA group recalled a proportionally lower number of episodic details for remote events, integrated the memories into a larger life context, and produced more references to emotional state and thoughts during recall of remote memories. The AS/HFA group scored significantly lower than controls, but still within the average range for their corrected age, on most aspects of the Tower Test.

Conclusions: The results of this study suggested that adults with AS/HFA exhibit unique autobiographical memory abilities. Executive function was significantly correlated with autobiographical memory recall; however, the relationship is complex. Implications for treatment will be discussed.

70 156.24 Do Adolescents with ASD Look at Eyes and Follow Them?. M. Freeth*, D. Ropar, P. Chapman and P. Mitchell, *University of Nottingham*

Background:
The ability to perceive and accurately interpret social cues is imperative to our understanding of the social world. Social impairment is a major characteristic of autism spectrum disorders (ASD). Conflicting findings have been reported in visual fixation patterns when participants are presented with stimuli containing another person's eyes (Klin et al. 2002; Dalton et al. 2005; Van der Geest, 2002).
Objectives:
1. To investigate whether visual fixation patterns for participants with ASD when free-viewing scenes containing a person are similar or different from the visual fixation patterns of typically developing control participants.
2. To investigate whether the eye-gaze direction of another person influences visual fixation patterns in typically developing participants and those with ASD.
Methods:
24 high-functioning adolescents with ASD and 24 control participants completed a free-viewing eye-tracking study.
A series of static scenes depicting a person looking straight out of the photo or towards an object in the photo were displayed for 5 seconds each.
Results:
Despite the face of the person in the photo only covering approximately 2% of the total area of the photo, ASD participants spent approximately 25% of their total viewing time fixating in this region. The total gaze duration on the top half of the face was significantly longer than on the lower half of the face - this was similar to matched controls, although participants with ASD were slower to first fixate the face.
Evidence for spontaneous eye-gaze following in both groups was found.
Conclusions:
Overall viewing patterns of adolescents with ASD are surprisingly similar to matched controls when photos of a person in a complex scene are viewed. This indicates that high-functioning adolescents with ASD have a strong spontaneous interest in people and their eye-gaze direction, contrary to previous suggestions by Klin et al. (2002) and Dalton et al. (2005).

71 156.25 Decision-Making Skills in Autism Spectrum Disorders: Performance on the Iowa Gambling Task. J. L. Mussey*, L. G. Klinger, M. R. Klinger and B. G. Travers, *University of Alabama*

Background:

The Iowa Gambling Task (IGT) is a decision-making task that requires implicit learning and executive function abilities. Performance on the IGT is related to the basal ganglia and frontal cortex of the brain, areas that are impaired in individuals with Autism Spectrum Disorders (ASD). Johnson, et al. (2006) used a computerized version of the IGT in adolescents with Asperger's disorder and typical development and found that participants with Asperger's disorder had an unusual selection pattern characterized by frequent shifts between decks.

Objectives:

This project examined whether individuals with ASD show implicit learning by increasingly choosing from advantageous decks across time rather than simply examining the average performance across all trials to compare individuals with ASD and typical development (TD).

Methods:

Participants were 14 high-functioning adolescents and young adults with ASD and 18 TD adolescents and young adults matched on age and verbal ability. Participants completed a computerized IGT composed of six blocks of 25 selections from four decks of cards that differed with respect to advantageousness (the amount of gain possible) and frequency of a loss.

Results:

Preliminary results indicate that individuals with TD showed strong early learning, selecting from advantageous decks 69% of the time by the 3rd block. Individuals with ASD showed slower, more gradual learning, selecting from advantageous decks 57% of the time by the 3rd block. This difference between diagnostic groups approached significance, p=.8, partial eta squared=.96.

Conclusions:

Preliminary results indicated differences between participants with ASD and TD in implicitly learning to make advantageous choices. Further data analyses are being conducted to examine performance and learning related to other aspects of the IGT such as the impact of frequency of loss and deck shifting. Funding provided by the University of Alabama Psychology Department and Graduate School.

72 **156.26** NEUROPSYCHOLOGICAL PROFILE IN A PAEDIATRIC HIGH-FUNCTIONING AUTISM SPECTRUM DISORDERS SAMPLE: RELATIONSHIP WITH CLINICAL VARIABLES.

O. Puig*, R. Calvo, E. De la Serna, S. Andrés, V. Sánchez and L. Lázaro, *Hospital Clinic de Barcelona. Neuroscience Institute. Department of Child and Adolescent Psychiatry and Psychology.*

Background: High-functioning autism spectrum disorders (HF-ASD) have been associated with neurocognitive deficits, especially, with a prominent executive dysfunction (Ozonoff et al, 1991; Pennington et al, 1991).

Objectives: This study examines the neurocognitive profile of a HF-ASD sample comparing with a healthy control group in a full range neurocognitive battery of tests, including executive function assessment. Also, we analyze the relationship of neuropsychological performance with symptoms' severity and comorbidities.

Methods: Participants include 15 individuals (ages: 8-13) with high-functioning autism spectrum disorders (HF-ASD group). Primary DSM-IV diagnoses in HF-ASD group are: high-functioning autism spectrum disorder and Asperger syndrome, without mental retardation. Control group include 10 healthy subjects sex and age matched. All subjects are being tested on a neuropsychological battery to assess intellectual functioning, working memory, process speed, verbal and non-verbal memory, sustained attention and executive functions (visual-spatial organization, response inhibition, set shifting, planning). Autism symptoms severity will be assessed with the High Functioning Autism Spectrum screening questionnaire (ASSQ) (Ehlers et al, 1999).

Results: Attending to neurocognitive profiles, executive dysfunction is hypothesised in whole

HF-ASD group. Also, we expect Asperger syndrome patients to show lower scores in visual-spatial functions, including non-verbal IQ, than healthy subjects. Regarding symptoms correlations, we hypothesy a negative relationship between executive dysfunction severity and symptoms measured with ASSQ. Comorbidities, if present, will be also negatively correlated with neurocognitive performance. ADHD comorbidity will implies worse performance in executive functions, sustained attention and verbal memory.

Conclusions: We expect results support the hypothesis that neurocognitive profile of HF-ASD patients is a valid source of information, which could help us to understand autism spectrum disorders and the relationship between their cognition and their symptoms.

73 156.27 Children with High Functioning Autism Spectrum Disorders Demonstrate Diminished Social Attribution to Ambiguous Visual Displays. G. L. Wallace*[1], B. E. Yerys[2], M. Celano[1], J. James[2], J. L. Sokoloff[2], L. Kenworthy[2] and J. N. Giedd[1], (1)*NIMH*, (2)*Children's National Medical Center, George Washington University*

Background: Individuals with autism spectrum disorders (ASDs) demonstrate a reduced tendency to ascribe social meaning to impoverished scenes of interacting shapes. However, most studies either have included intellectually impaired children with ASDs or have used cues such as character names to prime social attributions to animations of this type.

Objectives: The present study seeks to examine uncued social attribution to interacting geometric shapes in children with high functioning ASDs and its correlation with age.

Methods: 44 children with a high functioning ASD (diagnosed using DSM-IV criteria and scores from the ADI and ADOS) and 44 typically developing (TD) children matched group-wise on age (7-16 years), IQ (80+), and sex ratio (80% male) were shown the "Triangles Playing Tricks" task and asked to provide verbal descriptions of the animations. Data from two types of animations (goal-directed and 'theory of mind') were coded by a rater blind to diagnosis, providing two indices of performance: appropriateness and 'intentionality.'

Results: A significant main effect of group but no significant group by condition interaction was found for intentionality ratings, indicating that children with ASDs were less likely to ascribe intentionality to characters to both types of animations. This could not be explained by discrepant verbal output since no group difference in length of verbal descriptions was noted. Additionally, age was positively associated with both indices of performance on the theory of mind animations for TD, but not ASD children.

Conclusions: High functioning children with ASDs demonstrate a diminished likelihood of assigning intentionality to uncued, impoverished animations of interacting geometric shapes. In contrast to the pattern observed among TD children, theory of mind performance did not improve with age among high functioning children with ASDs.

74 156.28 Effects of enhanced prosody on narrative recall in children with autism. L. Black*[1], J. Van Santen[1], R. Coulston[1], R. Paul[2] and J. De Villiers[1], (1)*OHSU*, (2)*Yale Child Study Center, Southern Connecticut State University*

Background: Professionals are known to use enhanced prosody in working with children with autism spectrum disorders (ASD). However, no scientific evidence exists that enhanced prosody facilitates engagement, comprehension, or retention of information in ASD.

Objectives: The purpose of the study was to measure the effects of prosodic style on narrative recall performance in children with ASD vs. Typical Development (TD).

Methods: Participants (ages 4-7) underwent diagnostic and neurocognitive assessment. Two stories were developed depicting interpersonally dynamic and affectively-charged events, rich in factual and social

cognitive information. They were produced in three prosodic modes. (E) Enhanced: Prosody highlights story content and meaning at multiple levels (using affective, pragmatic, and grammatical prosody); it differs from "storyteller" style which captures attention but does not necessarily highlight meaning. (S) Standard. (D) Disconnected: Words were recorded randomly, concatenated into sentences, and acoustically modified to have continuous pitch and energy contours. Additional signal modification methods were used to match the modes on average pitch, energy, speaking rate, and pause duration. Separate questions were developed for factual and social-cognitive aspects of the story.

Results: For ASD, a clear trend was observed for story recall to be best in E mode, next in S mode, and worst in D mode. No such trend was observed in the TD group. TD performed better than ASD in all modes. There was a significant interaction between the E vs. D contrast and Group (ASD vs. TD); in E compared to D, the TD-ASD difference was significantly reduced. Social-cognitive questions were more difficult than factual questions for both groups.

Conclusions: The results suggest that enhanced prosody specifically targeted to highlight the multiple levels of information in complex verbal communication may help comprehension and retention of information in children with ASD. This has potentially important implications for intervention as well as for assessment.

75 156.29 REY-OSTERRIETH COMPLEX FIGURE PERFORMANCE IN HIGH-FUNCTIONING CHILDREN WITH ASD: DISTINCTIONS FROM TYPICALLY DEVELOPING AND CLINICAL CONTROL GROUPS?. K. D. Tsatsanis*[1], I. L. J. Noens[2], D. L. Pauls[2], A. Klin[1], C. L. Illmann[2], F. R. Volkmar[1] and R. T. Schultz[3], (1)*Yale Child Study Center*, (2)*Massachusetts General Hospital*, (3)*Children's Hospital of Philadelphia and the University of Pennsylvania*

Background: Children with an Autism Spectrum Disorder (ASD) are reported to show a cognitive bias toward a detail-oriented processing style. Deficits in some executive processes are also found. A widely used neuropsychological measure, the Rey-Osterrieth Complex Figure Test (ROCF), provides a novel and complex stimulus figure by which to investigate the effects of organizational strategies and processing style during the encoding phase on subsequent recall. There are few published studies to examine ROCF performance specifically in children with ASD, and, of those, limitations include sample size and characteristics, comparison groups, and methodology.

Objectives: This study seeks to examine the ROCF performance of children with ASD with comparisons to typically developing children and other clinical groups (children with TS, OCD, and/or ADHD). These clinical groups were selected because of overlap in symptom expression as well as reported presence of EF dysfunctions.

Methods: The ROCF was administered to 34 high functioning children with ASD, 30 typically developing children, and 52 children with TS, OCD, and/or ADHD between the ages of 8 and 14 years of age. The Developmental Scoring System (Bernstein & Waber, 1996) was used as it provides normative scores for this age group along four parameters of performance: organization, style, errors, and recall.

Results: We are conducting a detailed quantitative analysis of performance to examine differences in processing style, visuospatial planning/organization, and figure distortion both within the ASD group and relative to typical and clinical comparison groups. The differential impact of each of these factors on immediate and later recall is being analyzed.

Conclusions: The results of this study are expected to provide a picture of how children with ASD respond to novel and complex information, in a way that distinguishes them from typically developing children and other clinical groups.

76 156.30 Dual Task Performance in Children and Adults with Autism. I. M. Eigsti*, K.

Markoff, M. Helt, M. Rosenthal, E. Troyb and D. Fein, *University of Connecticut*

Background:Many of us have experienced the negative effects of divided attention (e.g., conversing while driving) due to "resource limitations" on attention and response selection (e.g., Watter & Logan, 2006). Negative effects may depend on functional connections between the relevant "dual" tasks, as performance of tasks that are more functionally and anatomically similar will be relatively more impacted by multitasking. Individuals with ASD might exhibit *less* impairment in multitasking, due to hypothesized decreases in functional connectivity. Alternatively, if multi-tasking critically depends on effective executive functioning, ASD may be characterized by poor multitasking. In addition to these theoretical implications, multi-tasking performance is highly relevant for everyday functioning.

Objectives:To explore functional connectivity through a behavioral dual-task paradigm.

Methods:19 Participants with ASD and 42 typically developing controls ages 11-54, matched on PPVT, completed a well-studied dual-task paradigm, in which they were asked to tap with their right or left index fingers while simultaneously describing a visually-presented image. Tapping rate was also recorded in a baseline "single-task" condition.

Results:All participants tapped at equivalent rates in the baseline condition (p's > .3), and rates decreased in the dual-task condition for both groups. However, the ASD group was significantly *more* slowed when multitasking (2.9 fewer taps in TD group, 4.8 in ASD group, p = .008). There was a group by handedness interaction, with left-handed ASD participants (n = 5) showing a significantly greater decrease than left-handed controls (n = 15).

Conclusions:Findings indicate that all individuals with ASD, and especially left-handed individuals, experienced more, rather than less, interference when multi-tasking. This suggests two possibilities: ASD may not be characterized by a lack of functional connectivity; alternatively, dual task performance reflects higher-order executive processes, in addition to interference between closely-related anatomical regions, in ASD.

77 156.31 McGurk Effect in Asperger Syndrome and High-functioning Autism. J. H. Schroeder*[1], J. A. Weiss[1], J. M. Bebko[1], K. Wells[1], L. Hancock[1], C. McMorris[1] and J. J. A. Holden[2], (1)*York University*, (2)*Queen's University*

Background: Bebko and colleagues (2006) suggest that deficits in intermodal processing (IMP) may be related to some of the language impairments that characterize autism. The McGurk effect is an illusion that demonstrates how we integrate what is seen and what is heard during speech. The McGurk effect involves visually presenting a face saying a sound that is synchronous with but different from a sound presented auditorily. Most typically developing individuals integrate the mismatched stimuli and report hearing a sound that was never presented. This illusion requires IMP of the auditory and visual components of the linguistic stimuli. Weiss and Bebko (submitted) found that children with autism were significantly less likely to show the McGurk effect relative to typically developing children and a cognitively impaired control group, suggesting that children with autism may have difficulty with IMP of speech information. The current study aims to extend this research by exploring these processes in individuals with Asperger syndrome (AS) and high-functioning autism (HFA).

Objectives: To determine whether impairments in IMP of speech are related to autism in general, or if they are related specifically to the developmental language delays and difficulties in current language that characterize autism.

Methods: Twenty children (6-16 years) with AS/HFA are compared to typically developing children and individuals with classic autism.

Results: We report data with AS/HFA which is currently being collected, compared to the performance of typically developing individuals and those with lower-functioning autism (data collection completed). Initial analyses indicate that only the lower functioning children with

autism report less of a McGurk effect (i.e. less IMP) than the other two groups.

Conclusions: This research will help to determine how individuals with AS and HFA integrate what they see and what they hear relative to individuals with lower-functioning autism and typically developing peers.

78 156.32 LEARNING OF WELL-DEFINED AND ILL-DEFINED CATEGORIES IN AUTISM. A. Froehlich*[1], J. Miller[1], M. DuBray[1], E. Bigler[2] and J. E. Lainhart[1], (1)*University of Utah*, (2)*Brigham Young University, Psychiatry, Interdepartmental Neuroscience Program, Brain Institute, University of Utah*

Background: The cognitive process of categorization is fundamental to the organization and generalization of knowledge, both of which are impaired in autism. Of particular interest have been categories based on well-defined rules versus those in which category membership is not easily defined.

Objectives: We examined performance with ill-defined categories that were based on a prototype, or central tendency, and those on that were based on individual category exemplars. Also examined was performance with well-defined categories based on a rule about a single diagnostic feature. Categorization of trained category examples versus novel examples, differences in rates of learning between participant groups, and the role of recognition memory for learned exemplars was measured.

Methods: Twenty-six high-functioning adults with an autism spectrum disorder and 26 typically-developing controls participated. Categorization tasks involved alternating training and transfer phases and a recognition phase, similar to the task structure used by Kolodny (1994). Stimuli for ill-defined categories included random dot patterns (Posner, Goldsmith, & Welton, 1967), and landscape paintings of the European Volga region. Stimuli for well-defined categories included computer line drawings of imaginary bugs and animals, each containing six varying features, only one of which was diagnostic of category membership.

Results: Participants with autism performed as well as controls with the well-defined categories. Performance with the ill-defined categories varied. Participants with autism demonstrated evidence of prototype formation similar to that of controls although were less able to categorize new exemplars that were high distortions of the prototype. Overall performance with ill-defined categories based on individually learned exemplars was poorer for the autism group.

Conclusions: Individuals with autism appear to be better able to learn categories that are well-defined, and prototype formation may be preserved in autism. Possible reasons for discrepancies in the literature and finer evaluation of categorization performance will be discussed.

79 156.33 'Sticky' attention: Children with autism's ability to disengage their attention without an external cue. J. M. Bebko*[1], C. A. McMorris[1], K. Wells[1], J. H. Schroeder[1] and J. J. A. Holden[2], (1)*York University, Toronto*, (2)*Queen's University*

Background: An important aspect of social-communicative functioning is children's ability to disengage and shift attention from one stimulus to another. Compared to typically developing children, children with autism appear to have difficulty, indicated by slower eye movements to a second stimulus. Previous studies examining disengagement have utilized a visual orientation task, where a peripheral stimulus is presented while a central fixation remains (disengagement) or disappears (shifting). In previous research, the peripheral stimulus provides an indication for children to shift attention. It is unknown if the observed difficulties in shifting attention are specific to these single-shift paradigms. The present study aims to understand children's ability to disengage attention beyond the first shift, in a self-directed task, in order to understand limitations in ongoing, 'in-line attention' capabilities.

Objectives: To examine how children with autism's attention abilities are controlled when

the cue to disengage must be self-generated versus externally cued, providing a better representation of their shifting capabilities in their everyday interactions with the environment.

Methods: Numbers and durations of eye fixations are compared to typically developing children matched for age and verbal ability. Children were presented with two separate images on the right and left sides of a screen. Stimuli were divided into high (man reciting story), low (man counting) and non-linguistic (mouestrap) conditions, which were further categorized by high and low emotion.

Results: If disengagement of attention is an in-line problem, effecting more than the first attention shift, then number of and time between fixations should be fewer and longer for the autism group; stimulus type and emotion level may also iinfluence the findings (Bahrick et-al., IMFAR poster 2007). Data are collected and currently being analyzed.

Conclusions: This study addresses an important difference between attention skills in tasks which require frequent disengagement and shifting of attention ("in-line attention") versus single-shift paradigms.

80 156.34 The Victoria / Yale Face Processing Battery: Psychometric Properties of the Original and Shortened Forms. S. S. Stahl*[1], J. M. Wolf[1], J. T. Tanaka[2], C. Klaiman[1], K. Koenig[1], J. Cockburn[2], L. Herlihy[1], C. Brown[1], M. South[1] and R. T. Schultz[1], (1)*Yale University School of Medicine*, (2)*University of Victoria*

Background:
Prior research indicates that individuals with autism spectrum disorders (ASD) have deficits in face processing ability. The Victoria / Yale Face Processing Battery (VYFPB) is a comprehensive, computer-based face processing skills battery that assesses facial identity recognition including part/whole processing, eye/mouth processing, and facial expression recognition.

Objectives:
To develop a shortened version of the VYFPB and to examine the psychometric properties of both the original and shortened versions of the battery. The reliability of the original and shortened forms of the VYFPB was examined in individuals with ASD and typically developing individuals. The relative validity of the shortened form was assessed by comparing the between-group differences found using the two forms.

Methods:
Participants were 55 high functioning children and adults with ASD and 103 typically developing individuals. The original form of the VYFPB was administered as previously described and reported (J. Wolf et al., IMFAR 2006 Abstracts, pg. 149). To shorten the battery, items with high item-total correlations and acceptable alphas were retained, while maintaining most of the original battery structure. This resulted in a battery that has 309 items compared to the original 570 items and takes approximately half as much time to administer.

Results:
Nearly all the scales for both the original and shortened forms demonstrated adequate to excellent reliability. Chronbach's alpha's for the scales of the original form ranged from .56 to .95; alpha's for the shortened form ranged from .55 to .95. Previously reported (Wolf et al., 2006) significant between-group differences in part/whole processing, eye/mouth processing, and facial expression recognition were maintained with the shortened battery.

Conclusions:
Both original and shortened forms of the VYFPB have clinical utility. The shortened form takes substantially less time to administer and appears to be nearly as effective at detecting face processing deficits in individuals with ASD.

Poster Presentations Program

157 Cell/Animal Model Posters

81 157.1 ABNORMALITIES OF EARLY SEROTONERGIC DEVELOPMENT IN THE EMBRYOS OF THALIDOMIDE / VPA-INDUCED AUTISM MODEL RATS. M. Narita*[1], A. Oyabu[1], Y. Imura[1], N. Kamada[1], A.

Uchida[1], M. Tazoe[2] and N. Narita[3], (1)*Mie University*, (2)*JAPAN LUTHERAN COLLEGE*, (3)*Bunkyo University*

Background: Chemicals including thalidomide (THAL) and valproic acid (VPA) are known to induce autism when taken at early gestational stage in human. We have previously established autism model rats by exposing THAL or VPA to embryonic (E) day 9 rats (Pediatr Res, 52; 576: 2002, Int J Dev Neurosci, 23; 287: 2005). Migration disorder of serotonergic (5-HT) neurons was observed in the adult.
Objectives: Our objectives were to elucidate whether abnormalities of 5-HT neuronal development are also observed even in the embryonic stage. Molecular basis of 5-HT developmental abnormalities were also elucidated.
Methods: THAL, VPA, or vehicle was orally administered to early pregnant rats corresponding to human embryopathy related to autism, and then, embryos were dissected out for anti-serotonin immunohistochemistry. Embryos were also analyzed for the expression of certain genes including sonic hedgehog (shh), a modulator for serotonergic development, using whole mount in situ hybridization and real time PCR technique.
Results: Dramatic delay of serotonergic development was observed in the embryos of autism model rats. Expression of shh were perturbed in the embryos of autism rats.
Conclusions: These results indicate that two potential autism-inducing teratogens, THAL and VPA, may disrupt early 5-HT neuronal development in the embryos through the perturbation of shh signal pathway, and thus may cause irreversible changes observed in the adult.
Supports: Long-range Research Institute from the Japan Chemical Industry Association and Grants-in-Aid for Scientific Research (C) of Japan Society for the Promotion of Science.

82 157.2 Identification of regional molecular markers in the cortex, hippocampus, and amygdala for fine structural analysis in animal models of autism. M. Howell*, A. Bernard, C. Thompson, L. Ng, M. Hawrylycz and E. Lein, *Allen Institute for Brain Science*

Background: Microscopically, autistic patients have been reported to show alterations in the neocortex, hippocampus, and amygdala. The precise nature of these abnormalities is largely undefined due to limited sample size and limited resolution of traditional histological techniques. Animal models have been generated to gain insight into how known etiologic factors contribute to changes in brain structure and function. Analysis of neuropathology in these models has also been limited by the resolution of Nissl stains and the paucity of histological methods for identifying unique cell populations.

Objectives: To identify molecular markers which delineate specific neuroanatomical subregions and neuronal subtypes within the cortex, hippocampus, and amygdala for analysis of fine cytoarchitecture.

Methods: To identify gene markers that delineate anatomical boundaries we mined the *in situ* hybridization (ISH) expression patterns of over 20,000 transcripts contained in the Allen Brain Atlas. We identified the genes that most specifically demarcate individual cortical layers, and subregions of the hippocampus and amygdala. ISH expression patterns were then analyzed during development to determine when this specificity is first observed. The Allen Institute has also generated ISH data for ~600 genes in human visual (BA 17/18) and temporal cortex (BA 21/22).These data were analyzed to identify genes that delineate discrete populations of excitatory and inhibitory cell types in human cortex.

Results: This approach has led to the identification of molecular markers that are uniquely expressed in discrete brain regions in mouse and human brain. These markers are currently being used to analyze cytoarchitecture in animal models of autism including the $Mecp2^{308/y}$, Fmr1 KO, and Ube3a KO mice.

Conclusions: These techniques will allow us to more clearly define neuroanatomical abnormalities in animal models. Cell type-specific markers in human neocortex will also allow an analysis of fine cortical cytoarchitecture in postmortem tissue from patients with autism in the future.

83 157.3 Neuropathogenic Consequences of Dysregulated Immune Responses to Concomitant Immune Challenges. G. Rall* and C. Matullo, *Fox Chase Cancer Center*

Background: Although viral infections have been proposed as etiological triggers for certain central nervous system (CNS) disorders, including autism, the identification of specific, causative pathogens--and determination of how such infections contribute to CNS disease--have been largely unsuccessful.
Objectives: To determine if peripheral infections can contribute to neuropathogenic disease, we developed a model in which mice are infected with two, concomitant viral infections: one restricted to the CNS, and the other restricted to the periphery.
Methods: In this model, mice are infected with CNS-restricted measles virus (MV; Edmonston strain, 5000 plaque forming units; PFU), and peripherally restricted lymphocytic choriomeningitis virus (LCMV; Armstrong strain, 5000 PFU).
Results: While infection by either virus alone results in no illness, simultaneous co-infection with both viruses causes neuropathology and consequent disease in ~50% of infected mice. Moreover, in 100% of doubly-challenged animals, a greater than 10-fold increase in the number of CD8+ T cells in the CNS is observed by flow cytometry, as compared to single infection alone. A substantial proportion (~40%) of these CNS infiltrating CD8+ T-cells are of LCMV-specificity, as shown by GP33 and NP396 epitope tetramer staining and chromium release assays, implying that LCMV-specific T cells are being "mis-recruited" to the MV-infected CNS. Despite no apparent cross-reactivity between the viruses, T cell-mediated CNS disease is MHC-I dependent, and appears to be due to severe edema and neuroinflammation, resulting in brainstem herniation.
Conclusions: These results indicate that concurrent immune challenges can result in novel pathogenic outcomes as compared to either challenge alone. We propose that immune cell misrecruitment may be a novel mechanism by which CNS disease can occur.
This work was supported by a grant from the NIH (NS 40500), and a Basic Science award from Autism Speaks.

84 157.4 Intraventricular Infusions of Propionic Acid Increases Locomotor Activity, Neuroinflammation, and Monocarboxylate Transporter Immunoreactivity in Rats: Spaced vs Chronic Administration. K. A. Foley*, M. M. Gordon, A. R. Taylor, F. Boon, L. 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). Neuroinflammatory changes, alterations in fatty acid metabolism, and blood brain barrier (BBB) permeability may be involved in the pathophysiology of ASDs. Propionic acid (PPA) is a short chain fatty acid, a by-product of enteric bacteria, and a food preservative that enters systemic circulation and the CNS by passive and active transport. We have found that PPA in rats produces behavioral and brain changes similar to that seen in ASD patients.

Objectives: Compare behavioral and neuropathological effects of spaced and chronic intraventricular PPA infusions in rodents.

Methods: Male adult Long-Evans rats received intraventricular infusions of buffered PPA (0.26 M, pH 7.5, 4 mL/infusion) or 0.1 M phosphate buffered saline (PBS) vehicle. Frequency of infusions varied from twice daily/7 days to once weekly/5 weeks. Immediately following microinfusion, animals were individually placed into an automated open-field for 30 min and locomotor activity was measured. 24h after last infusion, animals were perfused and brains examined immunohistochemically for markers of innate neuroinflammation, BBB permeability, and fatty acid transport.

Results: PPA treated animals displayed significant increases in locomotor activity and repetitive behavior compared to controls. Weekly PPA treated animals were significantly greater than daily treated PPA animals. Preliminary data suggest increased innate neuroinflammation (GFAP, CD68, Iba1, IL-6), BBB permeability (rat IgG), and

monocarboxylate transporter-1 immunoreactivity in the white matter of weekly PPA animals than daily PPA animals.

Conclusions: PPA administration in rats increases locomotor activity and induces neuroinflammatory processes in the hippocampus and white matter that may model human ASDs. It appears that spaced (weekly) treatment may exacerbate PPA's effects compared to chronic (daily) treatment. Recurrent PPA administration may mimic recurrent infections of PPA producing gut bacteria, offering further support for the PPA rodent model of ASDs.

85 157.5 Altered Function of Peripheral Blood Natural Killer Cells in Children with Autism. A. Enstrom, C. Onore, L. Lit, I. Hertz-Picciotto, R. Hansen, J. P. Gregg, I. N. Pessah, F. Sharp, J. Van de Water and P. Ashwood*, *University of California at Davis*

Background: There is evidence of enhanced immune activity in post-mortem brain specimens from subjects with autism spectrum disorders (ASD) as well as immune dysregulation and autoimmune phenomena in the peripheral circulation. However, the exact nature and extent of the immune dysregulations in ASD have yet to be fully characterized. Natural killer (NK) cells, in particular, may play an important role in the development and course of neurodevelopmental disorders such as ASD. **Objectives:** Previously, we performed a genomic screen in peripheral blood obtained from 35 children with confirmed ASD and 12 matched typically developing control children. Gene expression of NK cell receptors and NK-related effector molecules, such as granzyme B and perforin, were significantly upregulated in ASD compared with controls. Expanding on these initial studies, we carried out functional and cellular analysis of NK cells in ASD. **Methods:** We performed NK cytotoxicity assays and flow cytometric analysis of NK effector molecules on blood obtained from 17 children with ASD and 16 matched typically developing general population controls enrolled in the CHARGE study. **Results:** Flow cytometric analysis of NK effector molecules demonstrated that there was increased production of perforin, granzyme B, and interferon gamma (IFNγ) under resting conditions in children with ASD compared with controls ($p<0.1$). However, following stimulation in the presence of NK specific K562 target cells, the ability of NK cells from children with ASD to kill target cells was significantly reduced compared with controls ($p<0.2$). Furthermore, under similar stimulation conditions the presence of perforin, granzyme B, and IFNγ in NK cells from ASD children was significantly reduced compared with controls ($p<0.001$). **Conclusions:** These findings suggest possible dysfunction of NK cells in children with ASD. Abnormalities in NK cells may represent a susceptibility factor in ASD and may predispose to the development of autoimmunity and/or adverse neuroimmune interactions during critical periods of development.

86 157.6 The Development of a PKU Monkey Model to Study the Behavioral Phenotype and Neuropathology of Autism in Non-Human Primates. L. A. Martin*[1] and D. G. Amaral[2], (1)*Azusa Pacific University*, (2)*UC Davis*

Background:
Although the etiology of most autism spectrum disorders (ASD) is unknown, it is estimated that between 10-20% of ASD cases are caused by known medical conditions. Included in the list of medical conditions known to cause autism is Phenylketonuria (PKU). PKU is a genetic disorder of metabolism involving the failure to covert phenylalanine to tyrosine resulting in both social and cognitive deficits.
Objectives:
In this study, PKU was simulated through the delivery of a high phenylalanine diet to pregnant rhesus monkeys. These hyperphenylalaninemic monkeys provide a potentially reliable model in which the behavioral phenotype and neuropathology of autism can be explored in non-human primates.
Methods:
Beginning halfway through their pregnancy, 3 rhesus monkeys were given 1 g/kg body weight of phenylalanine daily until they gave birth. Five pregnant rhesus monkeys were left

untreated to serve as controls. An additional group of 4 controls from an unrelated study were also included with the 5 controls in this study. Each infant was raised with their mother, and each mother/infant pair was socialized daily with an adult male and 5 additional mother/infant pairs. The infants were tested in a variety of behavioral paradigms aimed at exploring social and motor deficits in these monkeys. These paradigms included preweaning social group and mother/infant-mother/infant tetrad observations and postweaning social group and familiar and unfamiliar pairings.
Results:
Preweaning social group and tetrad observations revealed significant differences in the frequency and duration of social and communicative behavior of hyperphenylalaninemic versus control infants. Postweaning observations of social groups and familiar and unfamiliar pairings did not reveal any significant differences between hyperphenylalaninemic and control groups.
Conclusions:
Hyperphenylalaninemic monkeys provide a promising model to study the behavioral phenotype of autism in non-human primates. Establishing a reliable non-human primate model can lead to detailed studies of the neuropathology of autistic behavior.

87 157.7 OXIDATIVE STRESS IN AUTISM: EXPRESSION OF OXIDATIVE STRESS MARKERS IN A RAT MODEL OF THE HUMAN POSTMORTEM PROCESS. E. M. Sajdel-Sulkowska*, *Harvard Medical School/BWH*

Background: Oxidative stress has been implicated in the autistic pathology. It is supported by our observations of increased levels of oxidative stress markers measured in the postmortem brains, that may be affected by the postmortem process.

Objectives: To evaluate potential contribution of artifacts due to the postmortem interval (PMI) and tissue handling on brain levels of oxidative stress markers.

Methods: Using a rat model of human postmortem process we compared brain levels of 3-nitrotyrosine (3-NT) in tissue derived from rats exposed to (1) increasing PMI; (2) different storage temperatures; and (3) between freshly dissected and previously frozen brain tissue. Weanling SD, WKY and SHR rats were euthanized by CO_2 asphyxiation. Cerebellum, brain stem, frontal and other cortical tissues were dissected out. The levels of 3-NT were measured in brain homogenates prepared in the presence of protease inhibitors by a commercial 3-NT ELISA.

Results: Remarkably, the PMI up to 4 hours either at 4^{o}C or at RT did not significantly affect cerebellar 3-NT levels ranging from 4-7 micromoles/gram. The most significant increase in 3-NT levels occurred between 4 and 8 hours at RT, with no further changes up to 24 hours at RT. On the other hand cortical regions appeared to be more sensitive to the PMI length and storage temperature with 7.8% increase at 4^{0}C and 23.5% increase after 4 hours at RT.

Conclusions: Considering the relative mass of animals, that determines the rate of body cooling, the postmortem changes in oxidative stress markers are likely to be relevant only under extremely long PMIs (>48 hours) in humans. Furthermore, the postmortem process appears to be brain region-specific with the cerebellum being relatively spared. Thus our previous data on the increased oxidative stress damage in the autistic cerebellum measured in cases matched for PMI is most likely related to autistic pathology.

88 157.8 Influence of prenatal exposition to valproic acid in juvenile play behavior in rats. M. L. R. Campos*[1], H. M. Cavalcanti[1] and M. T. Mercadante[2], (1)*Universidade Presbiteriana Mackenzie*, (2)*Federal University of São Paulo*

Background: The comprehension of cerebral dysfunctions related to the autism spectrum disorders (ASD) is important to develop new therapeutic interventions. Animal models are among the powerful tools to address this issue. The challenge is to build a model presenting behavioral alterations in the three domains of the ASD. Today, only one model seems to fulfill this demand, the BTBR mice (McFarlane et al, 2007). The prenatal

expositions to valproic acid (VPA) in rats may be an alternative to this task.

Objectives: The aim of this research is to analyze the interference of VPA in the juvenile social play in wistar rats.

Methods: Pregnant females were treated by "gavage" with 800 mg/kg of VPA (SIGMA) at 9th day of gestation (DG). At 28th and 29th postnatal days. pairs composed by animals from the same group were recorded for 10 min. each day. The juvenile play was evaluated by the intruder/resident paradigm. The exploratory locomotion, the playing soliciting and the social play were rated by blind investigators.

Results: The results of the experiment shows significant alterations in playing soliciting and social play in treated animals. Exploratory locomotion was preserved.

Conclusions:Prenatal exposure to valproic acid at 9th DG produces alterations in the juvenile social interactions that can be related to those described in autistic persons. In other study, the same animals showed impairments in learning processes and routine flexibility.

89 157.9 Intraventricular Propionic Acid - Induced Hyperactivity: Role of NMDA and Dopamine Receptor Antagonists in a Novel Propionic Acid Rodent Model of Autism. J. Martins*, K. A. Foley, J. E. Hoffman, F. Boon, L. Tichenoff, R. Taylor, Y. Mohammad-Asef, D. P. Cain, M. Kavaliers, K. -. P. Ossenkopp and D. F. MacFabe, *University of Western Ontario*

Background: Dietary or gut related factors have been proposed to alter behaviour in autism spectrum disorders (ASDs). Propionic acid (PPA) is an enterically produced short chain fatty acid and also a common food preservative. PPA can affect a variety of processes including cellular metabolism, gene expression, and neurotransmitter synthesis and release. Intracerebrocventricular (ICV) infusions of PPA in adult rats have been used to model ASDs. Pharmacological agents affecting glutamatergic and dopaminergic systems have been suggested as treatments for ASDs.

Objectives: To evaluate the role of NMDA and dopaminergic receptor antagonists on PPA induced locomotor activity increases in rats.
Methods: Adult male Long-Evans rats were habituated for 3 days in the locomotor activity system. Rats were then pretreated with intraperitoneal (IP) injections of either the NMDA receptor antagonist MK-801 (0.3 mg/kg), the dopamine D2 receptor antagonist raclopride (0.3 mg/kg), or vehicle (phosphate buffered saline, 0.1 M) 30 min prior to ICV infusions of PPA (500 µg/µL buffered to pH 7.5) or vehicle twice daily for 4 consecutive days. After the second PPA infusion on each treatment day, animals were individually placed into automated open fields (Versamax) where various locomotor activity variables were quantified and then analyzed.
Results: Rats pretreated with MK-801 prior to PPA treatment did not alter locomotor activity, with the exception of stereotypic movements. However, preliminary results suggested rats pretreated with raclopride prior to PPA treatment exhibited a decrease in hyperactivity.
Conclusions: The dopamine D2 receptor systems may play a role in the PPA enhanced locomotor response in rats.

90 157.10 Cytoarchitectonic abnormalities in the amygdala of mice infected with maternal influenza. I. Van Kooten*[1], L. Shi[2], H. W. M. Steinbusch[3], H. Van Engeland[4], P. Patterson[5] and C. Schmitz[3], (1)*School for Mental Health and Neurosciences, Div. Cellular Neuroscience*, (2)*California Institute of Technology*, (3)*Dept. Psychiatry & Neuropsychology, Div. Cellular Neuroscience*, (4)*University Medical Center-Utrecht*, (5)*Biology Division*

Background: Autism is a neurodevelopmental disorder with a strong genetic component and several known environmental risk factors, such as maternal viral infection, which has been shown to increase the risk for autism. In addition, its onset of etiology is likely to occur during prenatal development.
Objectives: We propose that intranasal human influenza virus infection to pregnant mice at embryonic day 9 will result in morphological alterations in the offspring's amygdala resembling alterations found in the amygdala

of patients with autism.
Methods: Using high precision design-based stereology, we investigated mean total volume of the amygdala (AMG), cortical grey matter (CGM) and total hemisphere of exposed, sham and control offspring at postnatal day 25 (P25). In addition, we examined mean total neuron number and mean total neuron density in the lateral and basolateral part of the amygdala.
Results: Preliminary results of the present study showed preserved volumes of the total hemisphere of the offspring at P25. We are currently focussing on a detailed analysis of the cytoarchitecture of the amygdala (i.e., analyzing neuron densities and numbers).
Conclusions: These results might contribute, as an animal model, to our understanding of the biological basis for interindividual differences in morphological alterations found in the brains of patients with autism.

91 157.11 Influence of prenatal exposition to valproic acid in learning process and flexibility routines in rats. C. S. Paula*[1], H. M. Cavalcanti[1], M. L. R. Campos[1] and M. T. Mercadante[2], (1)*Universidade Presbiteriana Mackenzie*, (2)*Federal University of São Paulo*

Background: The comprehension of cerebral dysfunctions related to the autism spectrum disorders (ASD) is important to develop new therapeutic interventions. Animal models are among the powerful tools to address this issue. The challenge is to build a model presenting behavioral alterations in the three domains of the ASD. Today, only one model seems to fulfill this demand, the BTBR mice (McFarlane et al, 2007). The prenatal expositions to valproic acid (VPA) in rats may be an alternative to this task.

Objectives: The aim of this research was to analyze the interference of VPA in the learning process and flexibility of routines in wistar rats
Methods: Pregnant females were treated by "gavage" with 800 mg/kg of VPA (SIGMA) at 9th day of gestation (DG). The sample was composed by 20 male rats – 10 from the control group and 10 from the experimental group. The learning capacity and capacity of maintaining flexible routines are evaluated by the T maze test at 120th post natal day (PND). At t 162nd PND, the capacity of habituate was measured by the open field test. The learning, discrimination and reversions capacity were evaluated by the box conditioning working at 198th PND.

Results: The results show that the VPA interfered in the capacities of learning, flexibility of routine, habituate and reversion of what is learned.

Conclusions:Prenatal exposure to VPA at 9th DG produces alterations in the learning processes and flexibility that can be related to those described in autistic persons. In other study, the same animals showed social impairments.

92 157.12 Time-of-Flight Secondary Ion Mass Spectroscopy (ToF-SIMS) of Brain Tissue in a Novel Propionic Acid Rodent Model of Autism - Evidence of White Matter Edema, Increased Oxidative Stress and Altered Lipid Profiles. D. F. MacFabe*, H. Y. Nie, J. T. Francis, A. R. Taylor, L. J. Tichenoff, M. J. Walzak, W. H. Chang and L. Lau, *University of Western Ontario*

Background: Altered neuroinflammatory, lipid and oxidative stress profiles are found in autism spectrum disorders (ASDs). Dietary, gastroenterological and immunological factors have been implicated in ASD symptomatology. Propionic acid (PPA) is a short chain fatty acid, a product of enteric bacteria, and a food preservative. PPA has widespread effects on the above factors and can elicit consistent brain and behavioural changes in rodents reminiscent of ASDs. Time-of Flight-Secondary Ion Mass Spectroscopy (ToF-SIMS) is a powerful imaging technique to examine widespread ASD related biochemical markers in brain.
Objectives: To examine the effects of chronic infusions of PPA on behaviour, ToF-SIMS molecular imaging and traditional immunohistochemistry .
Methods: Adult rats received intraventricular infusions of PPA (500ug/ul, pH 7.5) or PBS vehicle twice daily for 7 treatment days. Immediately following microinfusion, animals were individually placed into an automated open field (Versamax) and a variety of locomotor activity variables were assessed for 30min. Animals were sacrificed and brain

sections examined via ToF-SIM imaging, or neuropathologically (innate neuroinflammatory markers).
Results: PPA infusions produced increased locomotor activity. ToF-SIMS analysis of PPA treated rat brain revealed clear images of forebrain structures (neocortex , external capsule, thalamus, hippocampus) which were grossly similar to control brain. However, ToF-SIMS showed increased Na, Cl, and N derivatives in external capsule, consistent with extracellular edema and increased oxidative stress. PPA reduced signal intensity of cholesterol and phosphatidyl choline in white matter. Effects were more extensive than innate neuroinflammatory changes(GFAP, CD68, IbA1).
Conclusions: PPA infusions produced behavioural, neuropathological and molecular imaging changes in rats reminiscent of ASDs. Findings are consistent with ASD as a white matter disorder of increased oxidative stress, inflammation and altered lipid profiles. ToF-SIMs is a powerful technique to examine neurological disorders. Findings offer further support for PPA in rodent model for ASDs, providing a plausible dietary/gut/CNS link to this disorder.

93 157.13 THE AUTISM-ASSOCIATED GENE, ENGRAILED 2 (EN2), HAS AGE DEPENDENT EFFECTS ON CEREBELLAR GRANULE PRECURSOR PROLIFERATION AND DIFFERENTIATION WHEN OVEREXPRESSED IN VITRO. I. Rossman*[1], L. Lin[1], S. Kamdar[2], J. H. Millonig[2] and E. DiCicco-Bloom[1], (1)*UMDNJ-RW Johnson Medical School*, (2)*UMDNJ-Robert Wood Johnson Medical School*

Background: Given that *EN2* association with autism spectrum disorder (ASD) has been replicated in multiple datasets by several labs, and *En2* mutants display cerebellar neuropathology similar to ASD, we have been defining developmental functions. Previously we found *En2* expression promotes cerebellar granule neurogenesis in mice and rats.

Objectives: To determine whether *En2* ontogenetic functions in cerebellar granule neuron precursors (GNPs) exhibit age-dependent effects on proliferation and differentiation.

Methods: *En2* cDNA was cloned into an EGFP-containing over expression vector, as described (Benayed *et al* 2005). Cultured mouse or rat GNPs harvested at postnatal (P) day 4, P7, and P10 were transfected with GFP alone (control) or *En2*+GFP (*En2*), and fixed 24h later. Proliferation was assessed using thymidine analog BrdU immunocytochemistry. Neuronal differentiation was defined as cells bearing processes ≥ 2-cell bodies. GFP+ cells were immunostained for proliferation and cytoskeletal markers, and assessed by fluorescence microscopy.

Results: *En2* overexpression reduced mitotic marker BrdU 75% and 67% at P4 and P7, respectively, but had no effect at P10. Further, overexpression elicited a 2-fold increase in GNPs exhibiting neuronal processes at P4 and P7, but only a 25% increase at P10. Additionally, *En2* overexpression reduced BrdU labeling and increased differentiation identically in P7 wildtype and *En2* knockout mouse GNPs.

Conclusions: Overexpression of *En2* facilitates GNP cell cycle exit and neuronal process outgrowth, indicating the gene promotes the transition from proliferation to differentiation, consistent with postnatal patterns of gene expression. The magnitude of these effects diminished with increasing postnatal age, suggesting *En2* functions are modulated by cell-intrinsic signals. Additionally, since *En2*-naïve and WT GNPs respond identically to *En2*-overexpression, postnatal function is not dependent on earlier *En2* expression. Therefore these data imply that *En2* functions should be studied in each developmental epoch in which it is expressed to characterize potentially diverse roles.

94 157.14 Pediatric Vaccines Influence Primate Behavior, and Brain Stem Volume and Opioid Ligand Binding. A. Wakefield*[1], C. Stott[1], B. Lopresti[2], J. Tomko[2], L. Houser[2], G. Sackett[3] and L. Hewitson[2], (1)*Thoughtful House Center for Children*, (2)*University of Pittsburgh*, (3)*Washington National Primate Research Center*

Background:

Abnormal brainstem structure and function have been reported in children with autism. Opioid receptors play key roles in neuro-ontogeny, are present in brainstem nuclei, and may influence aspects of autism. Childhood vaccines are a possible causal factor in autism and while primates are used in pre-clinical vaccine safety testing, the recommended infant regimen (1994-1999) has not been tested.

Objectives:

The objective of this study was to compare brain stem volume and opioid binding in rhesus infants receiving the recommended infant vaccine regimen.

Methods:

Rhesus macaques were administered vaccines adjusted for age and thimerosal dose (exposed; N=13), or placebo (unexposed; N=3) from birth onwards. Brainstem volume was measured by quantitative MRI, and binding of the non-selective opioid antagonist [^{11}C]diprenorphine (DPN) was measured by PET, at 2 (T1) and 4 (T2) months of age. Neonatal reflexes and sensorimotor responses were measured in standardized tests for 30 days.

Results:

Kaplan-Meier survival analyses revealed significant differences between exposed and unexposed animals, with delayed acquisition of *root*, *suck*, *clasp hand*, and *clasp foot* reflexes. Interaction models examined possible relationships between time-to-acquisition of reflexes, exposure, [^{3}C]DPN binding, and volume. Statistically significant interactions between exposure and time-to–acquisition of reflex on overall levels of binding at T1 and T2 were observed for all 18 reflexes. For all but one (*snout*), this involved a mean increase in time-to-acquisition of the reflex for exposed animals. In each model there was also a significant interaction between exposure and MRI volume on overall binding.

Conclusions:

This animal model examines the neurological consequences of the childhood vaccine regimen. Functional and neuromorphometric brainstem anomalies were evident in vaccinated animals that may be relevant to some aspects of autism. The findings raise important safety issues while providing a potential animal model for examining aspects of causation and disease pathogenesis in acquired neurodevelopmental disorders.

95 157.15 Modeling reciprocal social interactions, and communication, in mice. D. C. Blanchard*, H. Arakawa and R. J. Blanchard, *University of Hawaii*

Background: Autism is defined in terms of three symptom groupings; deficiencies in reciprocal social interactions, deficiencies in communication, and the presence of restricted or ritualized behaviors. These three are not well correlated, nor do they necessarily respond similarly to treatment, suggesting that they may be under the control of different genetic and environmental mechanisms. Objectives: These factors indicate the desirability of selection and analysis of animal models that provide independent measures of the behaviors involved in these groupings. This abstract reflects a program of development of models of social interaction and communication. Methods: An ethological model of reciprocal social interaction involves C57BL/6J mice housed in stable groups in Visible Burrow Systems. Major measures include huddling during both active and inactive diurnal cycles, and approaches of mice, analyzed in terms of specific trajectory. An additional program on scent marking analyzes this major communication system in mice and protocol variations within the scent marking paradigm enable assessment of multiple aspects of commication in this species. Results: (VBS) Approaches from the rear elicit flight in the recipient suggesting that this is a nonamicable form of approach, whereas approaches from the front do not result in flight. Further, the response of the recipient to frontal approach provides further information about the reciprocity of the interaction. (Scent marking) Communication in mice can be precisely and selectively measured by scent marking, and the

behavioral response to urinary scent marks. We provide data assessing social communication; responsivity to social signals; social recognition; social and nonsocial learning. Conclusions: These results suggest that behaviors directly relevant to the major symptom-groupings of autism can be characterized in mice. Mice showing variation in these behaviors are not autistic, but such behaviors can provide a highly relevant approach to analysis of genetic and experimental factors modulating these behaviors in autistic individuals.

96 157.16 Microarray Analysis of GI Tissue in a Macaque Model of the Effects of Infant Vaccination. S. J. Walker*[1], E. K. Lobenhofer[2], E. Klein[3], A. Wakefield[4] and L. Hewitson[3], (1)*Wake Forest University Health Sciences*, (2)*Cogenics, a Division of Clinical Data*, (3)*University of Pittsburgh*, (4)*Thoughtful House Center for Children*

Background: There has been considerable debate regarding the question of an interaction between childhood vaccinations and adverse sequelae in the gastrointestinal tract, immune system, and central nervous system of some recipients. These systems, either singly or in combination, appear to be adversely affected in many ASD children. Although pre-clinical tests of individual vaccines routinely find the risk/benefit ratio to be low, previously there has not been a study to examine the effects of the comprehensive vaccination regime currently in use for infants.

Objectives: This study was designed to evaluate potential alterations in normal growth and development resulting from the vaccine regimen that was in use from 1994-1999. Specifically, this portion of the study was to compare the gene expression profiles obtained from gastrointestinal tissue from vaccinated and unvaccinated infants.

Methods: Infant male macaques were vaccinated (or given saline placebo) using the human vaccination schedule. Dosages and times of administration were adjusted for differences between macaques and humans. Biopsy tissue was collected from the animals at three time points: (1) 10 weeks [pre-MMR1], (2) 14 weeks [post-MMR1] and, (3) 12-15 months [at necropsy]. Whole genome microarray analysis was performed on RNA extracted from the GI tissue from 7 vaccinated and 2 unvaccinated animals at each of these 3 time points (27 samples total).

Results: Histopathological examination revealed that vaccinated animals exhibited progressively severe chronic active inflammation, whereas unexposed animals did not. Gene expression comparisons between the groups (vaccinated versus unvaccinated) revealed only 120 genes differentially expressed (fc >1.5; log ratio $p<0.001$) at 10 weeks, whereas there were 450 genes differentially expressed at 14 weeks, and 324 differentially expressed genes between the 2 groups at necropsy.

Conclusions: We have found many significant differences in the GI tissue gene expression profiles between vaccinated and unvaccinated animals. These differences will be presented and discussed.

Poster Presentations Program

158 Play Posters

97 158.1 Pretend play and communication in children with autism : about dysregulation. R. Blanc*[1], S. Roux[2], C. Barthelemy[2] and J. L. Adrien[3], (1)*University Paris5 and INSERM 619*, (2)*INSERM 619*, (3)*University Paris5*

Background: Autism is a severe developmental disorder characterized by social withdrawal, disorders of communication and symbolic play, resistance to change, and bizarre, stereotyped behaviors. We hypothesized that the difficulties of autistic child displays originate from basic disorders of organisation and regulation of actions according to environmental changes. Defined by difficulties in spontaneous production of actions and in maintaining and breaking off actions intentionally, this disorder impoverishes general mental representation skills, which are the basis of symbolic play and of development of communication.

Objectives: The main aim of this study was to investigate the regulation of actions involved in a symbolic activity, i.e.pretend play, in children with autism by comparing them to children with mental retardation and with normal development, strictly matched on developmental levels. A further aim was to investigate the relationship between the development and functioning of pretend play and the development of communication.

Methods: 21 children with autism were compared with 14 children with mental retardation and 15 normal children matched on overall and verbal developmental ages. Regulation of play activities was studied using original and appropriate clinical tools and from the assessment of two types of activity, one spontaneous and the other semi-directed. Communication development was assessed using ECSP.

Results: The results showed that regulation of play activities was very disordered in children with autism compared to the other groups, with breaking off, dissociation and instability of actions. However, in directed play their actions were more structured and corresponded to a better developmental level. In addition, dysregulation was associated with delayed, heterogeneous development of communication skills.

Conclusions: The results of this study are in line with our hypotheses and emphasize the role of the assessment of symbolic play for a differential diagnostic approach and the value for the therapeutic strategies based on regulation processes and symbolic play.

98 158.2 The Relation Between Joint Attention, Pretend Play, and Imitation in Younger Siblings of Children with ASD. L. E. McLean*, E. E. Malesa and T. A. Walden, *Vanderbilt University*

Background: Children with ASD (autism spectrum disorders) demonstrate early deficits in responding to joint attention (RJA), imitation, and spontaneous pretend play. These early abilities are of particular importance in early development, as empirical and theoretical evidence suggest that they are developmental precursors of subsequent deficits in ASD such as theory of mind. Parallel development of RJA, pretend play, and imitation in ASD and TD (typically developing) children is evidenced by the correlations in level of ability of these skills. While relations among RJA, pretend play, and imitation have been found in both TD and ASD, they have not yet been examined in younger siblings of children with ASD, who are at a higher risk for ASD and autism-related symptomology. Objectives: To examine the relation between RJA, imitation, and spontaneous pretend play in younger siblings of children with ASD (SIBS-ASD).
Methods: The Screening Tool for Autism in Two-Year-Olds (STAT) and an RJA research measure were administered to 65 SIBS-ASD (Mean CA=15.4 mos., range 12-24 mos.). Items from the STAT designed to assess imitation and spontaneous pretend play were used in analyses.
Results: RJA, pretend play, and imitation were significantly related (imitation and pretend play: $r=.28$, $p<.5$; imitation and RJA: $r=.43$, $p<.1$; pretend play and RJA: $r=.40$, $p<.1$) in this sample of SIBS-ASD.
Conclusions: The same relation between RJA, imitation, and pretend play found in ASD and TD is also present in SIBS-ASD. The finding that these three proposed precursors to theory of mind ability are related in SIBS-ASD may be valuable in future theory of mind research.

99 158.3 Are problems of pretend play in autism due to mentalising or executive difficulties?. C. Jarrold*, *University of Bristol*

Background: Individuals with autism show difficulties in pretence, but the cause of this deficit remains unclear. It may relate to a failure to grasp the metarepresentational nature of pretence, which in turn links to individuals' problems in theory of mind. Alternatively, executive impairments might make it difficult for individuals to inhibit the true state of affairs in pretence. Objectives: Experiment 1 varied the theory of mind requirements of pretend tasks, while Experiment 2 manipulated executive demands by comparing comprehension of object substitution and the attribution of absent properties in pretence; object substitution has a greater executive load because it involves inhibiting objects' true identity. Methods:

Experiment 1 presented 37 typically developing children, and 34 children with autism, with two tests of comprehension of pretence. Both involved scenarios in which protagonists held different pretend views, however only one condition required the participant to represent their mental states (ToM condition). Experiment 2 compared 16 typically developing children, and 16 children with autism, on tests of pretence comprehension involving object substitution or attribution of absent properties. Results: In Experiment 1, individuals' performance on the ToM condition was dependent on their theory of mind status, but theory of mind status had no effect on performance in the non-ToM condition. Once theory of mind status was accounted for, the two groups did not differ across the two pretend conditions, $p = .98$. In Experiment 2 there was a trend for an interaction, $p = .8$, such that individuals with autism had greater problems with object substitution. Conclusions: Experiment 1 shows that many pretend tasks do not require theory of mind. In contrast, there is evidence that executive difficulties make certain aspects of pretence particularly difficult for individuals with autism.

100 158.4 Deficits in object substitutions in autism: In search of an explanation. C. Dissanayake* and R. Kelly, *La Trobe University*

Background: The study on symbolic play in children with high-functioning autism (HFA) to be reported here builds on the results from an earlier study in which we found a specific, and not general, impairment in the symbolic or pretend play of young children with high functioning autism (HFA).

Objectives: The aim in this study was to explore whether either of two executive functioning hypotheses - the generativity and inhibition impairment hypotheses - can account for the difficulty children with autism have in engaging in object substitutions.

Methods: A group of 20 children with HFA and 20 typically developing (TD) children were matched on chronological age, verbal and overall mental age, performance IQ, full-scale IQ, and basic information processing speed. The groups were compared on their executive functioning abilities and symbolic play abilities, and the relationship between these abilities were also examined in order to explore the role of executive functions in their pretend play.

Results: The results, once again, indicated that the children with HFA displayed few symbolic play impairments relative to the TD children under both structured and unstructured conditions. However, they were specifically impaired in their ability to substitute objects in play. No significant group differences were found on the experimental measures of executive functioning, although parents reported inhibition difficulties amongst the children with autism. Although the results indicated that the executive functioning abilities of the children with HFA were associated with their symbolic play skills, the research findings did not support the generative or the inhibition impairment hypotheses.

Conclusions: While the results confirm our previous finding of a specific deficit in object substitution in autism, none of the current theoretical accounts of pretence can explain this finding.

101 158.5 TWO THEORETICAL MODELS OF PRETEND PLAY: AN EMPIRICAL STUDY IN AUTISM. E. Grandi*, C. Becchio, M. Del Giudice and L. Colle, *Center for Cognitive Science - University of Turin*

Background: A wealth of studies have pointed out pretend play is one of the areas of development most intensely affected in autism. Although the failure to use an object symbolically is considered one of the key marker of the pathology, there is a disagreement about the nature of this impairment. On one hand, the meta-representational hypothesis (Leslie, 1987), proposes that children with autism lack the fundamental ability of *decoupling* in order to either produce or comprehend pretend acts. On the other hand, the recent Cultural Learning approach (Rakoczy, 2006) considers pretence essentially a social activity, acquired, in its early forms, through imitation of adults' pretending acts whereas more

mature forms involve the ability to share intentions and creativity. In this view, the lack of the fundamental motivation to share might preclude cooperative forms of pretending in autism.

Objectives: To investigate early characteristics of pretend play deficit in autism in order to test the predictions deriving from two theoretical accounts.

Methods: 20 preschoolers with autism and 20 preschoolers with typical development, matched by mental age, were presented with a) four imitation tasks involving pretend actions (brushing teeth, washing hands, eating from a basket, drinking from a cup), b) a free pretend play situations (have a tea) and c) an object substitution task (using a banana like a telephone).

Results: Preliminary results reveal a preserved ability to comprehend and produce simple pretending actions in scaffolded situation (imitation tasks) in children with autism compared to control group, but their performance shows little imagination and creativity especially in free play situation, where they produced fewer novel acts and tend to imitate adult's actions.

Conclusions: Our results support Cultural Learning approach, showing that the ability to pretend is not totally affected in autism, but the deficit seems to be limited to forms of pretending that involve shared intentions.

102 158.6 PLAY GROUPS FOR CHILDREN WITH ASPERGER SYNDROME. A. Giannaka* and J. L. Adrien, *UNIVERSITY OF PARIS V - RENE DESCARTES*

Background: Studies have documented effective peer social intervention approaches for children with Asperger Syndrome. The children's success in establishing and maintaining friendships relates to their capacity to enter peer groups and coordinate enjoyed play activity. Objectives: This longitudinal study (3years) consisted of a psycho educative intervention aimed to develop the children social and imaginative potential, playing with peers, making friends and favour ting their social integration.
Objectives: n/a
Methods: 10 children with Asperger syndrome, 6-13 years old, participated in this study in Greece. Each child participated in a social skills group with 3 others "typical" children of the same age and development. Play group sessions met 1 time per week for 1 hour over 3 years period. The intervention was based upon a member of activities from different programs: Tacade skills for the primary school, J. Baker's programme, Battlori's artistic expression games, traditional Greek games, drama, music, role play based on friendship models in fairy tales, physical activities, group art work. At school, in the recreation ground, 10 educational assistants carried out a well-structured programme consisting of a variety of activities based on the interests of each child and his peers and encourage interactive play, the child participation in games and potential friendships. The assessment tools are the T. Attwood's Friendship Observation Schedule (2004), the J. Baker's rating form (2003), the C. Gray's questionnaire on rating social behaviour (1993), the Ingram-Troxell Playground Observation Checklist (2007).
Results: Children have improved their conversational ability, they start play and participate in a group in the recreation ground, they express their emotions more clearly and their social behaviour became more appropriate.
Conclusions: The participation of the children with Asperger Syndrome in play groups activities with typical children and the multidisciplinary approach of the intervention actualize their potential to socialize and reinforce their relations with peers.

103 158.7 THE RELATION BETWEEN SOCIAL ENGAGEMENT AND PRETEND PLAY: EVIDENCE FROM AUTISM. P. Hobson*, J. A. Hobson and S. Malik, *University College London and Tavistock Clinic, London*

Background:

What is atypical about symbolic play among children with autism? In a previous study (Hobson & Hobson, 2007), matched children with and without autism were similar in the 'mechanics' of play, but those with autism showed less 'playful pretence'.

Objectives:

To test predictions that:

(i) Across non-typically developing groups, limitations in pretend play would be associated with social/communication impairment

(ii) Children with autism would show specific deficits in 'playful pretend'.

(iii) 'Playful pretend' scores would correlate with social/communication impairment, even after controlling for limitations in pretend play ability.

Methods:

Participants were (i) 60 atypically developing children (28 with autism, 15 with autism spectrum disorders, and 17 with learning disabilities but without autism) between the ages of three and nine years, matched for chronological age, verbal mental age and gender, and (ii) 33 typically developing three to six year old children. Children were administered the Preschool Language Scales – III; Autism Diagnostic Observation Schedule (ADOS); and Test of Pretend Play (ToPP), also coded by two blind judges for four aspects of playful pretence: Investment in symbolic meanings (ICC = .93), Fun (ICC = .92), Creativity (ICC = .96) and Self-awareness in creating new meanings (ICC = .88).

Results:

Children in the atypically developing groups were not significantly different in ToPP scores. However, limitations in ToPP pretend play were associated with social/communication impairment (scores on the ADOS), $r(60) = -.28$, $p < .5$, two-tailed). Children with autism, but not those with ASD, showed specific deficits in playful pretence relative to the LD group, $t(43) = 2.55$, $p < .5$, two-tailed. 'Playful pretend' scores were correlated with social/communication impairment, even after controlling for limitations in pretend play ability, partial-$r(57) = -.29$, $p < .5$.

Conclusions:

Specifically social/communicative contributions to creative pretend play are limited among children with autism.

104 158.8 The Development of Pretend Play in Pre-school Children with Autism. H. M. Marwick*, *University of Strathclyde*

Background: Recent theory on the absence or limitations of the pretend play of children with autism has centered on the limitations of social interactive engagement and joint attention for these children, which underpins pretend play development.

Objectives: This paper examines the development of pretence in play for a group of 8 preschool children with autism to compare the sequence of imaginative play development with that of typically developing children and to look at the role of joint attention and interactive context in this development.

Methods: The children had all taken part in a joint-play intervention over a 5 month period and had limited engagement and play at the outset of the study. All went on to present conventional symbolic representation in play and meta-representational abilities, and a smaller number became involved in joint-imaginative scenarios and role-play. The onset and development of episodes of symbolic representation and pretence for the children is tracked as they appeared within the intervention sessions over 14 weeks, and sequencing in symbolic representation, and the role of joint attention and interactive context is examined.

Results: Results showed that for several children the entry into pretend play began with contingent imitation within joint attention. Conventional representation in 'functional' use of toys and objects appeared before meta-representation. Soft toys and puppets were used facilitatively by adult play partners to model interactions in imaginative scenarios and 6 of the children went on to give perspective giving responses to soft toys in pretend play. Of these children, 4 went on to become involved in imaginative play scenarios where they pretended to 'do' something, such as going shopping

Conclusions: It is concluded that the sequence of symbolic representation and imaginative play development for children with autism mirrors that of typically developing children and rests on joint attention in social interactive engagement.