Hyatt Regency Montreal
Montreal, Canada

Thursday, June 1\textsuperscript{st}, 2006 –
Saturday, June 3\textsuperscript{rd}, 2006
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<th>Time</th>
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<th>Friday, June 2, 2006</th>
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<tbody>
<tr>
<td>7:30 – 8:30</td>
<td>Breakfast (Grand Salon Foyer)</td>
<td>Breakfast (Grand Salon Foyer)</td>
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<tr>
<td>8:30 – 9:30</td>
<td>Tom INSEL Autism: What do we Know? What do we Need? (Grand Salon A, B, C)</td>
<td>Sally ROGERS Imitation Difficulties in Autism (Grand Salon A, B, C)</td>
<td>Conrad GILLIAM Genomic and Bioinformatic Approaches (Grand Salon A, B, C)</td>
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<tr>
<td>9:30 – 9:50</td>
<td>Coffee break</td>
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<tr>
<td>9:50 – 11:30</td>
<td>Invited Educational Symposia Early Detection (Grand Salon AB)</td>
<td>Neuroimaging (Grand Salon AB)</td>
<td>Invited Educational Symposia Psychopharmacology (Grand Salon C)</td>
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<tr>
<td>11:30 – 1:00</td>
<td>LUNCH /Poster 1</td>
<td>LUNCH /Poster 3</td>
<td>LUNCH /Poster 5</td>
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<tr>
<td>1:00 – 2:20</td>
<td>Oral Sessions 1, 2, 3 Brain Structure1 (Grand Salon AB)</td>
<td>Oral Sessions 7, 8, 9 Early Diagnosis (Grand Salon AB)</td>
<td>Oral Sessions 13, 14, 15 fMRI (Grand Salon AB)</td>
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<td>2:20 – 2:50</td>
<td>Coffee break</td>
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<tr>
<td>2:50 – 4:10</td>
<td>Oral Sessions 4, 5, 6 Brain Structure2 (Grand Salon AB)</td>
<td>Oral Sessions 10, 11, 12 Early Detection (Grand Salon AB)</td>
<td>Coffee break</td>
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<tr>
<td>4:10 – 6:30</td>
<td>Poster Session 2</td>
<td>Poster Session 4</td>
<td>Poster Session 6</td>
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- **Poster Sessions are held in the Jeanne-Mance room on Level 6.**
- **Poster sessions (5-hour each):** Posters must be up by 8:00 AM for morning sessions and by 1:00 PM for afternoon sessions. Poster presenters must be next to their poster for the last 1.5 hours: from 11:30 to 1:00 (morning sessions) and from 4:30 to 6:00 (afternoon sessions).
- **Invited Education Symposium:** Each has 3-4 thematic state-of-the-art lectures of approximately 30 minutes each.
- Each oral session has 3 or 4 talks with 5 minutes of discussion each.
- **General Reception:** *Hors d'oeuvres* and beverages will be served on the terrace adjacent to the poster session in the Jeanne-Mance room on level 6.
- **Breakfast & Lunch can be eaten in the Alfred-Rouleau room (level 4) or on the terrace connecting to Jeanne-Mance on level 6.**
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<td>Poster Session #6 ........................................ 198-221</td>
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Welcome to the 5th annual International Meeting for Autism Research (IMFAR). We are very pleased to be able to host this International Meeting in Montreal – the first meeting outside of the USA since the inception of the International Society for Autism Research (INSAR) 4 years ago. Montreal is noted for its international ambience and many fine restaurants, and it is typically quite beautiful this time of year.

IMFAR is growing! We received more than 500 abstract submissions this year, which is about 30% more than last year. Anticipating this growth, we had already planned to extend the meeting from two and a half days, to three full days. We hope that the increase in length still meets most of your needs.

We have made a number of other changes to the format of the meeting. In response to feedback from last year, we have reduced the number of oral sessions running in parallel, so that this year there are only two or three symposia running concurrently at any one time and only 87 oral presentations in total (about a third less than that of last year). Commensurate with this, we have increased the number of poster presentations, a format that many presenters find preferable since it allows more in depth intellectual exchanges. For each poster session, there is included a range of different themes, covering topics that should be of interest to basic scientists, as well as the more clinically-oriented researcher.

This year’s meeting also has dedicated the morning sessions to Keynote Addresses and Invited Educational Symposia. The goal of these is to provide a broad audience with digestible, up to date information in areas of autism research outside one’s own specific specialty. New research findings will be presented in the Poster Sessions, as well as in groups of three parallel Oral Presentation Sessions each afternoon.

Clearly these changes to the format will alter the feeling of the meeting and we will be eager to hear from each of you about the effectiveness of these changes as we make plans for next year’s meeting. Please give us your appraisal by completing the online feedback form on the IMFAR home page.

We wish to thank the many contributors to INSAR and IMFAR. The success of the meeting is due to the dedication and hard work of many individuals, including the INSAR board, the Scientific Program Committee, and the generosity of those who provide funding for the meeting. We are also extremely grateful for the continued financial support for this meeting from several private foundations, including Cure Autism Now (CAN), the National Alliance for Autism Research/Autism Speaks (NAAR/AS), the Autism Society of America (ASA), as well as for grant support from the National Institutes of Health to Sally Rogers (R13 MH70772-01), funded by the NIDCD, NICHD, NINDS and the NIMH. If you have the opportunity, please express your gratitude to members of these groups. Finally we are extremely indebted to Teresa Brown and Cheryl Klaiman who were instrumental in all aspects of the meeting planning; we could not have done this without them!

Bob Schultz
Conference Chair

Eric Fombonne
Program Chair

Sally Rogers
President, INSAR
General Information

Hotel Information:
Hyatt Regency Hotel, Montreal Centre-Ville Phone: 514.982.1234
1255, Jeanne-Mance, PO Box 130 Fax: 514.285.1243
Montreal, Quebec, Canada

Currency: Canadian currency is the dollar (100 cents) in denominations of 5, 10, 20, 50, 100 dollar bills, and one and two dollar coins (sometimes called "Loonies"). **Tipping:** Service is not included in restaurants, so it is customary to add a 15% tip to the total.

Language: French is the official language of Québec. While English is widely spoken, Montrealeans will really appreciate your efforts to greet them in French. Just say, Bonjour!

Things to do: Please consult the IMFAR.org web page for an extensive list of things to do in Montreal + web links. Tourism information can also be obtained at Québec's Infotouriste Centre, 1255 Peel Street, open: daily, 8:30 a.m. to 7:30 p.m

Transportation
- A **taxi** ride from anywhere in town to Trudeau Airport costs a flat rate of $31.
- **Aerobus** shuttle bus service: $12 to or from Trudeau, from the downtown bus terminal (514-842-2281) with several stops.
- **Subway.** The city's underground métro system links all of downtown and major tourist destinations, as well as connecting to Montréal's frequent bus service and the train. Look for the big blue signs with the white arrows
- **Fares:** You can purchase individual tickets, or convenient one- or three-day passes for unlimited travel on bus and métro. Adult fare (bus and métro): $2.50; Strip of 6 tickets: $11.25; The STM Tourist Card: 1 day, $8; 3 days, $16.

The next International Meeting for Autism Research: May 2 - 5, 2007, Seattle, Washington
Acknowledgments

The International Society for Autism Research (INSAR) is the parent organization that operates the annual International Meeting for Autism Research (IMFAR). INSAR is responsible for all committees that govern the organization and the annual meeting.

INSAR Governing Board
Sally Rogers, Ph.D., President
Marian Sigman, Ph.D., Ex Officio
Peter Szatmari, M.D. Vice President
Wendy Stone, Ph.D., Secretary
Bob Schultz, Ph.D., Treasurer

INSAR Committees
IMFAR 2006, Bob Schultz, PhD, Conference Chair; Eric Fombonne, MD, Program Chair
IMFAR 2007, Geri Dawson, PhD, Conference Chair; Susan Bookheimer, PhD, Program Chair
Membership Committee, Bob Schultz, PhD, Chair
Nominations Committee, Joseph Piven, MD, Chair
Publications Committee, David Amaral, PhD, Chair

IMFAR 2006 Scientific Program
Eric Fombonne, MD, McGill University, Canada, Scientific Program Chair
Margaret Bauman, MD, Harvard University, USA
Jan Buitelaar, MD, University Medical Center Nijmegen, Netherlands
Sophia Calamarino, PhD, Cure Autism Now, USA
Kasia Chawarska, PhD., Yale University, USA
Lisa Croen, PhD, Kaiser Permanente Division of Research, USA
Emmanuel Dicicco-Bloom, MD, University of Medicine & Dentistry of New Jersey, USA
Stewart Einfeld, MD, University of New South Wales, Australia
Alan Evans, PhD, McGill University, Canada
Joaquin Fuentes, MD, Policlinica Gipuzkoa, Spain
Jonathan Green, MD, University of Manchester Medical School, UK
Francesca Happé, PhD, King’s College London, UK
Susan Hyman, MD, University of Rochester, USA
Connie Kasari, PhD, University of California, Los Angeles, USA
Chantal Kemner, PhD, University Medical Center Utrecht, Netherlands
Young Shin Kim, MD, Yale University, USA
Pat Levitt, PhD, Vanderbilt University, USA
Ghislain Magerotte, Ph.D, Mons-Hainaut University, Belgium
Gail McGee, PhD, Emory University, USA
William McMahon, MD, University of Utah, USA
Marcos T Mercadante, MD, Universidade Presbiteriana Mackenzie, Brazil
Declan Murphy, MD, King's College London, UK
Kevin Pelphrey, PhD, Duke University, USA
Cathy Pratt, PhD, Autism Society of America, USA
Wendy Robert, MD, The Hospital For Sick Children, University of Toronto, Canada
Bernadette Roge, PhD, University of Toulouse, France
Laura Schreibman, PhD, University of California, San Diego, USA
Andy Shih, PhD, National Alliance for Autism Research/Autism Speaks, USA
Isabel Smith, PhD, Dalhousie University, Canada
Tristam Smith, PhD, University of Rochester, USA
Matthew State, MD, PhD, Yale University, USA
Ryuro Tagaki, MD, Takagi Psychiatric Clinic, Japan
Helen Tager-Flusberg, PhD, Boston University, USA
Nurit Yirmiya, Ph.D., The Hebrew University of Jerusalem, Israel
Paul Yoder, PhD, Vanderbilt University, USA
Lonnie Zweingenbaum, MD, McMaster University, Canada
## IMFAR 2006

### PROGRAM AGENDA

**Thursday June 1<sup>st</sup>**

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<td>7:00am – 5:30pm</td>
<td>Registration</td>
<td>Outside Grand Salon Foyer</td>
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<tr>
<td>7:30am – 8:30am</td>
<td>Breakfast</td>
<td>Grand Salon Foyer</td>
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</table>
| 8:00am – 1:00pm | **Poster Session #1** (Presenters will be by their posters from 11:30-1)  
| 8:25am – 9:30am | **WELCOME**  
Robert Schultz  
**KEYNOTE ADDRESS**  
Tom Insel  
*Autism: What do we Know? What do we Need?* | Grand Salon ABC            | 4     |
| 9:30am – 9:50am | Coffee Break                                                          | Grand Salon Foyer         | 4     |
| 9:50am – 11:30am | **INVITED EDUCATIONAL SYMPOSIUM #1**  
EARLIEST DETECTION OF AUTISM: INSIGHTS FROM HIGH-RISK SAMPLES  
Lonnie Zwaigenbaum  
"Design, Analytical And Clinical/Ethical Issues In Early Detection Studies"  
Sally Ozonoff  
"Studying Autism in the First Year of Life: Constructs and Caution"  
Amy Wetherby  
"Identifying High-Risk Samples Through Population Screening"  
Wendy Stone & Lynnette Henderson  
"Challenges In Screening Young Toddlers At High Risk For Autism" | Grand Salon AB             | 4     |
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<th>Time</th>
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<tr>
<td>9:50am – 11:30am</td>
<td><strong>INVITED EDUCATIONAL SYMPOSIUM #2</strong>&lt;br&gt;UNDERSTANDING GENETIC STUDIES OF AUTISM&lt;br&gt;Linda Brzustowicz&lt;br&gt;“Understanding Genetic Studies Of Autism – Basic Principles And Approaches”&lt;br&gt;Veronica Vieland&lt;br&gt;“Understanding Genetic Studies Of Autism: Common Pitfalls In Interpretation”&lt;br&gt;James Millonig&lt;br&gt;“Understanding Genetic Studies Of Autism – Candidate Gene Validation”</td>
<td>Grand Salon C</td>
<td>4</td>
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<tr>
<td>11:30am – 1:00pm</td>
<td><strong>LUNCH</strong></td>
<td>Alfred Rouleau</td>
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<td><strong>EXHIBITORS</strong></td>
<td>Grand Salon Foyer</td>
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<td>1:00pm – 6:30pm</td>
<td><strong>Poster Session #2</strong> (Presenters will be by their poster from 4:30-6)&lt;br&gt;Neuropathology, Genetic Disorders, Genetic Studies (Molecular), Developmental Trajectory, Early Detection, Early Development</td>
<td>Jeanne-Mance</td>
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<td>1:00pm – 2:20pm</td>
<td><strong>ORAL SESSION #1</strong>&lt;br&gt;<strong>BRAIN STRUCTURE/NEUROANATOMY</strong>&lt;br&gt;F. Toal et al.&lt;br&gt;“The relationship between clinical phenotype and brain anatomy in autism spectrum disorder: An smri study”&lt;br&gt;D.A. Ziegler et al.&lt;br&gt;“Corpus Callosum Volume Is Reduced Relative To Overall White Matter Volume In Autism And Developmental Language Disorder”&lt;br&gt;N. Chabane et al.&lt;br&gt;“Superior Temporal Sulcus Anatomical Differences Between Autism And Williams Syndrome: An MRI Study In Children Using Voxel Based Morphometry (VBM)”&lt;br&gt;M. Lazar et al.&lt;br&gt;“A diffusion tensor imaging study of the thalamus in autism”</td>
<td>Grand Salon AB</td>
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<td>1:00pm – 2:20pm</td>
<td><strong>ORAL SESSION #2</strong>&lt;br&gt;<strong>COGNITION</strong>&lt;br&gt;J. Lawson&lt;br&gt;“Towards A Unifying Conception Of Autism”&lt;br&gt;A. Hamilton &amp; U. Frith&lt;br&gt;“Imitation And Action Representation In Autistic Spectrum Disorders”</td>
<td>Grand Salon C</td>
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<tr>
<td>Time</td>
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<td>1:00pm – 2:20pm</td>
<td><strong>ORAL SESSION #3</strong></td>
<td>Hospitality 5</td>
<td>S. White et al.</td>
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<td>M.A. Thioux et al.</td>
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<td>K.C. Thomas et al.</td>
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<td>D.S. Mandell &amp; L. Brookman-Frazee</td>
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<td>C. Burns et al.</td>
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<td>L.A. Ruble &amp; J.H. McGrew</td>
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<td>2:20pm – 2:50pm</td>
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<td>2:50pm – 4:10pm</td>
<td><strong>ORAL SESSION #4</strong></td>
<td>Grand Salon AB 4</td>
<td>S. Durston et al.</td>
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<td>T. A. Keller et al.</td>
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<td>M.T. Williams et al.</td>
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<td>A.Y. Hardan et al.</td>
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<tr>
<td>Time</td>
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| 2:50pm – 4:10pm | **ORAL SESSION #5** | **NEUROPHYSIOLOGY**  
C. Bolduc et al.  
“EEG activity during REM sleep in autism: Primary vs. non-primary visual areas”  
C.D. Saron et al.  
“Sensorimotor And Multisensory Deficits Of Integration: A Behavioral And ERP Investigation Of Children With Autism Spectrum Disorders”  
R. Bernier et al.  
“EEG Correlates Of Mirror Neuron Activity And Imitation Impairments In Autism”  
T. Lepisto et al.  
“The Processing Of Invariant Speech Features In Autism” | Grand Salon C |
| 2:50pm – 4:10pm | **ORAL SESSION #6** | **REPETITIVE BEHAVIOR**  
J.W. Bodfish et al.  
“Empirically-Derived Phenotypes Of Repetitive Behavior In Autism Spectrum Disorders”  
S. Goldman et al.  
“Longitudinal Study Of Stereotypies In Preschool, 7 And 9 Year Old Autistic Versus Non-Autistic Developmentally Disabled Children”  
M.H. Lewis & Y. Tanimura  
“Repetitive Motor Behavior In A Mouse Model: Associations With Procedural Learning And Cognitive Flexibility”  
E. Anagnostou et al.  
“fMRI Of Response Inhibition In Autism” | Hospitalité |
| 5:30pm – 6:30pm | **GENERAL RECEPTION** |                                                                       | Terrace off Jeanne-Mance |
### Friday June 2nd

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<td>7:30am – 6:00pm</td>
<td>Exhibits</td>
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<tr>
<td>7:30am – 8:30am</td>
<td>Breakfast</td>
<td>Grand Salon Foyer</td>
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</table>
| 8:00am – 1:00pm     | **Poster Session #3** (Presenters will be by their poster from 11:30-1)  
                       | *Neurochemistry, Neurophysiology, Alternative Medicine, Immunology, Medical,  
                       |                   | Jeanne-Mance | 6     |
|                     |                       |                   |       |
|                     | **PRESIDENTIAL ADDRESS**                                               | Grand Salon ABC   | 4     |
|                     | **Sally Rogers**                                                       |                   |       |
|                     | *"Imitation Difficulties in Autism: Findings and Potential Mechanisms"* |                   |       |
| 9:30am – 9:50am     | Coffee Break                                                          | Grand Salon Foyer | 4     |
| 9:50am – 11:30am    | **INVITED EDUCATIONAL SYMPOSIUM #3**                                  | Grand Salon AB    | 4     |
|                     | A PRIMER ON NEUROIMAGING STUDIES OF AUTISM: KEY CONCEPTS AND STATE-OF-THE-ART FINDINGS  
                       | *Susan Bookheimer*                                                     |                   |       |
|                     | *"Key Concepts in Functional Neuroimaging in Atypical Development: Application to Autism"*  
                       | *Heather C. Hazlett*                                                  |                   |       |
|                     | *"A Developmental Perspective on Structural Imaging in Autism"*         |                   |       |
|                     | *Marcel Just*                                                          |                   |       |
|                     | *"Cortical Underconnectivity in Autism"*                               |                   |       |
| 9:50am – 11:30am    | **INVITED EDUCATIONAL SYMPOSIUM #4**                                  | Grand Salon C     | 4     |
|                     | PSYCHOPHARMACOLOGY IN AUTISM: RESEARCH CONSIDERATIONS, CURRENT FINDINGS & FUTURE DIRECTIONS  
<pre><code>                   | *Michael Aman*                                                        |                   |       |
</code></pre>
<p>|                     | <em>&quot;Medication Use In Autism Versus Evidence&quot;</em>                           |                   |       |
|                     | <em>Larry Scahill</em>                                                        |                   |       |
|                     | <em>&quot;Research Considerations&quot;</em>                                           |                   |       |
|                     | <em>Eric Hollander</em>                                                       |                   |       |
|                     | <em>&quot;Future Directions&quot;</em>                                                 |                   |       |
| 11:30am – 1:00pm    | Lunch                                                                 | Alfred Rouleau    | 4     |</p>
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<td>1:00pm – 6:30pm</td>
<td><strong>Poster Session #4</strong> (Presenters will be by their poster from 4:30-6)</td>
<td>Jeanne-Mance 6</td>
<td>Genetic Studies (Family), Broader Phenotype, Structural Imaging, Brain Structure/Neuroanatomy, Emotion/Faces</td>
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| 1:00pm – 2:20pm | **ORAL SESSION #7** **EARLY DIAGNOSIS** | Grand Salon AB 4 | E.R. Crais et al.  
“Developmental Patterns Of Gesture Use In Infants With Autism Spectrum Disorders”  
I.M. Smith et al.  
“Comparison Of Old And New ADOS Algorithms In The Classification Of Infant Siblings”  
P. Ventola et al.  
“Differentiating Between Autism Spectrum Disorders And Other Developmental Disabilities In Children Who Failed A Screening Instrument For ASD”  
G. Baranak et al.  
“Comparison Of The First Year Inventory And The Autism Observation Scale For Infants In The 12-Month Old Siblings Of Children With Autism” |
| 1:00pm – 2:20pm | **ORAL SESSION #8** **PERCEPTION** | Grand Salon C 4 | R.M. Joseph et al.  
“Mechanisms Underlying Superior Visual Search In Autism”  
S.E. Morgan & W.L. Stone  
“Do Children With Autism Display The “Pop-Out” Effect?”  
D. Annaz et al.  
“Dots Buzzing Around? Perception Of Biological Motion In Autism”  
L. Mottron & M. Caron  
“Cognitive Mechanisms, Specificity And Neural Underpinnings Of The Block Design Peak In Autism” |
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<td>1:00pm – 2:20pm</td>
<td><strong>ORAL SESSION #9</strong>&lt;br&gt;GENETIC: FAMILY &amp; TWIN STUDIES</td>
<td>J. Parr et al. &lt;br&gt;“The Broader Phenotype In Parents And Siblings Of Affective Relative Pairs With Pdd”&lt;br&gt;R.L. Hefter et al. &lt;br&gt;“Determining The Heritability Of Early Autism Markers By Screening A Statewide Twin Sample”&lt;br&gt;L. Zwaigenbaum et al. &lt;br&gt;“Familiality Of Language Phenotypes In Autism Spectrum Disorder”&lt;br&gt;Autism Genome Project</td>
<td>Hospitalité</td>
<td>5</td>
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<tr>
<td>2:20pm – 2:50pm</td>
<td>Coffee Break</td>
<td></td>
<td>Grand Salon Foyer &amp; Hospitalité Foyer</td>
<td>4 &amp; 5</td>
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<td>2:50pm – 4:10pm</td>
<td><strong>ORAL SESSION #10</strong>&lt;br&gt;EARLY DETECTION</td>
<td>J.A. Brian et al. &lt;br&gt;“Predictive Validity Of The Autism Observation Schedule For Infants”&lt;br&gt;A.M. Wetherby et al. &lt;br&gt;“Social Communication Profiles Of Children With Autism Spectrum Disorders In The Second And Third Years Of Life”&lt;br&gt;L. Morgan et al. &lt;br&gt;“Measures Of Repetitive Behaviors Using The CSBS DP In Children With Autism Spectrum Disorders In The Second And Third Years Of Life”&lt;br&gt;D.M. Casenhiser et al. &lt;br&gt;“Early ID Of Autism”</td>
<td>Grand Salon AB</td>
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<td>2:50pm – 4:10pm</td>
<td><strong>ORAL SESSION #11</strong>&lt;br&gt;INSTRUMENTS</td>
<td>E.J. Honey et al. &lt;br&gt;“A New Measure For Imagination Within The ADOS”&lt;br&gt;C.J. Gray &amp; G.L. Burns &lt;br&gt;“The Psychometric Properties Of The Pervasive Developmental Disorder Behavior Inventory With Children On The Autism Spectrum”</td>
<td>Grand Salon C</td>
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### ORAL SESSION #12

**GENETIC STUDIES: CYTOGENETIC & MOLECULAR**

**E.M. Morrow et al.**
*“Identification Of Autosomal Recessive Genes For Familial Autism And Mental Retardation”*

**R.P. Nagarajan et al.**
*“Reduced MECP2 Expression Is Frequent In Autism Frontal Cortex And Correlates With Aberrant MECP2 Promoter Methylation”*

**M. Shinawi et al.**
*“Analysis Of Epigenetic Control Of MECP2 In Autism”*

**P. Malenfant et al.**
*“Microdeletions And Microduplications In Subjects With Autism Spectrum Disorders”*

### Schedule

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<tr>
<td>2:50pm – 4:10pm</td>
<td><strong>ORAL SESSION #12</strong></td>
<td>Hospitalité 5</td>
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<td>4:30pm – 5:30pm</td>
<td>Business Meeting</td>
<td>Hospitalité 5</td>
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<tr>
<td>5:30pm – 6:30pm</td>
<td>General Reception</td>
<td>Terrace off Jeanne Mance 6</td>
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### Saturday June 3rd

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<td>7:30am – 12:00pm</td>
<td>Registration</td>
<td>Outside Grand Salon Foyer</td>
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<td>7:30am – 12:00pm</td>
<td>Exhibits</td>
<td>Grand Salon Foyer</td>
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<tr>
<td>7:30am – 8:30am</td>
<td>Breakfast</td>
<td>Grand Salon Foyer</td>
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<td>8:00am – 1:00pm</td>
<td>Poster Session #5 (Presenters will be by their poster from 11:30-1)</td>
<td>Grand Salon Foyer</td>
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<td>8:30am – 9:30am</td>
<td><strong>KEYNOTE ADDRESS</strong></td>
<td>Grand Salon ABC</td>
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<td></td>
<td>Conrad Gilliam</td>
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<td>“Genomic and Bioinformatic Approaches to Mapping Autism Spectrum Disorder Susceptibility Loci”</td>
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<td>9:30am – 9:50am</td>
<td>Coffee Break</td>
<td>Grand Salon Foyer</td>
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<td>9:50am – 11:30am</td>
<td><strong>INVITED EDUCATIONAL SYMPOSIUM #5</strong></td>
<td>Grand Salon AB</td>
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<td>LATEST TRENDS IN RESEARCH ON PSYCHOSOCIAL INTERVENTIONS</td>
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<td>Tristram Smith</td>
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<td>“Evaluating the evidence base for current psychosocial interventions”</td>
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<td>Peter Mundy</td>
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<td>“Beyond preschool: Interventions for older high functioning children”</td>
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<td>Connie Kasari</td>
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<td>“What are the active ingredients of interventions?</td>
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<td>Paul Yoder</td>
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<td>“Why predicting outcome and growth is not the same as predicting”</td>
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<td>9:50am – 11:30am</td>
<td><strong>SPECIAL SYMPOSIUM</strong></td>
<td>Grand Salon C</td>
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<td>AUTISM EPIDEMIOLOGY: WHO COUNTS &amp; HOW DO WE COUNT THEM?</td>
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<td>Marshalyn Yeargin-Allsop</td>
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<td>“The Evolving Prevalence Of Autism”</td>
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<td>Tony Charman</td>
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<td>“The Influence Of Case Ascertainment And Case Definitions On Prevalence: How You Count, When You Count And What You Count As Autism Counts!”</td>
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<td>Craig Newschaffer</td>
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<td>“The Challenges Of Conducting Epidemiologic Studies In Developing Country</td>
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<td>9:50am – 11:30am</td>
<td><strong>INVITED EDUCATIONAL SYMPOSIUM #6</strong>&lt;br&gt;<strong>MOUSE MODELS OF AUTISM</strong>&lt;br&gt;<strong>Jacqueline Crawley</strong>&lt;br&gt;“Strategies For Designing Mouse Behavioral Tasks Relevant To The Symptoms Of Autism”&lt;br&gt;<strong>James Bodfish</strong>&lt;br&gt;“Modeling Stereotyped Movements, Restricted Interests, And Behavioral Rigidity”&lt;br&gt;<strong>Emanuel Dicicco-Bloom</strong>&lt;br&gt;“Manipulating Expression Of Engrailed (En2), An Autism Associated Gene, To Discover Mechanisms Of Developmental Dysfunction”</td>
<td>Hospitalité</td>
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<td>11:30am – 1:00pm</td>
<td>Lunch</td>
<td>Alfred Rouleau</td>
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<td>1:00pm – 6:30pm</td>
<td><strong>Poster Session #6</strong> (Presenters will be by their poster from 4:30-6)&lt;br&gt;Epidemiology, Screening, Families, Psychometry, Education, Comorbid Behavior</td>
<td>Jeanne-Mance</td>
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<td>1:00pm – 2:20pm</td>
<td><strong>ORAL SESSION #13</strong>&lt;br&gt;<strong>FUNCTIONAL NEUROIMAGING</strong>&lt;br&gt;N.M. Kleinhans et al.&lt;br&gt;“Reduced Neural Specificity For Objects And Faces In The Fusiform Gyrus In Autism Spectrum Disorders”&lt;br&gt;R.K. Kana et al.&lt;br&gt;“Hemispheric Differences In Resolving Lexical Ambiguity In High Functioning Autism”&lt;br&gt;T.L. Richards et al.&lt;br&gt;“Face Processing In Autism: fMRI/EEG Source Localization Correlations”&lt;br&gt;A.E. Pinkham et al.&lt;br&gt;“Do Similar Neural Profiles Underlie Social Cognitive Deficits In Schizophrenia And Autism?”</td>
<td>Grand Salon AB</td>
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<td>1:00pm – 2:20pm</td>
<td><strong>ORAL SESSION #14</strong>&lt;br&gt;<strong>EARLY DEVELOPMENT</strong>&lt;br&gt;F.S. McEwen et al.&lt;br&gt;“Early Imitation And Later Autistic Behaviour: A Longitudinal Twin Study”</td>
<td>Grand Salon C</td>
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**N. Watt et al.**  
“Repetitive And Stereotyped Behaviors In Autism Spectrum Disorders From 18-24 Months”

**S. Shumway et al.**  
“Communicative Acts Of Children With Autism Spectrum Disorders Between 18 And 24 Months Of Age”

**K. Wittemeyer et al.**  
“Can Children With Autism Spectrum Disorders Improve In The Pragmatic Aspects Of Communication? – A Comparative Early Intervention Study”

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<td><strong>ORAL SESSION #15</strong></td>
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<td>BIOMEDICAL ASPECTS</td>
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<td><strong>B. Goodlin-Jones et al.</strong></td>
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<td>“Sleep In Children With Autism, Developmental Delay, Or Typical Development”</td>
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<td><strong>D.A. Braunschweig et al.</strong></td>
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<td>“Increased Prevalence Of Maternal Autoantibodies Against Fetal Brain In Autism”</td>
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<td><strong>J.L. Mills et al.</strong></td>
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<td>“Elevated Levels Of Growth-Related Hormones In Autism And Autism Spectrum Disorder”</td>
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<td><strong>I. Hertz-Picciotto et al.</strong></td>
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<td>“Blood Metal Concentrations In The Charge Study”</td>
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2:20pm – 2:50pm Coffee Break  
**Dissertation Awards**  
**Lifetime Achievement Award: Eric Schopler**
Keynote Address #1
Autism: What do we know? What do we need?

Thomas Insel, NIMH/NIH

Since the first IMFAR meeting in 2001, autism has received increased commitment from the research community, increased cooperation among advocacy groups, and increased awareness in the public. Nevertheless, we still know very little about the pathophysiology of this illness. Autism is a developmental brain disease, but we do not know what the ‘lesion’ looks like. Autism is a genetic disorder, but we have not identified genes of major effect nor have we found many of the associated alleles. Recent reports document increased prevalence (not incidence) for autism, but we have yet to identify a single environmental risk factor to explain this increase. And finally, autism is considered by many experts to be a cluster of disorders, but we have no consistent approach for sub-typing the various ‘autisms’ into valid syndromes.

While advances are being made on all of these fronts, to maximize progress we will need a coordinated, strategic effort. In spite of flat budgets at NIH, the research community will need (a) to expand to include developmental neurobiologists and others who can bring powerful new tools to autism research, (b) to build cooperative research networks that can share protocols and data across labs via a common database, and (c) to partner with advocacy groups and families to ensure that research is relevant and results are disseminated. We There is also an urgent need for studies to delineate the biological and behavioral subtypes of this complicated disorder so that we can identify the genetic, environmental, and interactive etiologies of autism, and develop new treatments and preventive strategies.
Invited Educational Symposium #1
Earliest detection of autism: insights from high-risk samples

Speakers:
Lonnie Zwaigenbaum, McMaster University
Sally Ozonoff, M.I.N.D. Institute, UC Davis Medical Center
Amy Wetherby, Florida State University
Wendy L Stone & Lynnette Henderson, Vanderbilt University Kennedy Center

ABSTRACTS

DESIGN, ANALYTICAL AND CLINICAL/ETHICAL ISSUES IN EARLY DETECTION STUDIES Lonnie Zwaigenbaum, McMaster University
Current knowledge about early signs of autism comes mainly from retrospective reports from parents and analysis of early home videotapes. This lecture will summarize the unique advantages of prospective, longitudinal studies of autism, including the potential for broader ascertainment, standardization of assessment methods across children and over time, and greater control over testing hypotheses regarding key developmental constructs. Design issues in prospective studies in high-risk infants will also be discussed, including ascertainment strategy; high-risk samples can be identified on the basis of genetic risk (infants with an older sibling with autism; 'baby sibs'), or by population screening. Analytical issues such as sample size/power and statistical approaches to longitudinal data will also be discussed, as will clinical and ethical dilemmas that can arise in the context of assessing the early development of high-risk infants.

STUDYING AUTISM IN THE FIRST YEAR OF LIFE: CONSTRUCTS AND CAUTION Sally Ozonoff, M.I.N.D. Institute, UC Davis Medical Center
Very few studies using retrospective methods have focused on development before the first birthday. The advent of prospective studies using high risk samples is providing, for the first time, a window into the development of children with autism spectrum disorders during early infancy. This talk will review constructs with potential utility in the early identification of autism prior to the first birthday, drawing on empirical evidence from retrospective studies and new findings from an ongoing study of infants at genetic risk for autism. For example, initial data indicates that atypical social orienting and face and affect processing can be detected in some siblings of children with autism prior to 12 months of age. However, the utility of these early behaviors as risk indicators of autism remains to be examined. Initial experience with sibling samples shows that some infants present unusual and unexpected phenotypes, including atypicalities in some (but not all of) early language and joint attention skills, social engagement, and imitation skills. These infants show considerable variability in subsequent developmental course. Challenges related to identifying specific markers for autism in infancy will be discussed in the context of the broader range of phenotypes observed in siblings.

IDENTIFYING HIGH-RISK SAMPLES THROUGH POPULATION SCREENING Amy Wetherby, Florida State University
An alternative to 'baby sibs' samples is to identify children at increased risk of ASD by population screening based on known risk factors. Although the search for 'red flags' may shift to the second year of life rather than early infancy, population-based sampling may yield more generalizable findings. This presentation will highlight the utility of this strategy by summarizing findings from the FIRST WORDS Project, a prospective, longitudinal study of children based on screening of a general pediatric sample for communication delays. Children are identified using a two-stage screening and referral process—a broadband, parent-report surveillance checklist to determine if a child is at-risk for a communication delay followed by autism-specific parent-report and interactive tools. Core deficits in social communication and repetitive and stereotyped behaviors that distinguish children with ASD in the second year of life from children with typical development and other developmental delays will be delineated and discussed in the context of improving early identification.
CHALLENGES IN SCREENING YOUNG TODDLERS AT HIGH RISK OF AUTISM
Wendy L Stone, Lynnette Henderson, Vanderbilt University Kennedy Center

Background: Findings from longitudinal studies of high risk samples may have major implications for clinical practice and health care delivery. However, the application of findings from early identification research to community practice settings may be difficult. Interactive screening tools may play an important role in providing community-based detection and intervention services.

Objectives: To illustrate the potential utility and challenges of: (1) using high risk populations to develop interactive screening tools for children under 24 months; and (2) using interactive screeners for broader clinical applications. Examples from the Screening Tool for Autism in Two-year-olds (STAT), an interactive measure originally developed for 2-year-olds, will be provided.

Methods: The STAT was administered to samples of low-risk (no developmental concerns) and high-risk (later-born siblings of children with ASD or children for whom there were developmental concerns) toddlers under the age of 24 months. After a follow-up diagnostic evaluation, signal detection was used identify optimal scoring algorithms for different screening ages.

Results and Conclusions: Preliminary data suggest that with a revision of the scoring algorithm, the STAT can be used as young as 15 months to discriminate between children who receive a later diagnosis of autism and those with typical development or other developmental disorders. Limitations of early screening and the stability of early diagnosis will be discussed.

Sponsor: NAAR, NICHD#R01HD043292

Invited Educational Symposium #2
Understanding genetic studies of autism

Speakers:
Linda Brzustowicz, Rutgers University
Veronica J Vieland, University of Iowa
James Millonig, UMDNJ-Robert Wood Johnson Medical School

ABSTRACTS

UNDERSTANDING GENETIC STUDIES OF AUTISM - BASIC PRINCIPLES AND APPROACHES Linda Brzustowicz, Rutgers University
This lecture will review the epidemiologic background of autism and outline the major scientific strategies that are commonly used in the identification of candidate genes for complex human behavioral disorders. The importance of accurate phenotypic definition will be discussed. The basic principles of conducting a genome scan analysis for linkage as a method of identifying potential genomic regions harboring susceptibility genes will be presented. The concepts of linkage disequilibrium and allelic association will be introduced, along with their utility as approaches to assess specific genes as susceptibility candidates.

UNDERSTANDING GENETIC STUDIES OF AUTISM: COMMON PITFALLS IN INTERPRETATION Veronica J Vieland, University of Iowa
The primary literature describing the analysis of complex human genetic disorders can be very intimidating for people outside the field (and even for those in the field), due to the diversity of statistical methods utilized. The wide variety of analytic approaches can make the comparison of results across studies difficult, and can make it challenging for the reader to determine whether the results of a given study are scientifically compelling or not. This lecture will attempt to clarify some of the confusion that arises due to the use of different statistics for standard gene-mapping study designs, illustrating the implications of some of the implicit and explicit assumptions of various methods. The issue of multiple testing will also be discussed.

UNDERSTANDING GENETIC STUDIES OF AUTISM-CANDIDATE GENE VALIDATION James Millonig, UMDNJ-Robert Wood Johnson Medical School
Amassing compelling statistical evidence supporting a particular candidate gene is only the first
step in demonstrating the role of that gene in disease etiology. This lecture will review some of the
different reasons that a statistical signal may be detected at a given location, and functional
approaches to validating that a particular gene is involved in the disorder. Candidate gene
validation by bioinformatics, transfection studies, human post-mortem analyses, and forward and
reverse genetic approaches in animal models will be presented.
Oral Session #1
Brain structure/neuroanatomy

Chair: Alan Evans

Speakers:
Fiona Toal, Eileen Daly, Lisa Page, Bill Cutter, Quentin Deeley, Brian Hallaghan, Sarah Curran, Dean Robertson, C Murphy, Francesca Happe, Patrick Bolton, Kieran CM Murphy, Declan GM Murphy, Royal College of Surgeons, Dublin
David A Ziegler, Nikos Makris, David N Kennedy, Verne S Caviness, Pauline A Filipek, Martha R Herbert, MIT
Nadia Chabane, Monica Zilbovicius, Arnaud Cachia, Fanny Mochel, Isabelle Meresse, Stanislas Lyonnet, Marie-Christine Mouren, Francis Brunelle, Arnold Munnich, Yves Samson, Jean-François Mangin, Nathalie Boddaert, Service de Pédiopsychiatrie, Hôpital Robert Debré, AP-HP, Paris, France

ABSTRACTS

THE RELATIONSHIP BETWEEN CLINICAL PHENOTYPE AND BRAIN ANATOMY IN AUTISTIC SPECTRUM DISORDER: AN sMRI STUDY. Fiona Toal, Eileen Daly, Lisa Page, Bill Cutter, Quentin Deeley, Brian Hallaghan, Sarah Curran, Dean Robertson, C Murphy, Francesca Happe, Patrick Bolton, Kieran CM Murphy, Declan GM Murphy, Royal College of Surgeons, Dublin

Background: It is unknown if differences in the clinical phenotype of Autistic spectrum disorder (ASD) are associated with differences in brain structure.

Methods: We investigated, as part of the MRC UK A.I.M.S. program, brain anatomy in 87 adults with ASD (58 people with Asperger syndrome, 18 with High Functioning Autism, 11 with Classical autism) and 46 controls using volumetric magnetic resonance imaging.

Results: People with ASD had significant reduction in white matter in cerebellar brainstem and parahippocampal regions; Further, we found significant differences within people with ASD according to clinical phenotype. Those with Asperger syndrome had reduction in grey matter in both cerebellum and ‘social’ brain regions including medial temporal and fusiform gyrus; whereas those with High functioning autism and Classical autism had an increase in grey matter in fronto-striatal and tempo-parietal regions. Finally when we compared people with High functioning autism and Classical autism to Asperger syndrome we found excesses in grey matter in language specific regions.

Interpretation: People with ASD have significant differences from controls in the anatomy of brain regions implicated in behaviours characterizing the disorder. These may arise from abnormalities in at least two neurodevelopmental processes, one associated with a regionally specific excess of grey matter, and another with deficits in both grey and white matter. Further, variation in the behavioural phenotype of ASD is associated with differences in brain anatomy. Our findings may also partially explain the variable results from prior studies of ASD; because many studied people from different parts of the autistic spectrum

CORPUS CALLOSUM VOLUME IS REDUCED RELATIVE TO OVERALL WHITE MATTER VOLUME IN AUTISM AND DEVELOPMENTAL LANGUAGE DISORDER
David A Ziegler, Nikos Makris, David N Kennedy, Verne S Caviness, Pauline A Filipek, Martha R Herbert, MIT

BACKGROUND: Morphometric analyses of corpus callosum (CC) in children with autism (AUT) have shown reduced CC area compared to controls (CTR). Paradoxically, other studies show marked increases in superficial white matter (WM) volume.

OBJECTIVES: We address this paradox by analyzing the relationships between CC size and other
cerebral morphometric features.

METHODS: We collected MRI data from school-aged children: high-functioning AUT (n=17), developmental language disorder (DLD; n=24), and CTR (n=30). Whole-brain segmentation delineated all major cortical/subcortical brain structures and allowed gyral-based cortical parcellation. We obtained midsagittal CC areas and parcellated WM to derive CC volumes. CC volumes and areas were subdivided into 7 geometrically defined subregions.

RESULTS: While CC areas did not differ between groups, CC volumes were significantly reduced in AUT and DLD in posterior CC (divisions 6 and 7) compared to CTR, even after covarying for total brain volume. Regression analyses showed significant positive correlations between cerebral WM volume and both CC volume and area, while cerebral gray matter (GM) volume only correlated with CC volume. The WM-CC regression slope was significantly steeper in CTR compared to AUT and DLD while GM-CC regression slopes showed the opposite pattern.

CONCLUSION: CC is smaller, relative to overall WM volume, in AUT and DLD. This pattern might be consistent with the notion of decreased global and increased local connectivity in AUT, and also in DLD.

SUPPORTED BY: CAN, NS20489, NS02126

SUPERIOR TEMPORAL SULCUS ANATOMICAL DIFFERENCES BETWEEN AUTISM AND WILLIAMS SYNDROME: AN MRI STUDY IN CHILDREN USING VOXEL BASED MORPHOMETRY (VBM) Nadia Chabane, Monica Zilbovicius, Arnaud Cachia, Fanny Mochel, Isabelle Meresse, Stanislas Lyonnet, Marie-Christine Mouren, Francis Brunelle, Arnold Munnich, Yves Samson, Jean-François Mangin, Nathalie Bogaert, Service de Pédiatrie, Hôpital Robert Debré, AP-HP, Paris, France

Background: Autism and Williams Syndrome (WS) are neurodevelopmental disorders characterized by a mirror neurobehavioral phenotype. Social and communication skills are impaired in autism and are quite spared in WS. In opposition, visuo-spatial constructive disabilities are constant hallmark in WS and relatively spared in autism.

Objectives and Methods: In order to compare structural abnormalities in both pathologies, we processed anatomical MRI in 9 WS children (11.6 ± 3.1 years), in 11 normal control children (11.8 ± 2.2 years) and 21 children with autism (mean age 9.1 ± 2.6 years) using VBM. All subjects were scanned on 1.5 tesla using T1-weighted-3D-FSPGR. Data were pre-processed and analyzed using SPM99.

Results: A significant grey matter concentration decrease was detected in bilateral superior temporal sulcus (STS) in autistic children compared to controls and WS children (p<0.05 corrected). Grey matter concentration in the STS showed a continuum relationship in regard to the diagnosis (WS > controls > autistic children). Moreover, a significant grey matter concentration decrease was detected in parieto-occipital region in WS children compared to controls and autistic children (P < 0.05 corrected) with the same relationship concerning the diagnosis (WS < controls < autistic children).

Conclusions: STS is now recognized as a key cortical area of the "social brain" and is highly implicated in social perception that are characteristically impaired in autism and exaggerate in WS. In addition, the parieto-occipital abnormalities are consistent with the severe visuospatial construction and numerical cognition deficits in WS. Our study provides additional support for the use of advanced structural imaging techniques in children with developmental disorders.

Sponsor: France Telecom Foundation and France Foundation.


Background: Previous studies indicated abnormal thalamic morphology and function in autism. Objectives: Investigate the microstructural integrity of the thalamus in autism using DTI.

Methods: DTI data were acquired for subjects who met ADI-R and ADOS-G criteria for autism and typically developing control subjects. Two age groups were investigated: a prepubescent (8 - 12 years old, 12 control and 13 autistic subjects) and a young adult group (18 - 25 years old, 10 control and 11 autistic subjects). For each age group, the autism and control subjects were matched for age and for performance and verbal IQ. Only right-handed male subjects were included in this study. The mean diffusivity (MD), and fractional anisotropy (FA) were used to characterize thalamus. Thalamic volumes were manually segmented in each subject. The mean values of FA and MD across the thalamus were calculated for each subject in the subject's native space. Subsequently, the subjects' images were registered to a common space and statistical
analyzes were performed at each voxel to investigate for local differences between groups. Results: The mean FA of the thalamus was significantly decreased in the older autistic group while MD was significantly increased. Voxel-based analyzes showed that smaller FA appears to characterize medial geniculate and dorsomedial nuclei and larger MD appears to be increased in autism in the pulvinar, dorsomedial, and anterior thalamic nuclei. No significant differences were found in the prepubescent group. Conclusion: These preliminary results suggest microstructural differences in several thalamic regions in young autistic adults compared with control subjects. Sponsors: NARSAD, NICHD CPEA.

Oral Session #2
Cognition

Chair: Isabel Smith

Speakers:
John Lawson, University of Cambridge
Antonia Hamilton & Uta Frith, Institute of Cognitive Neuroscience, University College London
Sarah White, Elisabeth Hill, & Uta Frith, Institute of Cognitive Neuroscience, University College London
Marc A Thioux, Cheryl Klaiman & Robert T Schultz, Yale University Child Study Center

ABSTRACTS

TOWARDS A UNIFYING CONCEPTION OF AUTISM John Lawson, University of Cambridge
Overview: For the last decade or so autism research on the cognitive level has been dominated by three main models; the Executive Dysfunction, Central Coherence and Theory of Mind/Emathising-Systemising models. However, a problem exists in that none of these models seem able to fully explain all of the behavioural features of the condition e.g. some individuals with autism successfully complete certain tasks that require high levels of executive function (Lawson, Baron-Cohen et al, 2004, JADD), simultaneously, some demonstrate difficulties in areas that don’t require Theory of Mind/empathising abilities (Lawson, in press, Routledge). Recently a theory has been developed to address these problems and move towards a synthesis of the main models (Lawson, 2003, JTSB). This theory is in part a response to the observation that people with autism demonstrate difficulties in some, but not all, aspects of life. Reflecting this, the theory draws on ideas developed within the philosophy of science concerning the nature of the world. More specifically, it draws on a distinction between ‘open’ and ‘closed’ systems and the different approaches that are required to engage appropriately with them. The central idea proposed is that autism can fruitfully be conceptualised as a difficulty or even inability when dealing with open systems. Such a conceptualisation seems better able to comprehensively explain the behavioural features of autism. It is also highly congruent with emerging evidence concerning neural connectivity deficits.

IMITATION AND ACTION REPRESENTATION IN AUTISTIC SPECTRUM DISORDERS Antonia Hamilton, Uta Frith, Institute of Cognitive Neuroscience, University College London
It has recently been suggested that children with autism have specific impairments in imitation abilities, that these impairments may be due to a dysfunctional mirror neuron system, and that such dysfunction might also contribute to impaired social skills and mentalising in children with autism. To test this hypothesis, it is necessary to understand the component skills which contribute to imitation in a systematic and detailed fashion. We have used a battery of motor, imitation and theory of mind tasks, and tested a group of fourteen children with autistic spectrum disorder
(chronological age 4;5 to 12;1, Verbal mental age 2;4 to 6;1) and a group of twelve control children (CA 3;4 to 4;4, VMA 3;1 to 5;11). We found that the children with ASD performed as well as the controls on tests of goal directed imitation, gesture recognition and motor planning. However, they performed worse than controls on tasks requiring visual perspective taking, theory of mind, and body posture matching. Thus, we suggest that the hypothesis of a specific imitation deficit in ASD is in need of refinement, so that links between social impairment in ASD and dysfunction of the mirror neuron system can be specified more precisely and tested more rigorously.

Funded by MRC grant 65013

HOW DO COGNITIVE IMPAIRMENTS AFFECT INTELLIGENCE TEST PERFORMANCE IN ASD? Sarah White, Elisabeth Hill, Uta Frith, Institute of Cognitive Neuroscience, University College London

Background: The performance of individuals with Autism Spectrum Disorder (ASD) across intelligence subtests is characterised by an uneven profile.

Objectives: To relate performance on cognitive tests, generated by three major theories of the core symptoms of ASD, to standardised intelligence subtests.

Methods: 57 high-functioning children (6-12 years) with ASD and 27 controls were tested on the WISC, as well as a battery of tests tapping theory of mind (ToM), central coherence (CC) and executive function (EF) abilities.

Results: Children with ASD who had a personal peak on the block design subtest showed elevated performance on a test of weak CC compared to the remaining children with ASD. Performance on these two tests was also correlated across the whole ASD group, as well as within the control group. In line with previous research, ASD children with a personal dip on the comprehension subtest had weaker ToM performance than the remaining ASD children, and these tests were correlated across the whole ASD group but not in the controls. EF performance was not related to one particular subtest but more generally to verbal intelligence in the children with ASD, whilst correlating with the object assembly subtest in the controls.

Conclusion: ToM impairment and weak CC both contribute to the uneven profile characterising ASD intelligence test performance. EF impairment appears to have a wider effect across verbal intelligence. These same relationships were only seen in the control children for weak CC, indicating a cognitive style rather than a deficit in this domain.

Sponsor: Medical Research Council (MRC), UK*

UNDERSTANDING THE EXCEPTIONAL AUTOBIOGRAPHICAL MEMORY OF AN AUTISTIC SAVANT Marc A Thioux, Cheryl Klaiman, Robert T Schultz, Yale University Child Study Center

Background: Some autistic savants with calendar computation skills are believed to have virtually unlimited memory for autobiographical events. Surprisingly, no scientific investigation of this phenomenon has been conducted to date.

Objectives: Discovering the basis of exceptional autobiographical memory.

Methods: Standardized and unstandardized tests of memory functions were administered to a 21 year-old male with Autism displaying outstanding calendar calculation skills.

Results: The patient was largely impaired on standardized tests of episodic and semantic memory. Nevertheless, he had an exceptional memory for events of his own life. For instance, he could accurately remember the weather for the last 7 years, and he was able to recall virtually all the dates when he met with the researchers over a period of 3 years. Furthermore, he seemed able to recall detailed contextual information for all these dates. In a remember-know paradigm he claimed to remember meeting with the researcher in about 90% of the cases. He was also able to learn lists of non-meaningful future dates with a level of performance well beyond the performance of undergraduate students. However, in this task he reported knowing rather than remembering in most of the cases.

Conclusion: The results of this study suggest that autobiographical memories are actually retrieved from the medial temporal lobe episodic memory system (rather than from a semantic memory store as factual information would be). It is likely however that the patient only encodes a limited subset of information in episodic memory that matches his circumscribed pattern of interests.

Sponsor: NAAR, NICHD
FAMILY USE OF EFFECTIVE ELEMENTS OF PROGRAMS FOR AUTISM
Kathleen C Thomas, Alan R Ellis, Carolyn McLaurin, Julie Daniels, Joseph P Morrissey, Cecil G. Sheps Center for Health Services Research, University of North Carolina at Chapel Hill

Background: A growing literature describes family difficulties accessing services for children with ASD. However, these studies do not make distinctions about the quality of services despite growing consensus on the central features of successful treatment and care of ASDs.

Objectives: This study examines family and child use of effective program elements in order to identify barriers and facilitators to effective care. The analysis expands the current literature by
1. basing analyses on a community sample of families
2. including a wide range of family and child characteristics
3. distinguishing family involvement in the provision of treatment protocols from general caregiving.

Methods: A combined telephone and in-person survey in North Carolina, 2003-5, was completed by 383 families with a child having ASD, 11 years or younger. Ordinary least squares regressions measure family and child characteristics associated with age at diagnosis, number of services per week, and proportion of services provided by family.

Results: Children with Asperger’s are more likely to receive their ASD diagnosis at a later age. Minority children and those whose families are not following one of the major treatment approaches for ASD fall behind others in the receipt of the three elements of effective care studied here. Findings underscore the extensive amount of time families devote to their child with autism in the provision of treatment interventions.

Conclusions: Implications highlight the need to develop family-level interventions such as information dissemination, decision-making tools, and parent supports to assure adequate access to effective service elements for all children with ASD.

Sponsors: NIMH (R21 MH066143), CDC through NC-CADDRE

OVERLAP OF SPECIAL EDUCATION AND PUBLIC MENTAL HEALTH SYSTEMS IN CARING FOR CHILDREN WITH AUTISM
David S Mandell, Lauren Brookman-Frazee, University of Pennsylvania School of Medicine

Objective: To examine the overlap among children diagnosed with autism spectrum disorders (ASD) served in the special education and public mental health systems, and their use of public mental health services.

Methods: Special education and Medicaid records from Philadelphia, PA, for calendar year 2002 were merged to identify children ages 6-17 years who had received ASD services in either system (n = 969). Characteristics of children served in one or both systems were compared.

Results: There were 675 children in the special education autism category and 418 diagnosed with ASD in the mental health system; 124 (12.8%) received autism services in both systems. Half (50.2%) of children receiving autism special education services were Medicaid eligible and 23.4% used public mental health services; 70.0% of children receiving mental health services for ASD received no special education services or through a category other than autism. Average expenditures were highest for children receiving mental health services for ASD and special
education in a category other than autism ($38,035) and lowest for those receiving special education services for autism and mental health services for other diagnoses ($18,247).

Conclusions: First, the results suggest that mental health system plays an important role in providing autism services. These data illustrate the complexities of the service system for children with ASD and suggest the need for stronger coordination between the two to promote efficient and effective care. Second, epidemiologic studies that rely on special education data as a first-stage screen may be missing an important source of cases.

PARENTAL PERCEPTIONS OF CARE COORDINATION FOR CHILDREN WITH AUTISM SPECTRUM DISORDERS Christine Burns, Abidin Tuncer, Erin Sheeder, Kristen Pullano, Jacalyn Yingling, Mark Orlando, Steven Sulkes, University of Rochester

Background: Care for children with autism is fragmented, challenging parents in their coordination efforts. Emerging electronic information sharing systems (EIS) hold particular promise for improving the coordination of care of children with autism.

Objectives: Evaluate parent perception of effort and beneficial components of coordination services for their children who have autism.

Methods: Mailed surveys to 300 families of children with autism spectrum disorder using randomized selection from established clinical database. Demographic information, understanding of child’s condition, care coordination effort and services received were collected. Data were analyzed using Statistical Package for Social Sciences - PC to determine predictive variables that contribute to the likelihood of receiving care coordination services.

Results: Significant barriers exist in communication with providers in health care, financial and school settings and accessing information about community resources. Satisfaction with care coordination was associated with the number of providers working the child. Being involved in decision-making, receiving immediate responses to problems, and assistance with treatment plan implementation were highly valued.

Conclusion: Considerable variability in models for care coordination and fragmentation of services continues to exist. Patient and family participation must be increased to assure family-centered care and improved care coordination to enhance health and functional outcomes of children with ASD.

Sponsor: HRSA, Maternal and Child Health Bureau, LEND*

CAREGIVER PERCEPTION OF SERVICE EFFECTIVENESS Lisa A Ruble, John H McGrew, University of Louisville

Background: In an era in which evidence based practices are becoming the standard of care in both the medical and psychosocial arenas, there is virtually no evidence that the current array of services commonly delivered for those with autism are even helpful, much less that they could meet these more rigorous standards.

Objectives: To provide information on service effectiveness.

Methods: A survey was distributed to a community sample of caregivers of children with autism spectrum disorder. Outcomes were selected based on symptoms of autism and on family factors. Caregivers used a Likert scale to rate the outcomes of the services they had received the past six months.

Results: Effectiveness was rated separately for home and school settings, and findings differed depending on whether child or overall family outcomes were examined. In-home behavior services were rated as the most effective service affecting the child in home and school. For child domains, in-home behavior therapy was rated as the most effective service for 2 outcomes (communication and behavior). Medication was rated as the most effective intervention for one outcome area (social skills). For the fourth child outcome area, problem solving, occupational therapy was rated as the most effective intervention. For family outcomes, respite care was ranked consistently as the most effective service in reducing caregiver, family, and financial and personal stress.

Conclusions: New information on the types of services important for meaningful and ecologically relevant outcomes is provided.
Poster Abstracts – 1
8:00 am – 1:00 pm

PS1.1
MUTIMODAL (INDIVIDUAL AND GROUP) COGNITIVE BEHAVIORAL THERAPY (CBT) SOCIAL SKILLS TRAINING (SST) FOR HIGH FUNCTIONING (HF) CHILDREN WITH AUTISM SPECTRUM DISORDER (ASD) Nirit Bauminger, School of Education, Bar Ilan University
Background: The focus of the social-communication deficit in HF children with ASD comprises the child's lack of intuitive, spontaneous learning about the social and emotional world. Despite, growing agreement regarding the potential value of SST that incorporate CBT techniques for HF children with ASD, very few studies have empirically tested it.
Objective. Current study evaluated the effectiveness of a CBT SST for HF children with ASD aiming to enhance social emotional understanding and dyadic and group cooperative social interaction with peers over two years: individual training in the first year (Study 1) and group training in the second year (Study 2).
Design/Method: Participants (aged 8 to 12 years) included 19 in Study 1 and 26 in Study 2. Both interventions implemented in the child’s school setting (each lasting 7 months) combined CBT components (e.g., affective education, problem solving) and behavioral techniques (e.g., role playing, behavioral rehearsal) using peer and adult mediation.
Results: Both studies demonstrated improvement in children’s social cognition (e.g., emotion recognition, social problem solving). In Study 2, generalization of treatment gains into other social cognition capabilities such as theory of mind and executive functioning also emerged. Mixed results found in social interaction capabilities, with an advantage to the individual treatment over the group treatment, presumably due to the implementation of a more comprehensive ecological treatment, where practice was more oriented toward generalization.
Conclusion: Discussion focuses on the efficacy of CBT SST treatment models for the enhancement of social-emotional functioning in HF children with ASD, underscoring the importance of individual differences.

PS1.2
A MODEL OF COMMUNITY-BASED EARLY INTERVENTION USING PIVOTAL RESPONSE TREATMENT Susan E Bryson, Daniel Openden, Isabel M Smith, Robert L Koegel, Lynn K Koegel, Dalhousie University-IWK Health Centre
Responding to the need for effective, feasible, and sustainable models of early intervention in autism, we are translating the university-based Pivotal Response Treatment (PRT) program to a province-wide community-based program. PRT is an ABA-based naturalistic intervention that targets core autism deficits in motivation and social-communication skills.
Objective: To determine the effectiveness of the Nova Scotia early intervention program, evaluating (1) training of parents and service providers, and (2) child and family outcomes.
Methods: An initial cohort of 27 preschoolers with autism [mean CA = 4.4 yr; mean Developmental Index (Merrill-Palmer-Revised) = 52] is enrolled in an early intervention program based on PRT. A parent-training model was supplemented by 15 hours/week of naturalistic behavioural intervention by trained 1:1 interventionists, in the home and/or in daycare/preschool settings. Parents and workers were trained together in a workshop format utilizing video feedback on acquisition of PRT skills.
Results: Social validity data were gathered from 67 parents, professionals, and paraprofessionals, yielding highly positive ratings of the form and content of training, and of participants’ perceptions of their increased skills. Analysis of videotaped intervention sessions confirmed that interventionists met pre-established criterion levels of fidelity in implementing PRT procedures. Preliminary six-month child and family outcome data will also be presented.
Conclusion: A community-based behavioural intervention model can produce substantial functional improvements for preschoolers with autism. Discussion will focus on the essential elements of the workshop-based training and ongoing support of parents and service providers that are associated with early indicators of the program’s success.

PS1.3
THE RELATIONSHIP BETWEEN THE EARLY LEARNING MEASURE AND OUTCOMES ON THE VINELAND ADAPTIVE BEHAVIOR SCALES FOLLOWING INTENSIVE BEHAVIOURAL INTERVENTION IN YOUNG CHILDREN WITH AUTISM Tessen Clifford, Jane Summers, Queen's University
Background: Intensive behavioural intervention (IBI) for young children with autism has been associated with unprecedented developmental gains for some children; however, not every child achieves such success.
Objectives: Use learning rates to identify early in treatment those children who will make gains following IBI, and those who might require modifications in instructional format and focus.
Methods: Thirty-two children with a diagnosis of either Autistic Disorder or PDD-NOS, who had received IBI for at least 1 year, participated in the study. Early learning rates in several domains, receptive commands, nonverbal
imitation, verbal imitation, and expressive labels, were collected prior to treatment and every month for the first 4 months of treatment. The Vineland Adaptive Behavior Scales were used to measure adaptive functioning at intake and after 6 and 12 months of treatment.

Results: Early learning rates are correlated with adaptive behaviour scores after one year of treatment. As well learning rate groupings are associated with outcome groupings, such that children with poor early learning rates have poor outcomes, and children with the best early learning rates have the best outcomes.

Conclusions: Preliminary findings suggest that early learning rates may be useful in identifying those children who will benefit from IBI, and those who require alternative interventions.

PS1.4

Background: This 4-year study addresses a significant concern; that is, how to assist families in facilitating language development, socialization, and quality family interactions in children with autism. This presentation summarizes results from our first NIH/NINR-funded father-training study (1998-2003) and how these results have been incorporated into a revised intervention.

Objectives of our current study are to: (a) evaluate the effects of training fathers of autistic children with an expanded training module, (b) evaluate the effects of the expanded father training on skill acquisition by mothers, (c) evaluate the effects of the in-home training on parental stress and family cohesion, and (d) develop an Internet-based investigator-father feedback system and evaluate its feasibility during the training protocol and maintenance phases.

Methods: Study 1 showed that fathers can be trained to use two specific child training skills, imitating with animation and expectant waiting, and that fathers, in turn, can effectively train mothers to use these skills. Building on this, we are in the process of training 24 additional families, adding clinically supported training components, and empirically evaluating intervention efficacy using the videotaping, observational, and coding methods developed and tested during previous projects.

Results: Preliminary Year 1 results indicate that it is possible to expand the earlier intervention and develop it into a web-based training booster site. As with the earlier study, families continue to be enthusiastic about the in-home intervention and eagerly participate.

Conclusion: While results of our current study are preliminary, important methodological lessons have been learned and intervention questions are being addressed.

PS1.5
Evaluating a Selectively Archived Video Recording System for Functional Behavior Assessment in Schools
Gillian R Hayes, Juane Heflin, Gregory D Abowd, Lamar

M Gardere, Ellen Matthews, Julie A Kientz, Ron Oberleitner, Trevor Pering, Georgia Institute of Technology

Background: Identifying behavioral function can lead to the development of interventions that are more effective for addressing challenging behavior. Teachers conduct functional behavior assessments (FBA) in schools, but the task load of recording the data manually and the challenge of accurately identifying antecedents and consequences while interacting with students have resulted in incomplete information capture. New software, CareLog, allows teachers to conduct FBAs in their classrooms more easily and enhances the capture of relevant information for subsequent review or consultation.

Objectives: Compare traditional and technology-augmented FBA processes and outcomes for children with autism.

Methods: Four teachers were recruited from a behavior center in the public school system. Each teacher identified two children with an autism diagnosis and severe behaviors and conducted one FBA with traditional methods and one using CareLog. Experts in FBA determined the function of each child’s behavior and compared this with the teacher’s conclusions. Efficiency in making this determination and the task load of each method were compared.

Results and Conclusion: Preliminary findings support the idea that teachers can successfully identify functions of behavior in their classrooms. Furthermore, use of software and selective video recording to augment the process can ease the data collection burden and enhance teachers’ abilities to analyze and communicate collected data.

PS1.6
FRANKFURT SOCIAL SKILLS TRAINING FOR INDIVIDUALS WITH AUTISM SPECTRUM DISORDER (ASD) Evelyn Herbrecht, Child and Adolescent Psychiatry; J.W.Goethe University Frankfurt

Background: Displeasure and complain about isolation of adolescents with autism and offering a structured group therapy could fill a gap towards an attractive treatment approach.

Objective: The aim of this study is to evaluate the effectiveness of group intervention for children and adolescents with ASD.

Methods: Principles of intervention are structured formats, combination of theoretical and practical elements, predictable rules, consideration of individual difficulties and sequential and progressive learning (includes structured games, training of facial and quasi real life affect recognition, group activities, role play, team discussions, feed-back and homework). Three groups (5-7 participants) of different age met weekly for one hour with two therapists who vary during the program, and who met regularly with the parents to provide details of the program. Types of assessment are questionnaires, ratings and behavioral observation conducted by therapists, parents, teachers and unconcerned raters.
Results: Acceptance and satisfaction with the program as well as recognition and tolerance of their respective problems are high among participants. Feedback from parents indicates distinct improvement of verbalization and contact abilities.

Conclusion: Qualitative data and results of the pilot-evaluation may lead to options for improvement and specification of the training program.

**PS1.7**

**FUNCTIONAL COMMUNICATION TRAINING USING MILIEU THERAPY PROCEDURES: A PILOT INVESTIGATION WITH A YOUNG CHILD WITH AUTISM SPECTRUM DISORDER**

*Richmond Mancil, University of Florida*

Background: There is concern about the generalizability and maintenance of traditional FCT procedures.

Objectives: Determine the effectiveness and efficiency of FCT with milieu procedures on decreasing aberrant behaviors, increasing communication mands, and increasing spontaneous communication with a child with ASD.

Methods: The subject was referred by his mother who was seeking assistance to teach her child to functionally communicate. The subject’s diagnosis of Autism Spectrum Disorder was confirmed by a review of records and the completion of the CARs. A functional analysis was completed to identify the function of the subject’s tantrums. The subject was then taught picture communication using milieu therapy procedures in play routines. Training was done by the researcher and then faded to the parent. Sessions were videotaped, coded, and then graphed using a multiple baseline format.

Results: The subject’s FA indicated a tangible function. The subject obtained efficient use of four picture communication cards within 59 five-minute sessions. Aberrant behavior decreased to zero and latency to respond to an opportunity leveled at 2 seconds. Further, the subject’s verbal vocabulary increased from two words to 56 words. The mean length of utterance (MLU) of the subject’s verbal speech also increased from one to four.

Conclusions: Findings of this pilot study show the utility of milieu procedures in FCT to simultaneously decrease aberrant behaviors, increase communication mands, and increase the diversity and complexity of verbalizations.

**PS1.8**

**THE EFFECTIVENESS OF EARLY INTERVENTION PROGRAMS FOR CHILDREN WITH AUTISM: A ONE-YEAR FOLLOW-UP STUDY OF INTENSIVE BEHAVIOURAL INTERVENTIONS VERSUS INTEGRATED PRESCHOOL CLASSROOMS**

*Amanda C Morgan, Barbara D’Entremont, Paul M McDonnell, University of New Brunswick*

Background/Objectives: The current study evaluates the success of community-based early intervention services for preschool children with autism spectrum disorder.

Methods: One group of children with autism (N=6) received 1:1 home-based Applied Behavioural Analysis (ABA) interventions for a minimum of 20 hours per week. Another group of children with autism (N=4) attended integrated preschool classrooms with Teacher’s Assistants. Examiners administered standardized tests including the Child Developmental Index (CDI), Childhood Autism Rating Scale (CARS), Vineland Adaptive Behavior Scales: Survey Form (VABS-SF), and the Psycho-educational Profile-Revised (PEP-R), to all participants twice, approximately 12 months apart in time.

Results: The groups’ mean standardized scores were similar on all standardized tests at intake. At follow-up the ABA group had higher mean standard scores on each of the standardized tests than the Preschool group. Mean improvement scores across the PEP-R, CDI, and Vineland, were 15.9 months for the ABA group and 5.5 months for the Preschool group. Individual mean improvement scores ranged from -2.3 to 44.0 months for the ABA group and from 1 to 16 months for the Preschool group. Preliminary analyses yielded group by time interaction effect sizes ranging from eta-squared = 0.179 to eta-squared=0.269.

Conclusions: Data collection is ongoing with thus far only 1/3 of follow-up assessments completed. Preliminary findings of this study support the results of previous research showing that ABA is more efficacious than integration in mainstream classrooms.

**PS1.9**

**TRACKING CHANGES IN ATTENTION STATES IN PRESCHOOL CHILDREN WITH AUTISM ATTENDING THE EARLY CHILDHOOD PARTIAL HOSPITALIZATION PROGRAM**

*Tanya Paparella, Stephanny F. Freeman, Jenny Lee, Bonnie Auyeung, University of California Los Angeles*

Background: How children with autism engage with their environment impacts their development, particularly in the language and social domains.

Objective: To assess change trajectories in attention states in preschoolers with autism participating in ECPHP, a 12-week treatment program that links research to practice in targeting the joint attention core deficit.

Methods: Children were previously diagnosed with autism. Children were assessed with the Mullen and Vineland. An observational measure of attention was developed to examine the proportion of time spent in the language and social domains.

Results: Data are presented for 10 children (mean age = 38 months), six males, four low functioning (<18 months on the Mullen). All children decreased in proportions of time spent in unengaged and onlooking states, and increased time in supported and coordinated joint attention. Higher functioning children showed dramatic declines in passive states (unengaged, onlooking) and increases in social states (joint attention). All children significantly increased in sustained attention at 8 weeks.

Conclusion: Intensive intervention programs that specifically target joint attention can affect change in children’s attention states. The findings also suggest
differences in trajectories of change may be related to functioning level. Other variables, such as duration of intervention may also be related to improvement.

PS1.10
EARLY INTENSIVE INTERVENTION IN YOUNG CHILDREN WITH AUTISM, A PROGRAM IMPLEMENTED IN FRANCE AND ITS EFFECTS ON DEVELOPMENT AND QUALITY OF LIFE
Bernadette Rogé, Carine Mantoulan, Kerstin Wittmeyer,
Laurence Frezefond, Jeanne Fremolle, Ghislain Magerotte, Université de Toulouse le Mirail
There is increasing international interest in early intervention in autism. Nevertheless, in France, a majority of clinicians remain unconvinced, when parents themselves demand early implementation of intervention.

The objective of our research was to establish an early intervention program for children with autism and to assess its effects on child development and on the quality of life.

The program was based on ABA and TEACCH methodology. 17 children with autism (ADI-R, ADOS) were included in the program. 10 children living too far to be included constituted the control group. All children were assessed using the Vineland, the CARS, and the Griffiths Scales before intervention and two years later. 14 families involved in the program and a control group of 13 families completed Quality of Life questionnaires and the Beck Depression Inventory.

A significant difference was noted between the two groups showing advanced development in the treatment group: higher intellectual performance, superior developmental level, better language development, higher Vineland scores, and lowered CARS scores. Experimental group parents, were more depressed than control group parents. After a period of 2 years, the depression scores had lowered significantly. The QOL scores were significantly lower in mothers before the treatment. At the end of the program the QOL scores had significantly increased in mothers but had dropped for several fathers.

Initial findings support the efficacy of our program on child development. The positive effects for quality of life is clear for mothers but not fully evidenced for all fathers.

PS1.11
PEER-MEDIATED AND TEXT-BASED COMMUNICATION INTERVENTIONS FOR STUDENTS WITH ASD
Kathy Thiemann, Juniper Gardens Children’s Project, University of Kansas
Background: Studies have documented effective peer-mediated social intervention approaches; however, recent research reveals that school-age children experience restricted time with peers, and limited social programming using recommended data-based strategies.

Objectives: To examine the effectiveness of a multi-component social intervention (e.g., peer training, direct instruction, written text-based cues) on the social communicative interactions between children with and without autism.

Methods: A multiple-baseline design across three social communication skills replicated across 8 children with autism spectrum disorders was used to measure the effectiveness of the peer-mediated intervention. A network of 5 to 6 peers without disabilities was formed around each child with ASD. The peers rotated in dyads twice per week to form a triad with the focus child, and participated in two 20-min social activities across one school day. After stable baseline observations, school staff was trained to implement the peer-mediated intervention for the remainder of the school year.

Results: All of the children with ASD increased their repertoires of targeted communication skills (both initiations and responses) such as gaining attention, questions, suggestions, social niceties, and talking about turns. The overall quality of the child-peer social interactions also improved based on social validity measures.

Conclusions: Findings support recommendations for integrating evidence-based approaches to enhance child-peer social interactions across typical school routines, with the ultimate goal of improved relationships and friendships.

PS1.12
TREATING JOINT ATTENTION DEFICITS THROUGH THE USE OF HIGHLY PREFERRED INTERESTS FOR YOUNG CHILDREN WITH AUTISM
Laurie A Vismara, UC Davis M.I.N.D. Institute
Background: Joint attention involves coordinating attention between social partners with respect to objects and events in order to share the experience of the object or event. Various explanations have been offered in the literature on the underlying cause of joint attention deficits in autism. The literature suggests that children with autism do not engage in joint attention behaviors because these exchanges typically involve unpredictable, complex, and social stimuli. One possible explanation is that children with autism are capable of producing joint attention but are lacking the social motivation to share their interests with others.

Method: Three children with autism between the ages of 24 to 36 months of age participated in this study. Their language abilities ranged from nonverbal to no more than ten words used for communicative purposes. A single-subjects reversal design with alternating treatments was used to test whether a motivational Pivotal Response Treatment condition consisting of highly preferred versus non-preferred interests may result in an immediate increase and generalization of joint attention initiations.

Results: Data indicate a large and significant difference in the mean number of joint attention initiations for the motivational treatment condition consisting of highly-preferred interests. As intervention continued, joint attention initiations for shared affect were also found to generalize to non-preferred interests without direct teaching. Lastly, findings included improvements in the quality of interaction between the participants and their caregivers.
Conclusion: Findings are discussed in terms of theoretical and clinical implications for understanding the role of motivation in facilitating the development of joint attention in autism.

PS1.13
A Psycho-educative intervention with social skills groups in children with Asperger’s Syndrome

Anastasia Yannaca, JL Adrien University of Paris V-Rene Descartes, Laboratory of Clinical Psychology and Psychopathology

Background: There is concern about the social abilities training in children with Asperger syndrome

Objectives: This research is a longitudinal study based on a programme of psycho-educative intervention with 6 children. The purpose is to develop their capacity for autonomy and comprehension of social codes and promote their social integration

Methods: 6 children ages 7-13 diagnosed with Asperger Syndrome by the DSM IV, the scale CARS and Australian scale for Asperger’s syndrome (Garnett and Attwood) participate in this study. The evaluation of this psycho-educative treatment is carried out with the help of Atwood’s friendship scale « Understanding and teaching friendship skills », J. Baker’s skills rating form ‘and C. Gray’s questionnaire on rating social behaviour. The intervention takes place in various settings: a) on an individual basis, b) in a group of « social abilities » with 3 other non-autistic children (18 children) and c) in a school setting (in the recreation courtyard). The programme is based upon a number of activities from different programmes: Tacade « Skills for the primary school », the programme of J. Baker « Social Skills treatment for children and adolescents with Asperger Syndrome », the social scenarios of Carol Gray., Greek traditional games, artistic expressions games. The activities are of different sorts: symbolic interactive games, role-playing, group design, physical activity, as well as strategies for listening, co-operation and the expression of feelings

Results: The results to date show the effectiveness of the procedures and techniques utilised; the children have made notable progress in communication, imagination and social interaction.

Conclusion: The participation of children with Asperger Syndrome in these activities, surrounded by non autistic children, helps them to realize their potential for socialisation and improves their relationships with their peers.

PS1.14
EFFECTIVENESS OF PARENT-IMPLEMENTED SOCIAL COMMUNICATION INTERVENTION FOR TODDLERS WITH AUTISM SPECTRUM DISORDERS
Juliann Woods, Amy M. Wetherby, Early Social Interaction Project, Department of Communication Disorders, Florida State University

Objective: The Early Social Interaction Project (ESI) was designed to extend the recommendations of the National Research Council (2001) to toddlers with autism spectrum disorders (ASD) using a parent-implemented social communication intervention embedding naturalistic teaching strategies in everyday routines. The purpose of this study was to evaluate the effectiveness of the ESI parent implemented intervention on social communication outcomes with a group of parent-toddler dyads.

Method: This quasi-experimental study evaluated whether there were differences in measures of social communication from pre- to post-intervention in a group of 17 children with ASD who entered ESI in the 2nd year of life and participated in ESI for a year. The ESI group was compared with a contrast group of 18 children with ASD who entered early intervention during the 3rd year of life on measures of social communication and developmental outcome.

Results: Results indicated significant improvement for the ESI group on 11 of 13 social communication measures from pre- to post-intervention. The 3rd year contrast group was comparable to the ESI post-intervention group on communicative means and play but had significantly poorer performance on all other measures of social communication and on verbal and nonverbal developmental level at 3 years of age.

Conclusions: These findings provide preliminary evidence that ESI is a feasible model that may be able to provide the intensity of active engagement recommended for children with ASD in a cost-efficient method and offers promise for the use of parent-implemented intervention to impact social communication in toddlers with ASD.

PS1.15
IMITATION EFFECTS ON NON VERBAL AUTISTIC CHILDREN
Cedric Galera, Kattalin Etchegoyhen, Myriam Pasco, Jacqueline Nadel, Manuel Bouvard, Department of child and adolescent psychiatry, Charles-Perrens Hospital

Background: Previous work suggested an effect of repeated imitation session on autism (Field et al, 2001).

Objectives: To evaluate and confirm the pro-social effects of imitation using the Still Face (SF)/ Imitation paradigm.

Methods: Patients were recruited from the autism clinic of Charles-Perrens hospital. The diagnosis of Autism/Pervasive Developmental Disorder was based on DSM-IV criteria. To be included it was necessary to be non verbal. Developmental level was assessed with the Psycho-Educative Profile Revised. Preverbal communication was assessed with a scale adapted from the Early Social Communication Scale. Pro-social behaviors were assessed with the standardized Nadel and Mahe instrument. Selected subjects were applied the following 3 phases-protocol (1 hour between each phase) 3 times the same day: 1/ SF first period (3 minutes), 2/ Imitation period (3 minutes), 3/ SF second period (3 minutes).

Results: Data were collected on 9 autistic children (mean age= 6 years 9 months; age range= 4 years to 12 years). Pro-social behaviors (including eye contact, search of physical contact and social gesture) increased between SF1 and SF2 of each phase and throughout the protocol.

Conclusion: Preliminary findings of the study suggest an
effect of repeated imitation sessions on non verbal autistic children.

**PS1.16**
**PRELIMINARY FINDINGS FROM A DOUBLE-BLIND PLACEBO-CONTROLLED STUDY OF DONEPEZIL IN PERVERSIVE DEVELOPMENTAL DISORDERS**

**Benjamin L Handen, Antonio Hardan, Cynthia Johnson, University of Pittsburgh School of Medicine**

**Background:** Pervasive developmental disorders (PDD) are neurodevelopmental disorders characterized by impairments in social interactions, communication, as well as restricted stereotyped patterns of behavior, interest, and activity. While several psychotropic agents are available to treat associated behavioral features, no medication has been found to be effective in treating the core symptoms of these disorders, including language and cognitive abnormalities.

**Objectives:** To assess the safety and efficacy of donepezil in the treatment of cognitive dysfunction in children and adolescents with PDD.

**Methods:** Performance on tasks tapping verbal and executive function (Delis Kaplan Executive Test: DKET) abilities was assessed for 20 non-mentally retarded children with pervasive developmental disorders (mean age: 11.6 years; range: 8 to 16 years) during a placebo-controlled, double-blind trial of 10 mg of the cholinesterase inhibitor, donepezil. Behavioral measurements were also obtained using the child behavioral checklist (CBCL).

**Results:** Significant benefits were observed in the active medication but not in the placebo group on the California Verbal Learning Test and on the Color-Word Interference and the Design Fluency subtests of the DKET. No changes were noted in both groups on Verbal Fluency and Sorting Tasks of the DKET. Relative to placebo, improvements were found with donepezil on externalizing but not internalizing measures of the CBCL. Transient and mild adverse events were reported including diarrhea and headaches.

**Conclusion:** Based on these preliminary results, donepezil may be beneficial in targeting language and cognitive deficits observed in PDD. This is consistent with neuropathologic and neurochemical abnormalities of the cholinergic pathways in autism and warrants further examination of the effectiveness and safety of donepezil and similar agents in large samples of individuals with PDD and a wide range of age and intellectual functioning.

**PS1.17**
**PILOT EFFICACY OF TREATMENT WITH BUSPIRONE IN AUTISTIC CHILDREN: A RANDOMIZED DOUBLE BLIND STUDY IN CHILDREN 2 TO 6 YEARS OF AGE**

**Robert R Rothermel, Michael E Behen, Emily Geenen, Angela Fish, Harry T Chugani, Diane C Chugani, Children's Hospital of Michigan-PET Center**

**Background:** Few pharmacological interventions aimed at altering neurodevelopment. Brain serotonergic abnormality has been demonstrated in children with autism.

**Objectives:** Examine the efficacy of treatment with buspirone, a serotonergic agonist, in children with autism. It was expected that treatment with buspirone would be associated with improved outcome compared to placebo, with greatest benefit in younger than older children, and that pretreatment K-complex values would be associated with outcome.

**Methods:** Nineteen children (13 males/6 females; younger group=2 to 4 years, n=6; older group=>4 to 6 years, n=13) were randomly assigned to Buspirone-placebo or Placebo-buspirone conditions. Alpha[11C]methyl-L-tryptophan (AMT) PET scans and multiple neurobehavioral assessments were completed by caregivers and examiners blind to treatment condition.

**Results:** Multivariate analyses (MANCOVA) for competence, triad, and associated symptoms, controlling for age, gender, and pretreatment AMT (K-complex) values, revealed positive effects of buspirone on repetitive behavior, sensory functioning, and anxiety, and trends for social functioning. Age and K-complex values moderated response to buspirone, with younger children and those with higher baseline K-complex values demonstrating more benefit from buspirone.

**Conclusion:** Treatment with buspirone was associated with improvement in two triad symptoms, sensory problems and anxiety. Gains were greater for younger children, and associated with pretreatment K-complex values, suggesting that altering serotonergic levels has more impact in neurodevelopmentally less mature nervous systems. Greater responsiveness in younger children may reflect greater plasticity and susceptibility for change in the long term developmental course in the serotonin system involved in the expression of autism.

**PS1.18**
**A PLACEBO DOUBLE-BLIND STUDY OF DEXTROMETHORPHAN FOR PROBLEMATIC BEHAVIORS IN CHILDREN WITH AUTISM**

**Cooper R Woodard, June Groden, Matthew Goodwin, James Bodfish, The Groden Center**

**Background:** The effects of dextromethorphan in persons with autism are unclear, though case studies have shown decreases in problem behaviors.

**Objectives:** Compare the effects of dextromethorphan to placebo.

**Methods:** Participants were eight children with ASD who demonstrated moderate to severe behavior problems. Design was a double-blind, placebo-controlled, ABAB/BABA (A = medication, B = placebo) design lasting 10 weeks. Participants were given 30 mg of dextromethorphan (1 tsp. Delsym®), BID. Measures included the TESS, the ABC, the CGIS - Autism, and the Design Fluency subtest of the ABC. Transient or greater on the Irritability subscale of the ABC, and an improvement on the Hyperactivity subscale. For these
same participants, between two and four additional subscales had change scores at the 3rd 25% or 3rd 50% levels that included improvements on measures related to the core features of autism. Two of these three participants also showed significantly (p < .05) lower rates of problem behavior (e.g., out-of-seat behavior, aggression, non-purposeful verbalizations). No side effects occurred in both dextromethorphan phases for any of the participants. Conclusion: Preliminary findings suggest that dextromethorphan is safe and may have a positive effect on a subgroup of persons with autism.

PS1.19
INFANT STEREOTYPIES IN AUTISM: EXAMINING DEVELOPMENTAL TRAJECTORIES AND CURRENT PHENOTYPES
Brian A Boyd, Kristen S.L. Lam, Grace T Baranek, Raheleh Tschoepe, Linda R Watson, Elizabeth R Crais, University of North Carolina-Chapel Hill

Background: Relatively little research has focused on early displays of repetitive or stereotyped behaviors and the specific types or patterns associated with autism (Baranek, 1999). Predictable topographies of repetitive behaviors have been found in typically developing infants (Thelen, 1979); however, it is not known whether such topographies differ either quantitatively or qualitatively in autism.

Objective: To explore the longitudinal development of motor and object stereotypies at two time points in infancy to see if they aid in the early detection of autism.

Method: 10 minute segments of retrospective home videotapes of 74 children (ASD=31, DD=18, TYP=25) at 9-12 and 15-18 months of age are coded by blind raters for the presence of motor and object stereotypies using a validated interval coding system (see Baranek, 1999). Coded behaviors include repetitive stereotypies (e.g., arm waving) as well as non-repetitive stereotypies (e.g., posturing).

Results: Preliminary analyses with a subset of our sample (autism=21, DD=4, TYP=10) showed increased levels of repetitive behaviors at both time points for the autism and DD groups. The presentation will include data from the complete dataset to examine specific patterns that distinguish autism from DD or TYP, and examine predictive relationships with current manifestations of adaptive functioning (using Vineland), repetitive behaviors (using RBS-R), and autism severity (using CARS) in these same children with autism.

Discussion: Studying early development of motor and object stereotypies in infancy may prove important to the early detection of developmental disabilities, and may elucidate deficits that have implications for treatment as well as further research in autism.

PS1.21
COMPARISON OF REPETITIVE BEHAVIORS IN ASPERGERS DISORDER AND HIGH FUNCTIONING AUTISM
Michael L Cuccaro, Jason S Brinkley, Laura Nations, Ruth K Abramson, Alicia Hall, Harry H Wright, John R Gilbert, Margaret A Pericak-Vance Duke University Medical Center

Background: It is unclear whether in PDD there are distinct groups of repetitive behaviors with different specificity to autism.

Objective: Test the hypothesis that motor/sensory stereotypies are distinct from ‘quasi-obsessive’ behaviors, and that low cognitive abilities predict the former.

Methods: Individuals with an established autism/PDD diagnosis were retrospectively identified from a research pool and a clinic database at the Maudsley Hospital. A non-autistic control group of mentally retarded subjects (MR) was also identified from the latter. ADI and ADOS were used in all research cases and in most of the clinic sample. Developmental level was assessed with various cognitive tests. Data were extracted from the ADIs for all 62 autistic subjects of the research sample (mean age 14.1 years; age range= 5-22 years), and from the Maudsley Item Sheets for the others (502 with a PDD/Autism, mean age 7.7 years; and 119 with MR, mean age 10.3 years; age range=1-18 years). Proportional Odds and Structural Equation Modelling examined the goodness of fit of a two-factor model.

Results: Motor/sensory stereotypies and quasi-obsessive behaviors were distinct independent groups only in MR. Their correlation in PDD/Autism was small.

Motor/sensory stereotypies were predicted by low cognitive abilities across samples whereas the quasi-obsessive behaviors were significantly associated with ruminations in PDD.

Conclusions: These results suggest that motor/sensory stereotypies may be less specific to autism. The correlation between them and quasi-obsessive behaviors in PDD might reflect the end result of diffuse altered neural networks in these disorders.

PS1.20
REPEITIVE AND STEREOTyped BEHAVIORS IN PERVERsIVE DEVELOPMENTAL DISORDERS
Iris Carcanci-Rathwell, Sophia Rabe-Hasketh, Paramala J Santosh Child Psychiatry Department/ADCR building Institute of Psychiatry

Background: It is unclear whether in PDD there are distinct groups of repetitive behaviors with different specificity to autism.

Objective: Test the hypothesis that motor/sensory stereotypies are distinct from ‘quasi-obsessive’ behaviors, and that low cognitive abilities predict the former.

Methods: Individuals with an established autism/PDD diagnosis were retrospectively identified from a research pool and a clinic database at the Maudsley Hospital. A non-autistic control group of mentally retarded subjects (MR) was also identified from the latter. ADI and ADOS were used in all research cases and in most of the clinic sample. Developmental level was assessed with various cognitive tests. Data were extracted from the ADIs for all 62 autistic subjects of the research sample (mean age 14.1 years; age range= 5-22 years), and from the Maudsley Item Sheets for the others (502 with a PDD/Autism, mean age 7.7 years; and 119 with MR, mean age 10.3 years; age range=1-18 years). Proportional Odds and Structural Equation Modelling examined the goodness of fit of a two-factor model.

Results: Motor/sensory stereotypies and quasi-obsessive behaviors were distinct independent groups only in MR. Their correlation in PDD/Autism was small.

Motor/sensory stereotypies were predicted by low cognitive abilities across samples whereas the quasi-obsessive behaviors were significantly associated with ruminations in PDD.

Conclusions: These results suggest that motor/sensory stereotypies may be less specific to autism. The correlation between them and quasi-obsessive behaviors in PDD might reflect the end result of diffuse altered neural networks in these disorders.
(19M/4F) of participants with ASP (M age = 11.4 years) and HFA (M age = 12.3 years). Paired t-tests revealed no significant differences between the means for any of the RBS-R intensity or frequency scores (range of p-values 0.32 - 0.92). Analyses of individual items in RBS-R Stereotyped Behavior (6 items) and Restricted Behavior (4 items) scales also revealed no differences. Finally, ASP and HFA participants did not differ on the ABC Stereotypy scale (p = 0.55).

Conclusion: There appear to be no differences between IQ-matched individuals with ASP and HFA in the intensity or frequency of repetitive behaviors.

PS1.22
Special interests in Autism Spectrum Disorders Judith H Danovitch, Amanda B Merz, Elizabeth H Dohrmann, Fred R Volkmar, Ami Klin Yale School of Medicine

Background: Persistent unusual and intense interests are widely reported in children with Autism Spectrum Disorders (ASD), but limited quantitative data exists about these interests and how they relate to level of functioning.

Objectives: To characterize special interests in high functioning children with ASD

Methods: Participants were recruited from the Yale Developmental Disabilities Clinic and were assessed with the ADOS and ADI. Level of functioning was assessed with the Vineland Adaptive Behavior Scales. Parents of participants with ASD also completed a survey where they listed any unusually intense interests displayed by their child and indicated how frequently the interests interfered with social interactions. Two raters coded the special interests into 8 descriptive categories.

Results: Data are collected for 96 participants (91 males) with diagnoses of ASD. 90% reported at least one special interest. The majority (81%) of special interests involved the collection of facts within a system or topic involving verbal memory, followed by the collection of facts involving visual memory (27%). Parental ratings of interference were positively correlated with the ADI circumscribed interest item, and negatively correlated with Vineland scores for communication, daily living, and socialization. There is also evidence that the presence of a special interest is associated with an earlier emergence of language, measured by the age of first single words and first phrases on the ADI.

Conclusion: The presence of special interests and how often these interests interfere with social interactions is related to level of functioning and early language.

PS1.23
REPETITIVE BEHAVIORS AND OTHER PROBLEM BEHAVIORS IN PRESCHOOLERS WITH AUTISM SPECTRUM DISORDER COMPARED TO TYPICAL CONTROLS Robin Lea Gabriels, Kristen S. I. Lam, John A. Agnew, Tia N. Holtzclaw, Michael L. Cuccaro, James W. Bodfish, University of Colorado at Denver and Health Sciences Center

Background: Information is lacking regarding how other problem behaviors in ASD relate to restrictive and repetitive behaviors and interests (RBs) compared to matched controls.

Objectives: Compare caregiver frequency/severity ratings of RBs and other problem behaviors in preschool children with ASD and typically developing (TD) controls.

Methods: Sixty-two children (mean age = 50.5 mos.) diagnosed with an ASD by a licensed clinician recruited through the NDRC Autism Research Registry and 65 TD children (mean age = 46.5 mos.) recruited through local preschools and daycare centers. Repetitive Behavior Scale-Revised (RBS-R) and Nisonger Child Behavior Rating Form (NCBRF) were completed by caregivers.

Results: The ASD group had significantly more mood and behavior problems (p < 0.006) than TD controls. Within the ASD group, RBS-R total score was significantly correlated with all four NCBRF subscales (Conduct r = 0.61; Anxious r = 0.77; Hyperactivity r = 0.46; Overly Sensitive r = 0.70) with p < 0.000 for all analyses. Within this group, the six RBS-R subscales were compared to the four NCBRF subscales and of 24 comparisons, 21 were significantly correlated at p < 0.005, corrected for multiple comparisons.

Conclusions: Problem behaviors appear to be present at an early age in ASD and are related to RBs. Clarifying this relationship may help improve accurate co-morbid psychological diagnoses and ensure appropriate treatment.

PS1.24
AN EXAMINATION OF THE CONCEPTUAL MODELS OF THE STEREOTYPIC BEHAVIOR OF PERSONS WITH AUTISM David Brunell McAdam, University of Rochester School of Medicine

Background: Some conceptual models hypothesize that the stereotypic behaviors of persons with autism have internal causes. The specific internal mechanism (e.g., perceptual reinforcement, increased arousal) maintaining stereotypic behavior within these models varies from model-to-model. However, all of these models suggest that stereotypic behavior serves to reduce a heightened internal state or anxiety. Other models hypothesize that stereotypic behaviors are learned behaviors that are socially-mediated through the actions of other people.

Objectives: To use an analogue functional analysis assessment procedure to determine the degree to which the stereotypic behavior of persons with autism have internal causes. The specific internal mechanism (e.g., perceptual reinforcement, increased arousal) maintaining stereotypic behavior within these models varies from model-to-model. However, all of these models suggest that stereotypic behavior serves to reduce a heightened internal state or anxiety. Other models hypothesize that stereotypic behaviors are learned behaviors that are socially-mediated through the actions of other people.

Methods: Participants were recruited from the Yale Developmental Disabilities Clinic and were assessed with the ADOS and ADI. Level of functioning was assessed with the Vineland Adaptive Behavior Scales. Parents of participants with ASD also completed a survey where they listed any unusually intense interests displayed by their child and indicated how frequently the interests interfered with social interactions. Two raters coded the special interests into 8 descriptive categories.

Results: Data are collected for 96 participants (91 males) with diagnoses of ASD. 90% reported at least one special interest. The majority (81%) of special interests involved the collection of facts within a system or topic involving verbal memory, followed by the collection of facts involving visual memory (27%). Parental ratings of interference were positively correlated with the ADI circumscribed interest item, and negatively correlated with Vineland scores for communication, daily living, and socialization. There is also evidence that the presence of a special interest is associated with an earlier emergence of language, measured by the age of first single words and first phrases on the ADI.

Conclusion: The presence of special interests and how often these interests interfere with social interactions is related to level of functioning and early language.
PS1.25
EARLY FEATURES OF AUTISM: LONGITUDINAL STUDY OF REPETITIVE BEHAVIOURS IN YOUNG CHILDREN Erin Louise Mooney, Kylie M Gray, Bruce J Tonge, Deborah J Sweeney, Stewart L Einfeld, Monash University Centre of Developmental Psychiatry and Psychology

Background: Preliminary investigation of repetitive behaviours displayed in children with autism has suggested they can be divided into higher-level (more complex) and lower-level (more sensory/motor behaviours) categories, where higher-level behaviours may be differentiating features of autism at a certain developmental level while lower-level behaviours may be a function of developmental delay.

Objectives: To investigate the early manifestation of repetitive behaviours in developmentally delayed children with and without autism and how these behaviours change over a 12 month period.

Methods: Developmentally delayed children aged 18-51 months were referred by services and paediatricians practicing within the southern or western regions of Melbourne, Australia. All children received an initial assessment and a 12-month review. Standardised developmental and diagnostic assessments were administered at both time points.

Results: Data was collected on 73 developmentally delayed children with autism and 33 developmentally delayed controls. Preliminary analyses indicated that several measures of higher level repetitive behaviour, were associated with the probability of receiving a diagnosis of autism. The results of time series regression analyses used to investigate the relationship between age (chronological and developmental) and the presence of repetitive behaviours in children will be reported.

Conclusion: Preliminary findings strengthen existing literature suggesting that the presence of higher-level repetitive behaviour is a differentiating feature of autism in young children. Further longitudinal work will help to clarify relationships between age and the presence between repetitive behaviours in developmentally delayed children with autism.

PS1.26
REPETITIVE BEHAVIOUR IN AUTISM SPECTRUM DISORDERS: FACTOR STRUCTURE, RELATIONSHIP TO IQ AND SPECIFICITY Jenifer Tregay, Catherine Jones, Anita Jayne, Sarah Marsden, Gillian Baird, Emily Simonoff; Andrew Pickles, Susie Chandler, Tom Loucas, Tony Charman, Institute of Child Health, University College London

Background: Repetitive and stereotyped behaviour form part of the diagnostic criteria for autism spectrum disorders (ASDs), yet little is understood about how these heterogeneous behaviours group together, how they relate to IQ and which behaviours are specific to ASDs.

Objectives: To understand the structure of repetitive behaviours in ASDs using factor analysis of two informant-rated instruments (ADI-R and the CRI). To examine types of repetitive behaviour reported in high vs. low IQ groups and in individuals with and without ASD.

Methods: Participants were 255 individuals aged between 11-14 years. Diagnostic assessments (ADI-R and ADOS) were used to classify participants into one of three diagnostic groups (Autism, PDD or ‘No PDD’). Half of the participants in each diagnostic groups had IQ >70, whilst half had IQ <70. Two parent-report instruments were analysed: 12 items from ‘repetitive and stereotyped behaviour’ section of the Autism Diagnostic Interview (ADI-R) and 17 items from the Childhood Routines Inventory (CRI).

Results: Factor analyses of the ADI-R and CRI resulted in 4 and 5 factor solutions respectively. Multivariate analysis indicated that, across the 2 instruments, factors relating to unusual preoccupations, motor stereotypes and repetition were associated with low IQ. Behaviours relating to the maintenance of sameness, sensory hypersensitivity and attention to detail, while more common in individuals with an autism diagnosis, were not related to IQ.

Conclusions: Repetitive and stereotyped behaviours do show a coherent factor structure. Some factors are more highly associated with IQ, whilst others are more specific to autism.
the modified version of the predictive PRT profile assessment is reliable with the original version of the assessment for clinician scorers. Issues addressed are the importance of early and effective intervention for children with autism and dissemination of research based practice into applied settings.

PS1.28
REGRESSION IN AUTISM: DEFINITIONS AND PREVALENCE IN THE CHARGE STUDY Robin Lee Hansen, Sally Ozonoff, Paula Kracowiak, Carrie Jones, Lesley Deprey, Lisa A Croen, Irva Hertz-Picciotto University of California, Davis

Background: Developmental regression in children with autism spectrum disorders has been variably defined and, thus, studies have reported differing proportions. Objectives: To examine the prevalence of regressive autism using two different definitions based on the Autism Diagnostic Interview-Revised (ADI-R); and to describe the distribution of scores on another measure of regression, the Child Development Questionnaire (CDQ), between the children designated as `regressive' vs `early onset' based on the ADI-R definitions.

Methods: Subjects were participants in the population based CHARGE study, 2-5 years of age with ASD confirmed by ADI-R and Autism Diagnostic Observation Schedule (ADOS) scores. 158 met the definition of autistic disorder on both measures, while 59 met criteria for ASD. Two definitions for regression were used. The `narrow definition' required loss of both language and social skills, while the `broad definition' required loss of either language or social skills, defined by ADI-R questions 11 and 25.

Results: Using the narrow definition of regression, 30/217 (14%) met criteria for regression. 91/217 (42%) met criteria for regression using the broad definition. Using either definition of regression, the mean CDQ scores of children with regression and early onset autism were significantly different, but the group distributions overlapped, with losses reported for some children with early onset autism.

Conclusions: The rates of regression in a large sample of young children with ASD vary significantly depending on the definition used. Definitions that require language loss seem to significantly underestimate rates of developmental regression. Loss of skills appears to be distributed along a continuum, rather than falling into distinct categories. Measurement issues regarding regression need further investigation.

PS1.29
Autism and Head Circumference in the CHARGE Study Carrie Reynolds Jones, Robin Hansen, Paula Krakowiak, Nareg Kalanikarian, Lisa Croen, Irva Hertz-Picciotto UC Davis M.I.N.D Institute

Background: Increased rates of macrocephaly have been reported in children and adults with autism, but results were based on very small groups of autistic children and were rarely compared to control children from the same population. Objectives: Evaluate the association of head circumference with other growth parameters in young children with autism, and compare to typically developing children of the same age.

Methods: 186 Autism cases and 63 general population controls ages 2-5 from the CHARGE (Childhood Autism Risks from Genetics and the Environment) study in California had measurements of head circumference, weight and height plotted by age and sex on NHANES III growth charts and compared.

Results: Mean head circumference of both cases and controls was around the 50th percentile, with a higher-than-expected proportion of both cases (9%) and controls (12%) at or above the 95th percentile. Weight was a very strong predictor of head circumference in linear regression models (p < .0001), but autism vs. general population group membership did not predict head circumference (p =.21).

Conclusion: These data showed no difference in head circumference between children with and without autism, with head circumference predicted by weight rather than by diagnostic group. Trajectories over time and possible differences in autism subgroups will be examined next.

PS1.30
AUTISM IN VENEZUELA: BEYOND TRANSLATION, ACCULTURATION AND TESTING Cecilia Montiel-Nava, Joaquin A. Peña, Isabel C. Montiel-Barbero, Facultad de Humanidades_ La Universidad del Zulia

Background: There is lack of information regarding the epidemiology of autism, its clinical characterization and related disorders in Hispanic populations. The review of epidemiology and diagnostic of this disorder usually takes into account the studies done in the English language .

Objective: The main aims of this paper are to present some research findings and what the state of the study of autism is in Venezuela.

Method: thru the review of the Venezuelan literature we identified the scientific studies of autism and developmental disorders carried out in our country. The criterion for inclusion in this revision was that the article must have been published in a peer reviewed journal.

Results: After reviewing the published research related to ASD in Venezuela it was found that there is information regarding 1.) Some epidemiological data from where it can infer more detailed information and start planning more complete studies, 2.) information about metabolic characterization, 3.) Information about medical conditions related to autism 4.) Data from structural and functional neuroimaging, 5.) There is an ongoing project of standardization the diagnostic procedures to comply with the international guidelines.

Conclusion: Although there is still not enough information to draw conclusions, all the studies presented could be considered as pilot studies for planning the next steps in the investigation of ASD in Venezuela. Our progress in the field of ASD research is dependent on our ability to incorporate the research guidelines into our daily practice.
PS1.31
CHILDREN WITH AUTISM: MORBIDITY, CO-MORBIDITY AND FAMILY BURDEN Daniel W Mruzek, Gregory S Liptak, Christine M Wade, Lauren Benzoni, Karen W Nolan, Melissa A Thingvell, Edgar Fryer, University of Rochester Medical Center

Background: Autism is associated with multiple biopsychosocial health concerns for the child and family. Objectives: To investigate morbid and co-morbid conditions in children with autism as well as the burden of care experienced by families.

Methods: Secondary analysis of data obtained from the National Survey of Children’s Health, a nationally representative sample (CDC, 2003-4). Data were analyzed using SUDAAN statistical software.

Results: 473 children (weighted sample size 309,793) were identified by their families as having autism. 11% of children with autism were reported to have fair or poor general health compared to 3% of children without autism. Co-morbid conditions such as depression & anxiety, bone joint or muscle problems, and gastrointestinal allergy were significantly more common in children with autism (all p<0.001). Parents of children with autism reported that their children were much harder to care for than other children of the same age, that they had to make greater sacrifices than expected to meet their children’s needs, and that the mental and emotional health of the child put a great burden on the family (all p<0.001).

Conclusions: Children with autism are at significantly higher risk for multiple health concerns, including mental and physical problems, than children in the general population. Also, families with children with autism experience significantly greater burdens across a broad range of categories.

PS1.32
REMOTE AUTISM EVALUATION THROUGH TELEHEALTH TECHNOLOGY: 2 CASE STUDIES Ron M Oberleitner, Uwe Reischl, James Ball, John Harrington, Suhas Pharkute, Gregory Abowd, TalkAutism

Background: Due to limited availability of local professional services, families coping with autism encounter serious obstacles when attempting to access urgent autism services.

Objectives: To assess the impact of Telehealth technology on perceived quality of care.

Methods: Case #1: An Idaho family concerned about their child’s immediate health status used a preliminary version of the CareLog video capture system to record and transmit video clip data to a web-based Personal Health Record for subsequent review by an autism specialist in New York.

Case #2: Due to lost health records caused by Hurricane Katrina, a family relocated to Atlanta agreed to a formal autism evaluation of their child by using videophone connection with an autism specialist in New Jersey.

Results: In Case #1, the family declined to visit a local emergency room as suggested but opted to send video data remotely for consultation. The remote specialist responded quickly, which the family perceived as helpful while they waited for an appointment with a local specialist. Outcome of telehealth consultation was consistent with the in-person evaluation two months later. The Family in Case #2 opted for telehealth evaluation because it was unclear when a local in-person evaluation could be arranged. The family was delighted to be able to send their child to a new school much sooner than would have otherwise been possible.

Conclusion: Families with autism perceived Telehealth as a reliable vehicle for accessing specialty care. In addition, the application of the videophone technology demonstrated the practicality of accessing remote resources during a time of emergency.

PS1.33
ASSESSMENT PROTOCOL FOR CLINICAL, NEUROLOGICAL, AND NEUROIMAGING CHARACTERIZATION OF NON-VERBAL AUTISTIC CHILDREN IN VENEZUELA. A PILOT STUDY Joaquin A Peña, Cecilia Montiel-Nava, Enoe Medrano, Isabel Montiel-Barbero, Eduardo Mora-La Cruz, José A Chacín, Postgrado de Neurología Pediátrica-La Universidad del Zulia

Background: With the advent of standardized diagnostic tools expert clinicians are now able to diagnose autism reliably.

Objective: In this study we present preliminary findings of the assessment protocol developed to identify and characterize non-verbal autistic children in Venezuela.

Methods: participants of this study were recruited thru advertisement in local newspapers. The inclusion criteria was having a diagnosis of Autistic Syndrome according to the ADOS-G, receptive language lower than 36 months according to the VABS. Children with another medical condition were excluded. Written informed consent was obtained from all parents or guardians of the subjects. Each patient was assessed using: the VABS, a Developmental History, ADOS-G, Neurological Examination, karyotyping and screening of X-Fragile Syndrome, EEG, SPECT brain perfusion imaging with Tc-99m ECD, and H-MRS.

Results: Of the 33 children, 8 had receptive language abilities above 36 months; and 4 had an additional medical condition (ataxia, seizures, hemiparesis, and heart disease), causing them to be excluded. Patients exhibited less perfusion in the left brain hemisphere in all of the ROI. These findings represent a decrease in the values of brain perfusion and confirm the existence of a dysfunction in the areas related to language, which leads to an anomalous hemispheric specialization in non-verbal autistic children.

Conclusion By following a standardized assessment protocol the identification of ASD in our research facility is more accurate. Furthermore, data obtained through physical, neurological, neuroimaging and genetic information for each case will lead to a better understanding of the comorbid features of ASD.
PS1.34
DOES HIGH IQ IN AUTISM SPECTRUM DISORDERS TRANSLATE INTO REAL-LIFE SUCCESS? Celine A Saulnier, Ami Klin, Sara S Sparrow, Domenic V Cicchetti, Fred R Volkmar, Catherine Lord, Yale Child Study Center
Background: Despite an increase in the number of individuals with Autism Spectrum Disorders (ASD) who achieve independence in adulthood, there continues to be great variability in outcome, with many ‘higher functioning’ individuals failing to translate their potential to real-life success.
Objectives: The relationship between social and communicative adaptive functioning as measured by the Vineland Adaptive Behavior Scales and symptomatology as measured by the Autism Diagnostic Observation Schedule is investigated in relation to age and IQ in two clinical samples of individuals with ASD.
Methods: Participants included 187 males aged 7 to 18 years (84 through the Yale Child Study Center and 103 through the University of Michigan) with Verbal IQ scores above 70 (104.7 and 101.2, respectively).
Results: Impairments were found in communication (Vineland standard scores = 72.2 and 83.5, respectively) and social adaptive skills (Vineland standard scores = 52.0 and 67.0, respectively). Negative relationships were found between age and Vineland scores, suggesting that adaptive skills do not keep pace with chronological development. Yet, ADOS scores remained stable with age, indicating stability in symptomatology over time.
Conclusion: Despite their cognitive potential, individuals with ASD across two independent samples show significant deficits in adaptive functioning, with the greatest impairments in functional social skills.

PS1.35
DIFFERENTIATING AUTISM SPECTRUM DISORDER SUBTYPES USING THE ADI-R AND ADOS Christina P Chrysler, Peter Szatmari, Lonnie Zwaigenbaum, Catherine Lord, Susan Risi, McMaster University-Offord Centre for Child Studies
Background: While it is possible to reliably and accurately diagnose autism, the differentiation of autism from Asperger syndrome (AS) and PDDNOS is much more difficult.
Objective: To evaluate the ability of a diagnostic algorithm employing both the ADI-R and ADOS to accurately differentiate autism from other autism spectrum subtypes.
Method: The sample consisted of 404 individuals with autism, PDD-NOS and AS. All subjects were assessed using available clinical records, ADI-R, ADOS, and the Vineland Adaptive Behaviour Scales (VABS). Each individual was given a best estimate (BE) diagnosis. A new diagnostic algorithm was devised combining the ADI-R, ADOS and VABS and was compared to the BE diagnosis.
Results: Combining the standard ADI-R and ADOS cut-offs had a tendency to over-diagnose autism and to under-diagnose AS and PDDNOS. This tendency was minimized if the algorithm was implemented in a sequential fashion, diagnosing AS first before assessing for autism and by adding data from the VABS communication scores. With these amendments, it was possible to differentiate the ASD subtypes with acceptable sensitivity and specificity.
Conclusions: To differentiate autism from PDDNOS and AS, researchers will have to use supplementary information in addition to the ADI-R and ADOS. In addition, it appears best to employ a sequential approach diagnosing AS first, then autism then lastly PDDNOS.

PS1.36
DIFFERENTIATING ASPERGER’S FROM AUTISM IN ADULTS USING MEASURES OF CURRENT FUNCTIONING Lily A. Ield, Jessica Greenson, Lindsey Sterling, Kathryn Schoolcraft, Sara J. Webb, Elizabeth Aylward, Geraldine Dawson, University of Washington
Background: The DSM-IV differentiates Autistic Disorder from Asperger’s Disorder based on early language development/impairment. When these diagnoses are made later in life, diagnostic differentiation is based on parental recall of historical data.
Objectives: Similar to Howlin’s study (2003), this study examined current expression of language and social impairment in adults with autism and Asperger’s Disorder to determine if current functioning differentiates these two groups.
Methods: Current language and social functioning was assessed using the ADI-R, ADOS-G module 4, the comprehension and vocabulary sub-domains of the Wechsler Adult Intelligence Tests-III (WAIS-III) and two self report questionnaires on social interest.
Results: Preliminary analyses from 13 adults with autism and 10 adults with Asperger’s revealed that adults with autism use significantly more stereotyped utterances and delayed echolalia than adults with Asperger’s Disorder. Trends in the data revealed the autism group to have more impaired reciprocal conversation and to be more language-impaired on the ADI-R language score. There was a relation between ADI-R verbal items and the comprehension subtest of the WAIS-III in the autism group but not the Asperger’s Disorder group.
Conclusions: The results suggest that language differences continue to exist between individuals with autism and Asperger’s Disorder in adulthood. Further analyses with more subjects will also examine differences within the social domain.
Support: This study was funded by the National Institute of Mental Health (U54MH066399).

PS1.37
THE CONGRUENCY OF PARENT AND TEACHER REPORT OF SOCIAL SKILLS IN CHILDREN WITH AUTISM SPECTRUM DISORDER Donna S Murray, Lisa A Ruble, Heather N Willis, The Kelly O’Leary Center for Autism Spectrum Disorders, Cincinnati Children’s Hospital Medical Center
Background: There is a paucity of research analyzing the
congruency of parent and teacher responses on questionnaires evaluating social skills in children with ASD.

Objectives: To determine if there is overall congruency on the TRIAD Social Skills Assessment (TSSA) between parent and teacher report of social skills in children with ASD, determine if there is a correlation between parent and teacher report on areas of social development, and analyze areas reported to be more or less impaired.

Methods: Data were collected from the medical charts of 48 children with ASD who received a social skills assessment at one of two large regional autism centers. The TSSA questionnaires were distributed as part of the intake process, prior to treatment at the center.

Results: Data were collected on 48 participants of children with ASD (age range 5-14 years). Items evaluated four social development areas including; affective understanding, initiating interactions, responding to interactions and maintaining interactions. There was a strikingly similar pattern of parent and teacher report, but not a direct correlation for all social development areas.

Conclusion: This study lends support for use of multi-informants. The trend indicates that some social skills are consistent across settings; while other social skills are context dependant.

PS1.38
THE BOUNDARIES OF AUTISM: COMPARISONS INVOLVING CHILDREN WITH SPECIFIC LANGUAGE IMPAIRMENT AND OBSESSIVE COMPULSIVE DISORDER
Margot Ruth Prior, Suzanne Barrett, Zandt Fiona, Department of Psychology, University of Melbourne, Australia

Background: The symptoms and behaviours characteristic of autism overlap with those of other developmental disorders and can be a challenge for differential diagnosis.

Objectives: Comparison of symptoms of young children with diagnoses of autism, specific language disorders (LD), and of children and adolescents with diagnoses of obsessive compulsive disorder (OCD) or Autism Spectrum Disorders (ASD) (Autism and Asperger Syndrome).

Methods: Study 1: Using questionnaire and observation methods, 4-7 year old children with LD and autism were compared in social, communication, play, and repetitive behaviour domains. Study 2: Repetitive and obsessive behaviours were measured in children and adolescents with Autism or OCD, and in normal controls, via interviews with parents and children.

Results: Study 1. Children with autism showed greater deficits than those with LD in joint attention, functional play, repetitive behaviour and pragmatic language; however there were many areas showing no group differences. Cluster analysis of the 37 children identified three groups, each including a mixture of autistic and LD cases.

Study 2: All varieties of repetitive and obsessive behaviours were more prevalent in the OCD and ASD groups compared with controls, with a pattern of both similarities and differences. Children with OCD showed more compulsions and obsessions that those with autism especially the older probands.

Conclusions: This research indicated consistent support for the concept of a spectrum, underpinned by severity of social, communicative, and behavioural impairments.

This research was carried out with ethical approval from the ethics committee of the Royal Children’s Hospital Melbourne and the University of Melbourne. Funding was from the University of Melbourne.

PS1.39
NAVIGATING THE AUTISM DIAGNOSTIC SYSTEM: PARENTS’ EXPERIENCES IN ONTARIO
Alison Ann Spadafora, Marcia Nadine Gragg, Sylvia L. Voelker, University of Windsor

Background: Early identification of ASD facilitates effective intervention, but there is evidence that obtaining a diagnosis can be a lengthy process.

Objectives: Identify variables contributing to difficulties parents experience in obtaining ASD diagnoses for their children in the Canadian health care system.

Methods: Parents (N=79) were recruited from the Autism Society of Ontario. They completed questionnaires describing their initial concerns about their child, their subsequent contacts with the health care system, and their impressions of how the system worked and could be improved.

Results: Parents reported on 81 children (86.4% males) with ASD. Median year of diagnosis was 2000. Average age at initial concern, which was raised most often by the mother, was 19.7 months (SD = 13.5). Initial help seeking occurred 10.4 months later, on average. The first professional to see the child usually referred the child (43.4%) or delayed/reassured the parent (38.6%). Average age at diagnosis was 51.5 months (SD = 32.9). Child gender, ethnicity, birth order and SES were unrelated to study variables. Barriers to help seeking included long wait lists and concerns that doctors would not take parental complaints seriously.

Conclusion: Parents noticed ASD symptoms by about 1½ years, but diagnosis was typically delayed for another 2½ years, placing the children at risk for missing early intervention opportunities. Suggestions for increasing the efficiency of the diagnostic system are discussed.

Sponsor: SSHRC*

PS1.40
USING THE ADI-R AND ADOS IN YOUNG CHILDMREN WITH DEVELOPMENTAL DELAY: EVALUATING DIAGNOSTIC ACCURACY
Deborah Sweeney, Kylie M Gray, Bruce J Tonge, Stewart L Einfeld, Monash University, School of Psychology, Psychiatry & Psychological Medicine

Background: The ADI-R and ADOS have become established as the gold standard instruments in the assessment and diagnosis of autism. Whilst a number of studies have reported on the diagnostic accuracy of these tools in children and adolescents, less work has been reported on the efficacy of these tools in young children.

Funding was from the University of Melbourne.
presenting with developmental problems.

Objectives: This study aimed to assess the diagnostic efficacy of the ADI-R and the ADOS in a sample of young children with developmental problems aged 18 - 48 months.

Methods: Approximately 210 children aged 18-48 months referred to a developmental assessment clinic participated in the study. All children underwent a comprehensive assessment, including administration of the ADI-R and ADOS. Diagnoses were then made according to DSM-IV criteria based upon all available information.

Results: One-hundred and fourteen children received a diagnosis of a Pervasive Developmental Disorder (either Autistic Disorder or PDDNOS). Results will be reported on the efficacy of the ADI-R and ADOS in classifying these children. False positives and negatives will be examined in relation to age (developmental and chronological), language ability, and degree of behaviour and emotional problems.

Conclusion: Anecdotal reports suggest that referrals of young children suspected of autism are increasing. Investigating the diagnostic accuracy of assessment tools such as the ADI-R and ADOS in this population has therefore become increasingly important, particularly in terms of differentiating autism from developmental delay.

Sponsor: National Health and Medical Research Council

PS1.41
RAPID ASSESSMENT OF AUTISTIC SYMPTOMATOLOGY BY SCHOOL TEACHERS: CROSS VALIDATION WITH ADI-R AND ADOS
Anna M Abbacchi, Patricia D Lavesser, Yi Zhang, John N Constantino, AGRE Consortium, Washington University School of Medicine

Background: Methods of feasible and reliable quantitative characterization of autistic symptomatology in school settings can facilitate clinical diagnosis and aid in assessment of response to intervention.

Objectives: We examined the validity of teacher reports of autistic symptomatology using the Social Responsiveness Scale (SRS), a 65-item quantitative measure of autistic traits, against two established instruments utilizing trained examiners/interviewers (ADI-r and ADOS).

Methods: Subjects were recruited from the Washington University Child and Adolescent Psychiatry service and the Autism Genetic Resource Exchange (AGRE). The total sample involved 543 clinical subjects (age 4-18) with and without autism spectrum disorders (ASDs) and their siblings (affected and unaffected). Children were assessed by parent- and teacher-report SRS, ADI-r and ADOS.

Results: Correlation between parent- and teacher-report SRS scores in this clinically-ascertained sib sample was 0.60. Among children whose total SRS scores were greater than 85 by both parent- and teacher-report, 99% met criteria for an ASD by either ADI-r or ADOS (Fisher’s exact p=2.5 x 10-15). Principal components factor analysis at the domain level revealed that parent-report SRS and ADI-r domain scores (DSM-IV) loaded onto a first factor; while teacher-report SRS and ADOS domain scores loaded onto a second factor; this structure recapitulates a lack of separability of social and communication domains in autism.

Conclusion: Teachers’ SRS reports of observations in the naturalistic context of school appear consistent with what is ascertained by the ADOS. The combined use of parent- and teacher-report SRS represents a rapid and feasible method for quantitative assessment of autistic symptomatology.

Sponsors: NICHD, NIMH, Cure Autism Now

PS1.42
MEASUREMENT OF ACTIVITY IN CHILDREN WITH AUTISM
Jennifer Travis Foley, Danielle D Morris, Tristram H Smith, Susan L Hyman, University of Rochester

Background: Reliable measurement of behavior is necessary to measure effects of treatments.

Objective: We compared a subjective measure (Conners Abbreviated Rating Scale) completed by parents, teachers and researchers. All three groups’ ratings were compared to objective measurement by a motion sensor device (Actigraph).

Method: Observations were collected as part of a larger study of autism treatments. Children were observed for one hour in structured behavioral treatment sessions by the teachers and research staff. Parents rated a later unstructured interval. The motion sensor device was worn on a belt during the therapy sessions. Observations (143 complete pairs) were recorded over 18 weeks of study. Results: Subjects are 7 boys with autism (ages 3-4) who receive behavioral services from a single agency. Ratings on the abbreviated Conners did not correlate significantly between teachers and researchers (r2=.47), teachers and parents (r2=.23), or researchers and parents (r2=.25). The summed score for the motion sensor worn during the sessions was compared to the Conners Scale.

Conclusion: The Actigraph is a reliable, objective means to measure motor activity. Subjective data may reflect observation of other behaviors that influence the perception of the rater. The change in scores, rather than the actual score, may be more important for the assessment of treatment effect. Actigraph monitoring of the unstructured times rated by parents is planned.

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PS1.43
Characterizing Child Engagement and Predictors of Social Behaviors
Andrea Steele King, Lisa Ann Ruble, Demian Packett, University of Louisville

Background: Child engagement has been identified as an important predictor of treatment success and an essential ingredient in programs for young children with autism.

Objectives: To describe the Autism Engagement Scale (AES) as a reliable observational rating tool, and to examine the relationship between the AES and child sociocommunicative behaviors.
Methods: Participants were a community sample of children who received an intervention assessment at the Systematic Treatment of Autism and Related Disorders program. In this sample of 25 young children with autism, 24 were male (Mage 4.9; SD=1.3). Diagnosis was confirmed with the Autism Diagnostic Observation Schedule-Generic. Behaviors were videotaped and coded using the AES during a 10-minute free play activity with a parent. Parents completed a social skills survey of children’s interactions with adults and children.

Results: A direct correlation was found between the total score of the AES and summary of parent report of children’s social skills with children (Spearman’s rho=.481, p<.01) but not with adults (r=.076, n.s.). Spearman’s rho revealed that attention to others (r=.497, p<.01), cooperation (r=.428, p<.05), productivity (r=.506, p<.01), and consistency with others’ goals (r=.516, p<.01) were all related to better social skills with children.

Discussion: The AES shows initial promise as a tool for evaluating specific child engagement behaviors important for positive child outcomes and evidence based practices.

Sponsor: Department of Pediatrics, University of Louisville

**PS1.44**

**DEVELOPMENTAL SCREENING PRACTICES AND AUTISM AWARENESS OF UTAH’S PRIMARY CARE PHYSICIANS: 2004 SURVEY RESULTS**

**William M. McMahon, Jennifer C. Lloyd, Judith Miller, Judith P. Zimmerman, Dept. of Psychiatry, University of Utah Medical Center**

Background: Scientific literature regarding physician screening and referral patterns for developmental delays in children and Autism Spectrum Disorder (ASD) is sparse.

Objectives: To investigate the developmental screening and referral practices of Utah physicians.

Methods: A mail survey was conducted of Utah family physicians and pediatricians asking about developmental screening and referral practices, ASD awareness, and interest in Continuing Medical Education (CME). A response rate of 38% (n=335) was obtained.

Results: Eighty-six percent reported using an instrument to conduct developmental screening, 70% routinely screen for emotional and behavioral concerns in the birth to five population, and 20% were familiar with autism screening tools. Sixty-seven percent referred for further evaluation at least 25% of such children. Respondents mean rating on a scale of one (low) to 10 (high) for current knowledge of an ASD was 3.7 with comfort rating in identifying a child with an ASD as 3.4. Ninety-nine percent of all respondents were interested in CME about ASDs with high interest in how to screen and refer.

Conclusion: The results of this survey can provide useful information in understanding physician knowledge, screening and referral practices for ASD and developing future CME programs.

Sponsor: Partially funded by a grant from CDC.

**PS1.45**

**The York Measure of Quality of IBI: Development and Initial Psychometric Properties**

**Helen E Penn, E Alice Prichard, A Perry, York University**

Background: Professional consensus panels have strongly recommended Intensive Behavioural Intervention (IBI) as the treatment of choice for young children with autism.

Researchers have linked the quantity of treatment received to better results; however, few attempts have been made to link treatment quality to outcome. Little research has been carried out to determine the key characteristics of quality IBI and suggest how these characteristics should be measured.

Objectives: To develop an observational scale which captures information about IBI that experts believe is important to treatment success. To evaluate its reliability and validity and to determine whether a ratings-recording or an interval-recording approach is more psychometrically sound.

Method: The York Measure of Quality of IBI (YMQI) was based on previous research about important characteristics of IBI programs, existing IBI staff evaluation tools, and data from a survey of clinicians and parents. The pilot version of the YMQI has nine characteristics of IBI (e.g., appropriate use of reinforcers).

Six coders were trained to use the measure on a sample of 28 video-taped IBI sessions in order to evaluate reliability and construct validity. Expert ratings of overall quality from four psychologists and/or behavior analysts allowed for an assessment of criterion-related validity.

Results: The ratings-recording approach was more psychometrically sound than the interval-recording approach, with excellent internal consistency, fair to good inter-rater reliability and adequate criterion-related and construct validity for most characteristics of quality.

Conclusion: Revisions to the YMQI are in progress to improve its psychometric properties and clinical usefulness.

Sponsors: Ontario Graduate Scholarship (HP), Ontario Autism Scholar’s Award (EAP), Autism Society Ontario (HP, EAP), CIHR/NAAR Strategic Training Grant (EAP, HP).

**PS1.46**

**VALIDITY OF THE VINELAND -AUTISM PROFILE**

**Adrienne MD Perry, Jennifer Dunn Geier, Helen Penn, Nancy Freeman, York University; Thistletown Regional Centre**

Background: Level of adaptive behaviour is frequently assessed via parent interview using the Vineland Adaptive Behavior Scales (VABS, Sparrow, Balla, & Cicchetti, 1984). However, in autism, it is not just the absolute level of adaptive behaviour which is of interest but also the profile of subscores in different domains. Clinicians diagnosing autism frequently look for an ‘autism profile’ such that domains are ordered from highest to lowest, thus: Motor Skills, Daily Living Skills, Communication, Socialization.

Objectives: Previous research has been inconsistent in confirming this profile for autism as a whole. Studies vary
in terms of sample characteristics (size, age, cognitive level, etc.) and statistical procedures (standard scores vs. age equivalents, group comparisons vs. regressions, etc.). Thus, the purpose of this study was to explore the autism profile in a large and diverse sample.

Method: File review data have been compiled for 1,045 individuals from 3 clinical settings, spanning a range of ages (2-23 years) and a range of clinical diagnoses (481 with Autistic Disorder, 399 with other or unspecified ASD/PDD, and 165 with other developmental problems or delays). Childhood Autism Rating Scale (CARS) scores were available for most children. Cognitive measures were available for about one-third of the children and indicated a wide distribution from the average to the profound range.

Results: Results will be presented visually for standard scores and age equivalents broken down by clinical diagnosis, CARS category, age group, and IQ group. Conclusion: The validity of the ‘autism profile’ on the Vineland was, essentially, confirmed but there were interesting differences between children with Autistic Disorder per se, broader ASD, and non ASD-diagnoses. Profiles also varied as a function of severity of autism and severity of cognitive delay.

**PS1.47**

**INVESTIGATING THE SOCIAL RESPONSIVENESS SCALE: CONCURRENCE WITH DIAGNOSIS, CORRELATION WITH THE ADI-R, AND INTER-RATER AGREEMENT**

*Aimee E.N. Sullivan, Susan Risi, Jeff Burke, Stamping Qui, Catherine Lord, University of Michigan Autism and Communication Disorders Center*

Background: The Social Responsiveness Scale (SRS) has been indicated for use both as a screener and an aid to clinical diagnosis. It aims to provide diagnostic information and measure severity of autistic social impairments.

Objectives: To investigate the SRS as an autism screener. The measure’s agreement with clinician diagnosis, correlation with scores from Autism Diagnostic Interview, Revised (ADI-R), and agreement between multiple raters, were examined.

Methods: Data were collected from 196 subjects as part of a standard diagnostic evaluation (143 males; 66 autism, 51 PDD-NOS, 79 nonspectrum). Data were also collected from parents and teachers of 67 subjects participating in a longitudinal study (53 males; 41 autism, 12 PDD-NOS, 15 nonspectrum). ADI-R administrators were blind to subjects’ SRS scores.

Results: Agreement between diagnosis and the SRS screener cutoff was significant (p<.001). Comparing SRS total scores to ADI-R Social Domain scores demonstrated a correlation of .43 (p<.001), which was largely driven by nonspectrum subjects. Teacher and parent scores were not correlated (r = .16, p=.154) within the longitudinal sample.

Conclusion: The implications of this pattern of findings for research and clinical use will be further discussed. This research was sponsored by NIMH grant R01MH066496.
PS1.51  NEURAL BASIS OF BIOLOGICAL MOTION PERCEPTION IN CHILDREN WITH AND WITHOUT AUTISM  Elizabeth J Carter, Kevin A Pelphrey, Duke University  

Background: Children with autism exhibit poor visual perception of biological motion relative to nonbiological motion (Blake et al., 2003, Psychological Science). Previously, we found that the superior temporal sulcus (STS) activity in neurotypical adults was greater in response to biological motion than to nonbiological motion, but the more generally motion-sensitive area MT/V5 responded equivalently (Pelphrey et al., 2003, J. Neuroscience).

Objective: Investigate response patterns in the STS and MT/V5 in 6- to 10-year-old children with and without autism using functional magnetic resonance imaging.

Methods: Children viewed animated stimuli of four types: a walking human, a walking robot, a disjointed mechanical figure with the same components as the robot, and a ticking grandfather clock. We compared the neural correlates of the perception of biological motion by biological and nonbiological figures with both meaningful and unmeaningful nonbiological motion.

Results: For both groups, activity for all conditions is equivalent in area MT/V5. In the typically developing children (n=12), the STS region shows increased activation to the human walking only. However, the STS region in a group of children with autism (n=5) does not show any differential activation. We are continuing to collect data.

Conclusion: This could explain the poor performance on tasks involving the identification of biological motion in autism. This study demonstrates the feasibility of studying children with autism using fMRI.

Sponsor: NIMH

PS1.52  BRAIN ACTIVITY AND EYE MOVEMENT PATTERNS FOR INDIVIDUALS WITH ASD  Charles Norris Cartwright, Catherine Hanson, UMDNJ-New Jersey Medical School  

Background: Little is known about the neural correlates of gaze patterns for individuals with Autism Spectrum Disorders (ASD) when viewing objects that have been cued by either direction of eye gaze or an arrow.

Objectives: Record fMRI and eye movement data during the performance of visual tasks using face and arrow stimuli.

Methods: High functioning young adults, aged 18-35, with ASD (using ADOS/ADI-R diagnostic instruments) and their age-matched, typically developed controls were recruited through The Autism Center of UMDNJ-NJIMS. They were asked to make simple judgments about face and arrow stimuli while being scanned in a Siemens 3T Allegra magnet. Eye movements were simultaneously recorded.

Results: Preliminary analysis of the data (11 typical control subjects and 3 ASD subjects) demonstrate very different patterns of brain activation for individuals with ASD and typically developed individuals, including differences in activation patterns in the insula, fusiform gyrus, anterior cingulate, and superior temporal gyrus. The eye movement data indicate that individuals with ASD are less focused in their eye fixations and have shorter dwell times than do typically developed individuals.

Conclusion: Preliminary findings of this study suggest that individuals with ASD process face and directional cues differently than do typically developed individuals.

Sponsor: New Jersey Governor's Council on Autism

PS1.53  WHOLE VS. PART-BASED FACE PROCESSING IN AUTISM: AN FMRI STUDY  Kim M Dalton, Matthew M Nersesian, Andrea McDuffie, Brendon M Nacewicz, Emelia M McAuliff, Andrew L Alexander, Richard J Davidson, University of Wisconsin - Madison  

Background: Deficits in face processing and diminished gaze-fixation may be related and associated with unique brain activation patterns in autism.

Objective: To investigate gaze-fixation and brain activation during whole face versus part-feature processing in autism.

Method: Twenty individuals with autism (5 females) and 15 age-matched neurotypical controls (5 females) participated in the study. Structural and functional (BOLD) brain MRI images were acquired on a GE 3T scanner along with eye tracking. Participants were presented with 32 images of whole human faces and 32 images of isolated eyes versus mouths (16 each). Half of the images were inverted. Participants were instructed to decide if a target face matched a subsequently presented target face or feature-morphed foil face.

Results: The autism group made more errors on the facial discrimination task and tended not to show a face inversion effect in response time compared to the controls. The autism group also spent less time fixating on eye regions compared to controls.
the whole faces and more time fixating the isolated mouths. The amount of time spent fixating the face was related to response time in the control but not autism group.

Discussion: Relationships among these behavioral differences will be discussed along with between and within group analyses of functional brain results.

Sponsors: NIH-STAART, NARSADs to R.J.D. and K.M.D.

PS1.54
AGE RELATED CHANGES IN THE FUNCTIONAL ANATOMY OF FACIAL EMOTION PROCESSING: EVIDENCE FROM fMRI Quinton Deeley, Eileen Daly, Rayna Azuma, Simon Surguladze, Vincent Giampietro, Mary L Phillips, Declan GM Murphy, Kings College London

Background: processing faces is fundamental to social communication and behaviour. People with Autistic Spectrum Disorders (ASD) have impairments of facial emotion recognition, and show biological differences in brain function when processing faces compared to healthy controls. This may arise because of differences in the development of brain regions underpinning social cognition. Hence it is necessary to understand how brain regions supporting social cognition develop in order to understand how these processes differ in people with ASD.

Objectives: to investigate age-related changes in neural responses to facial emotion in typically developing individuals across the life span.

Methods: we measured brain activity with event related fMRI in 40 healthy male controls, age range 8 - 50, during implicit processing of neutral facial expressions, and expressions of fear and disgust.

Results: neural responses to all three expression types revealed a negative correlation between increasing age and activity in cortical midlines structures, particularly in medial and superior frontal gyri (BA 9/10). Conversely, there was a positive correlation between increasing age and activity in basal ganglia and thalamic structures.

Conclusion: activity in cortical midline structures may reflect a processing bias towards determining the self-relevance of facial expressions during the most formative period of social development, which attenuates as people age. Conversely, increasing activity in basal ganglia structures may reflect a shift towards a processing strategy associated with reduced cognitive and affective salience of facial expressions as people age.

PS1.55
DISRUPTION OF THE MIRROR NEURON SYSTEM IN AUTISM: AN FMRI STUDY OF SOCIAL AND INSTRUMENTAL GESTURE Nancy B Isenberg, Kimberly J. Montgomery, Matthew W. Roche, James V. Haxby Department of Neurology, 65 James St., Edison NJ 08818

During development, imitation lays the groundwork for peer interactions and learning of social and communication skills. Imitation is impaired in individuals along the autism spectrum. Mirror neurons, which respond to the observation and execution of actions, initially described in primates, are likely the neural basis for imitation. Previous neuroimaging experiments suggest a mirror neuron system (MNS) in the human brain, encompassing the right superior temporal sulcus, inferior parietal lobule, and frontal operculum.

We investigated the hypotheses that the observation, imitation and execution of gesture would produce activation along the MNS in controls, but not in autistics. Six subjects with high-functioning autism and six age and IQ-matched healthy, right-handed control subjects were scanned using fMRI. Activity along the MNS was found during the observation, imitation, and execution of social and instrumental gesture in normal controls. Between group comparisons of observation, imitation and execution of social and instrumental gesture revealed significant differences in the MNS with relative decreases in the autism subjects compared to control subjects. These results support the hypothesis that the MNS is disrupted in individuals along the autism spectrum.

PS1.56
DEVELOPMENTAL CHANGES OF PREFRONTAL ACTIVATION DURING VERBAL FLUENCY TEST IN INDIVIDUALS WITH AUTISM AND HEALTHY SIBLINGS Yuki Kawakubo, Department of Neuropsychiatry, University of Tokyo

Background: Individuals with autism have cognitive dysfunctions in language and attention. The cognitive dysfunctions are closely related to the prefrontal cortex. Objective: The present study investigated the change of oxyhemoglobin in the prefrontal cortex measured with near-infrared spectroscopy (NIRS) in adults and children with autism. Moreover, to clarify whether the dysfunction of the prefrontal cortex may be a specific trait-related endophenotype for studying the complex genetics of autism, we compared the data on autism with those on healthy siblings.

Methods: Fourteen children with autism (mean age=9.9), 13 healthy child siblings (mean age=10.3), 15 control children (mean age=11.2), 9 adults with autism (mean age=27.8), 7 healthy adult siblings (mean age=23.0) and 13 control adults (mean age=27.0) participated in this study. All participants and their parents gave written informed consent. The relative concentration of oxyhemoglobin [oxyHb] was recorded using 2-channel NIRS machine during the letter fluency test.

Results: In children, neither [oxyHb] change during the task or task performances were significantly different among three groups. [oxyHb] changes were significantly correlated with age in healthy sibling and control groups, but not in autism group. In adults, [oxyHb] increases during the task were smaller in individuals with autism than in their healthy siblings and control subjects, although task performances were similar.

Conclusion: The results suggest a poorer maturation during development in language-related function of the prefrontal cortex in individuals with autism, which is not likely a static trait marker of genetic liability for autism.
Financial support: This work was supported in part by grants-in-aid for scientific research (No. 16790675 and 17025015 to KK, 17790806 to KY) from Japan Society for the Promotion of Science and the Ministry of Education, Culture, Sports, Science and Technology, Japan.

PS1.57
MEG STUDY OF THE EFFECTS OF NOISE ON THE AUDITORY MISMATCH FIELD IN CHILDREN WITH AUTISM Tal Kenet, Michael M Merzenich, Srikantan Nagarajan, Massachusetts General Hospital

The autistic syndrome (AS) is a complex heterogeneous disorder of unknown etiology. Recent studies have revealed many abnormal aspects of cortical morphology and function in AS, including small minicolumns, reduced neuropil (implying weak cortical network inhibition and facilitation), degraded intrahemispheric connectivity, abnormal neuromodulator expression, and abnormal white and grey matter development, among others. These findings are consistent with a "noisy developing cortex hypothesis" for AS (proposed by Merzenich and Rubenstein, 2003), which argues that a high excitation to inhibition ratio (or, from another perspective, a poor signal to noise ratio) lies at the core of the disorder. This hypothesis predicts that a cortex with such history will have altered processing of input signal in the quiet and in noise, relative to a normal cortex. Despite a wide spectrum of manifestations of AS, language impairments are expressed to various degrees of severity in all affected individuals. We therefore chose to test this prediction in the auditory domain, by studying MEG-recorded auditory mismatch field in AS and control children, for acoustic stimuli varying in duration, spectral content and intensity. The responses were evaluated in the quiet, and with background ICRA (speech-like) noise (+5 dB signal to noise level). We found that for simple tone sounds, the presence of noise attenuated responses in AS proportionally to the control population. However, for complex tone stimuli (that recruit a larger neuronal population), noise did not attenuate the response to the deviant tone in the AS group, but did result in attenuation of response in the control group. The results indicate that AS results in hypersensitivity to change, in agreement with studies from other groups. It is likely that detection is enhanced at the expense of discrimination, which has been shown to be impaired in AS.

Support Contributed By: Cure Autism Now and the M.I.N.D. Institute

PS1.58
DIFFERENCES IN CEREBELLAR-CEREBRAL CIRCUITS IN AUTISM DURING FMRI OF SIMPLE SEQUENTIAL FINGER TAPPING Stephanie Kay Powell, Sunaina Fotedar, Joanna G Blankner, Melissa C Goldberg, James J Pekar, Stewart H Mostofsky*, Kennedy Krieger Institute

Background: Motor impairment may be a marker for dysfunction within parallel brain regions responsible for social and communication deficits intrinsic to autism. Though motor impairment is common in children with autism, few studies have used functional imaging to explore its underlying neural circuitry.

Objectives: To compare neural activation during simple motor execution in children with autism and their typically developing peers.

Methods: Subjects included 24 children (ages 8-13 years) within two diagnostic groups: high functioning autism (HFA) and age-matched typically developing controls. Subjects completed a standardized motor examination (PANESS; Denckla, 1985), then underwent fMRI scanning while performing a simple motor task comprised of alternating periods of right hand finger sequencing (RHFS), left hand finger sequencing (LHFS), and rest.

Results: While children with HFA had an overall poorer total PANESS score (p=.003), they were equivalent to controls in their sequencing speed (RHFS p=0.8, LHFS p=0.6). Between-group fMRI data revealed greater activation for controls during both RHFS and LHFS in the bilateral cerebellum and left occipito-temporal occipitoparietal regions. Controls also displayed greater activation in the right caudate during RHFS and left prefrontal cortex (BA9) during LHFS. Children with HFA showed greater activation during RHFS in bilateral premotor/supplementary motor areas (BA6), left thalamus, and right insula.

Conclusions: Findings suggest that dysfunction within cerebral-cerebellar circuits may contribute to motor deficits associated with autism, as evidenced by a lower ability to rely on the cerebellum and a greater recruitment of premotor regions during basic motor execution. This research was supported by grants from the National Alliance for Autism Research and NIH K02NS44850. R01NS048527, P30HD-24061, M01RR00052, K01MH01824

PS1.59
EMOTIONAL CONGRUENCE ACTIVATION ON FMRI IN AUTISM AND CONTROL SUBJECTS Joel L. Steinberg, Deborah A. Pearson, Stacy L. Reddoch, Rosleen Mansour, Sharoon Saleem, Katherine A. Loveland, University of Texas Health Science Center at Houston

We tested the hypothesis that altered neural circuits underlie impaired processing of multi-sensory emotional information in autism by acquiring fMRI scans from 5 autism and 4 healthy control adolescents during performance of an emotional congruence task. The task consisted of sequential visual presentation of human faces (Ekman faces) simultaneously paired with human emotional vocalizations. Two conditions were presented in alternating blocks for 10 minutes. The Gender condition was to press one of two buttons to indicate whether the voice and face genders were congruent or noncongruent. The Emotion condition was to press one of two buttons to indicate whether the voice and face emotions were affectively congruent or noncongruent. FMRI scans were acquired on a Philips 3 T MRI scanner using a BOLD-sensitive spin echo echoplanar pulse.
sequence that reduced distortion and dropout in the orbitofrontal and medial temporal regions. FMRI scans were corrected for slice-timing and motion, normalized to the Talairach atlas using AFNI, and smoothed spatially. The time-series was high-pass filtered and autocorrelation-corrected. Each condition was modeled with a smoothed boxcar, and regression parameters were estimated using SPM2 Fixed Effects. Statistical significance was defined as voxel or cluster p < 0.05 corrected for multiple comparisons. During Emotion relative to Gender, controls had significantly greater activation in the ventromedial prefrontal, superior temporal, parahippocampal, posterior cingulate gyri, and occipital regions compared to the autism subjects. Unlike the controls, the autism group showed significant prefrontal activation during Gender but not Emotion. These findings are consistent with the hypothesis regarding altered ventromedial and medial temporal circuits in autism.

**PS1.60 NEURAL BASIS OF IRONY COMPREHENSION IN CHILDREN WITH AUTISM: THE ROLE OF PROSODY AND CONTEXT**

A Ting Wang, Susan S Lee, Marian Sigman, Mirella Dapretto, Department of Psychology, University of California, Los Angeles

Objective: Little is known about the neural bases of higher-level pragmatic impairments seen in autism spectrum disorders (ASD). We used fMRI to examine the neural circuitry underlying deficits in understanding irony in high-functioning children with ASD.

Method: While undergoing fMRI, typically developing (TD) and ASD children listened to short scenarios and decided whether the speaker was sincere or ironic. Three types of scenarios were used where we varied the information available to guide this decision. Scenarios either included 1) both knowledge of the event outcome and strong prosodic cues (sincere or sarcastic intonation), 2) prosodic cues only, or 3) knowledge of the event outcome only.

Results: Children with ASD performed above chance, but were less accurate than TD children at interpreting the communicative intent behind a remark, particularly with regard to taking advantage of available contextual information. In contrast to prior research showing hypoactivation of regions involved in understanding the mental states of others, children with ASD showed significantly greater activity than TD children in the right inferior frontal gyrus as well as in bilateral temporal regions. Increased activity in the ASD group fell within the network recruited in the TD group and may reflect more effortful processing needed to interpret the intended meaning of an utterance.

Conclusion: These results confirm that children with ASD have difficulty interpreting the communicative intent of others and suggest that individuals with ASD can recruit regions activated as part of the normative neural circuitry when task demands require explicit attention to socially relevant cues.

Supported by the National Alliance for Autism Research, the UC Davis MIND Institute, the Cure Autism Now Foundation, the NIDCD (R03 DC005159), and the NICHD (P01 HD035470).

**PS1.61 REDUCED MEDIAL FRONTAL ACTIVATION IN AUTISM: A FUNCTIONAL MRI STUDY OF IRONY**

Diane L Williams, Rajesh K Kana, Timothy A Keller, Nancy J Minshew, Marcel A Just, Center for Cognitive Brain Imaging, Carnegie Mellon University

Background: Comprehension of irony requires common ground between speaker and addressee in shared beliefs and knowledge. For example, in the story, Tom and Mike planned to go on a picnic. In the morning it was raining very hard. Tom said, ‘Great weather for a picnic,’ the reader must recognize that the speaker’s mental state differs from the literal interpretation of the statement he makes, a process that may rely on ‘theory of mind’. Several neuroimaging studies have suggested the role of medial frontal regions in processing theory of mind, and the hypoactivation of these regions in autism.

Objective: Compare activation of brain areas involved in discourse processing and theory of mind in individuals with autism and matched controls.

Methods: 17 adult participants with autism and 14 age and IQ matched control participants read brief stories that concluded with either a literal or ironic statement made by one of the characters in the story during fMRI.

Results: Behavioral data showed that the participants with autism performed more poorly than controls on the ironic sentences, but not on the literal sentences. In the fMRI data, when the processing of ironic utterances was compared to processing of literal utterances, the participants with autism showed reliably lower activation than the controls in medial frontal cortex that included the anterior cingulate, paracingulate, and medial aspect of the superior frontal gyrus.

Conclusion: The autism group had less activation in areas involved in integrative aspects of sentence processing and in areas involved in ‘theory of mind’.

Source of Funding: NIH

**PS1.62 SOCIAL BRAIN ABNORMALITIES IN VERY YOUNG CHILDREN WITH AUTISM**

Claire Amiet, Isabelle Meresse, Nadia Chabane, Nathalie Boddart, Anne Philippe, Laurence Robel, Marie-Christine Mouren, Laurence Laurier, Arnold Munnich, Francis Brunelle, Yves Samson, Monica Zilbovicius. URM 0205 « Brain imaging in psychiatry », INSERM-CEA, Service Hospitalier Frédéric Joliot, CEA, Orsay, France

Background: Autism is a severe developmental disorder that impairs social and communication skills. Previous functional rest brain imaging studies detected temporal abnormalities in autism. These results concern school aged children.

Objectives: Here, we investigated whether these abnormalities could be detected precociously, before the age of 5 years.

Methods: Regional cerebral blood flow was measured at
rest with positron emission tomography in 22 autistic children (18 boys, mean age: 3.8 ± 0.6 years, mean IQ: 60 ± 15) and 11 non-autistic mentally retarded children (mean age: 7.2 ± 2.3 years, mean IQ: 52 ± 23). Images were analyzed with SPM99.

Results: The autistic group had a significantly hypoperfusion in the right temporal lobe (p<0.001, corrected), centered on the superior temporal sulcus, associated to a less significant and extended hypoperfusion in left temporal gyrus, cingular gyrus and bilateral inferior frontal gyri (p<0.001, uncorrected). In addition, temporal hypoperfusion was detected individually in 82% of autistic children.

Conclusions: PET and voxel-based image analysis revealed a dysfunction of temporal lobes and frontal and limbic regions. As these interconnected regions are important components in social cognition, we can postulate an early dysfunction of a cerebral network including temporal, frontal and cingular regions in autism. Indeed, these results should be replicated with age-matched groups.

Sponsor: France Telecom Foundation and France Foundation.

PS1.63
En2 KNOCKOUT MICE DISPLAY AUTISTIC-LIKE BEHAVIOR AND NEUROCHEMICAL ALTERATIONS Michelle A. Cheh, James H. Millonig, Xue Ming, Erin P. Jacobsen, Silky Kamdar, George C. Wagner, Department of Neuroscience, Rutgers University

Background: Twin, family and disease modeling studies support a polygenic multifatorial basis in the etiology of autism spectrum disorder (ASD). Recent data has demonstrated that two allelic variants in the human ENGRAILED2 (EN2) gene are inherited more often in individuals with ASD than unaffected siblings (Gharani et al., 2004; Benayed et al., 2005). En2-/- knockout mice display similar cerebellar phenotypes to those observed in post-mortem and MRI studies of autistic individuals. Recently, we have observed that En2-/- mice display various neurobehavioral and neurochemical deficits associated with ASD (Cheh et al., submitted).

Objective: To further examine behavioral alterations in En2-/- mice and determine their behavioral and neurochemical response to challenge drugs.

Methods: Social interaction, amicable behavior, and aggression were observed in pairs of juvenile and adult En2-/- and En2+/+ mice. In addition, behavior was monitored following exposure to various pharmacological agents and regional neurochemical analysis was conducted using HPLC-electrochemical detection.

Results: Deficits in social interaction, play behavior, and aggression were observed in En2-/- mice. These mice also displayed enhanced behavioral responses to challenge drugs, including increased seizure behavior and increased serotonin syndrome. In addition, region-specific alterations in 5-HT and 5-HIAA were observed under baseline conditions, as well as following drug exposure.

Conclusions: These results reveal that En2-/- mice display ASD-like behavioral and neurochemical changes as well as an enhanced response to pharmacological challenges. No other mouse mutant reported has demonstrated genetic association for the human gene with ASD and autistic-like anatomical and behavioral phenotypes, making the En2 knockout an appropriate animal model for studying the developmental and environmental basis of ASD.

Acknowledgements: NAAR, NS43981, ES05022, EPAR829391, J&J

PS1.64
MICE LACKING THE GABRB3 GENE EXHIBIT AN ABNORMAL LOCUS COERULEUS AND HYPOTONIA Timothy M DeLorey, Ezzat Hashemi, Peyman Sahbaie, Frances M Davies, Gregg Homanics, Molecular Research Institute

Background: The GABRB3 gene, which encodes the beta3 subunit of the GABAA receptor, remains a viable candidate for involvement in autism spectrum disorder (ASD). Mice deficient in the gabrb3 gene exhibit many phenotypic traits that overlap with ASD. A brain region that has received little attention, in regards to ASD, is the locus coeruleus (LC), despite its many projections to brain regions that have been implicated in ASD and its association with behaviors impacted in ASD.

Objectives: To investigate whether the developmental disruption of the gabrb3 gene in mice affects the resulting LC morphology and its associated behaviors, such as muscle tone.

Methods: The LC was examined in tyrosine hydroxylase stained coronal brain sections from both control and gabrb3 gene deficient male mice. In addition, muscle tone in mouse was assessed by the hanging wire test.

Results: The LC in gabrb3 gene deficient mice was observed to be significantly larger than in control mice. In addition, gabrb3 gene deficient mice exhibited hypotonia, as compared to controls.

Conclusion: The finding that gabrb3 gene deficient mice exhibit both an abnormally large LC and hypotonia, a behavioral feature that has been reported in ASD, adds to the growing list of phenotypic similarities shared between individuals with ASD and gabrb3 gene deficient mice. The above findings suggest that the LC may be an additional brain region worth considering in regards to ASD.

Research funded by NIMH RO1 MH065393.

PS1.65

Background: Self-injurious behavior (SIB) is a devastating behavior disorder that is exhibited by some individuals with autism and related developmental disorders. The factors that determine individual differences in vulnerability to exhibit SIB are not well characterized, but neurobiological and environmental variables are likely sources of these differences.

Objectives: We are evaluating the validity of the pemoline model of SIB as a research tool to investigate the
neurobiological basis of individual differences in vulnerability to acquire SIB.

Methods: We evaluated individual differences in expression of SIB across a range of doses of pemoline, and investigated the effects of antecedent stress and manipulations of environmental complexity. In addition, we examined biochemical and behavioral variables that underlie individual differences in acquisition of the behavior disorder.

Results: Pemoline-induced SIB was dose-orderly, and a dose was identified that induced SIB in approximately 2/3 of the rats. The expression of SIB was increased by pre-exposure to stressors or environmental impoverishment, and decreased by enrichment. Pre-screening for individual differences in responsiveness to a mild stressor reliably predicted which rats were vulnerable or resistant to pemoline-induced SIB.

Conclusions: Environmental variables that are associated with clinical SIB exert similar influences on pemoline-induced SIB, suggesting concordance between clinical SIB and the animal model. Furthermore, the individual differences in vulnerability for pemoline-induced SIB suggest that we can use this model to identify neurochemical/neurobiological factors that underlie vulnerability for SIB.

Sponsor: NIH - National Institute on Child Health and Human Development

PS1.66
INTRAVENTRICULAR INFUSIONS OF PROPIONIC ACID INDUCES INCREASED LOCOMOTOR ACTIVITY, AND NEUROINFLAMMATORY CHANGES IN LONG EVANS RATS

Jennifer Hoffman, Andrew Franklin, Roy Taylor, Francis Boon, Peter Cain, Martin Kavaliers, Klaus-Peter Ossenkopp, Derrick MacFabe, The Kilee Patchell-Evans Autism Research Group - The University of Western Ontario

Background: Dietary factors may alter behaviour in autism spectrum disorders (ASDs). Neuroinflammatory changes have been observed in ASD autopsy brain. Propionic acid (PPA) is a short chain fatty acid, a common food preservative, and a major by-product of many gut enterobacteria. We have found intraventricular PPA induces consistent neurobehavioural, electrophysiological and neuropathological changes in rodents. We hypothesized that increased oxidative stress is involved in PPA neurotoxicity.

Objective: to investigate the effect of PPA on the oxidative stress status in brain areas relevant to ASD.

Methods: Adult Long-Evans rats were subjected to intraventricular infusions of PPA (4µl/animal), twice daily for 7 days. Animals were euthanized, and brains were dissected out into cortex, hippocampus, thalamus, striatum, cerebellum and brain stem. Biomarkers of protein and lipid oxidation as well as activity of the antioxidant enzymes superoxide dismutase, and catalase were studied in the brain homogenates.

Results: PPA treated animals showed increased lipid and protein oxidation in all brain areas studied, although compared to the shams the differences were statistically different only in cortex, hippocampus, thalamus, and cerebellum. Antioxidant enzymatic activity also showed inter area differences for both sham and treated animals. Conclusions: 1) PPA induces oxidative stress; 2) different brain areas have dissimilar susceptibility to oxidant insult. Sponsor: GoodLife Charities

PS1.68
RELATION BETWEEN THE MEDIAL AMYGDALA NUCLEI AND THE SOCIAL RECOGNITION MEMORY: A POSSIBLE AUTISM ANIMAL MODEL

Paula J Moura, Lucila L Campos, Marcos T Mercadante, Gilberto F Xavier, SAO PAULO UNIVERSITY

Autism is characterized by impairments in communication and social relationships as well as a restricted as range of activities. This disorder is associated with specific impairments in the processing of social and
emotional information. The nature of these specific impairments suggests that autism involve dysfunctions of brain regions responsible for processing of social information. Animal models of autism have provided insights into the neuropathology of this disorder. In rodents, the intruder resident paradigm has been used to access the social recognition memory (SRM) that is revealed by reduced social investigation when meeting a co-specific for the second time within an interval shorter than 60 minutes. SRM is based on pheromonal information. The olfactory system seems to play a key role in the recognition. Rodent’s olfactory system includes the accessory olfactory system and the main olfactory system, each having different paths in the brain. The accessory olfactory system integrates information coming from the vomeronasal organ; it projects to specific nuclei in the amygdala including the medial amygdala nucleus (MEA). In the present study, rats were subjected to bilateral multiple site injections of ibutenate, to produce selective damage in the MEA, and subsequently submitted to an intruder resident paradigm. Preliminary results show that lesioned rats tend to reduce social investigation when reexposed to the same co-specific. This was indicated by a near-significant Group effect in the ANOVA (F1.7=4.67, p<0.067). The social investigation ability is the same in both groups when the intruder is unknown. Although we have suggested that MEA is involved in SRM, future studies are needed to determine whether MEA is important in the acquisition, recovery or both phases of SRM. Furthermore, another amygdalar structures could be involved in the modulation of SRM or in the motivation to the social recognition is the subject of on-going investigations.

PSI.69
SELF-INJURIOUS BEHAVIOR: PHARMACOLOGICAL STUDIES IN AN ANIMAL MODEL. Amber M Muehlmann, Darragh P Devine, University of Florida
Background: The most debilitating of all the maladaptive behaviors in autism is self-injurious behavior (SIB). SIB consists of stereotyped behaviors that can produce physical injury (e.g. head-banging, face-punching, self-biting). Pemoline, an indirect monoamine agonist, produces stereotyped self-biting in rats and is used as an animal model of SIB. Objectives: We have evaluated the predictive validity of the pemoline model using valproate, a clinically effective pharmacotherapy for SIB, and screened the potential effectiveness of topiramate, MK-801, and memantine. Methods: Individual groups of rats received daily injections of pemoline (200 mg/kg/day) and either valproate, topiramate, MK-801, or memantine twice daily for five consecutive days. SIB was measured by quantifying the duration of self-injurious oral contact with the skin, and by evaluating the severity of tissue injuries using a 5-point rating scale. Results: Valproate attenuated the severity of the pemoline-induced tissue injury without affecting the duration of stereotyped oral contact. Topiramate and MK-801 each attenuated the duration and severity of the pemoline-induced SIB. Memantine did not significantly affect either measure. Conclusions: The effectiveness of valproate demonstrates concordance in its efficacy for clinical and pemoline-induced SIB. The effectiveness of topiramate suggests that this drug may have pharmacotherapeutic potential. The effects of MK-801 and memantine have heuristic potential as they indicate that pemoline-induced SIB involves glutamate-mediated neuroplasticity. Sponsor: Cure Autism Now Foundation and the National Alliance for Autism Research.

PSI.70
DECREASED GLUTATHIONE CONCENTRATION IN BRAIN AREAS AFTER CHRONIC ADMINISTRATION OF PROPIONIC ACID IN LONG EVANS RATS. Karina Rodriguez-Capote, Yudith Ramos, Jennifer Hoffman, Andrew Franklin, Klaus Peter Ossenkopp, Fred Possmayer, Derrick MacFabe, University of Western Ontario
Background: Sensitivity to oxidative stress via impaired glutathione (GSH) metabolism has been suggested in autism spectrum disorders (ASDs). Propionic acid (PPA) is a common food preservative and a by-product of gut enterobacteria. Recently we reported PPA induces neurobehavioural changes and increases brain oxidative stress in rodents. We hypothesize that the oxidative stress induced by PPA is due to a decline in GSH. Objective: to investigate the effect of PPA on the glutathione system in rodent brain. Methods: Adult Long-Evans rats received intraventricular infusions of PPA (BID for 7 days). Following neurobehavioral studies animals were euthanized and cortex, hippocampus, thalamus, cerebellum and brain stem were dissected. Total GSH and GSH related enzymes were studied in brain homogenates. Results: PPA treated animals showed decreased total GSH in all brain areas, being statistically significantly for cortex, hippocampus, and thalamus. Glutathione peroxidase was also significant increased in those areas, suggesting increased oxidative stress. Glutathione reductase activity was relatively unaffected by PPA treatment, whereas the activity of glutathione S-transferase increased, suggesting that GSH is being used for removal of PPA or related catabolites. Conclusions: The decreased concentration of total glutathione induced by PPA is likely due to GSH consumption by its conjugation with xenobiotics. This decline in GSH concentrations may render the CNS more susceptible to oxidative stress. Sponsor: GoodLife Charities

PSI.71
NOVEL INTERACTIONS BETWEEN ENGRAILED2 (EN2), AN AUTISM-ASSOCIATED GENE, AND IGF1 CONTROL POSTNATAL CEREBELLAR DEVELOPMENT. Ian T Rossman, Silky Kamdar, James H Millonig, Emanuel DiCicco-Bloom, UMDNJ-Robert Wood Johnson Med Sch
Background: Previous studies demonstrate 1) EN2 is associated with autism spectrum disorder (ASD) in three separate populations, and 2) disrupted En2 expression in mice causes cerebellar abnormalities similar to autism neuropathology, including reduced numbers of Purkinje and granule neurons. Together, these data suggest En2 knockout (KO) mice provide a genetically relevant animal model to study possible pathogenetic roles of this gene during postnatal development.

Objective: To determine the molecular interactions between En2 and extracellular signals that together regulate postnatal cerebellar development.

Methods: DNA synthesis was examined in vivo as well as in granule neuron precursors (GNPs) in culture in response to growth signals, using BL6/129 (WT) and En2 KO mice. GNPs were isolated by genotype, cultured for 24h in defined media, and assessed for 3H-deoxythymidine or BrdU incorporation. Neuritogenesis was assessed live, or following fixation and Tuj1-immunostaining, and defined as cells with processes measuring 2-cell bodies in length.

Results: IGF1 elicited a 2-fold greater stimulation of DNA synthesis in KO GNP than WT cells. Additionally, IGF1 induced similar genotype dependent increases in vivo, suggesting En2 expression normally inhibits IGF1 mitogenic signaling. Conversely, KO GNPs grew fewer neurites than WT cells in response to IGF1 or PACAP (WT=42%; KO=25%; % neurite-bearing cells). There were no genotype-dependent differences in cell survival, or responses to other growth factors, suggesting cell cycle regulation is comparable between genotypes. Preliminary data suggest region-specific increases in BrdU labeling in KO cerebella compared to WT.

Conclusion: We identify previously unrecognized interactions between IGF1 and En2, suggesting altered En2 activity may impact cerebellar growth via aberrant IGF1 signaling.

Support: NS048649-01, ES11256; R01 MH076624; USEPA-R829391.

PS1.72

EPIGENETIC MECHANISMS OF AUTISM: A STUDY OF GENE-ENVIRONMENT INTERACTIONS. Christopher J Stodgell, Barbara K Tisdale, Linda Salamone, Patricia M. Rodier, University of Rochester School of Medicine & Dentistry

Introduction: Autism has multiple genetic and environmental etiologies. Embryonic exposures to teratogens may interact with genes and through epigenetic mechanisms result in autism.

Methods: On day 12.5 post-conception, rat embryos were exposed to valproic acid (VPA). This approximates the gestational age of days 20-24 in humans, a developmental period known to be critically important in the embryonic origin of autism. Other timed-pregnant rats were treated with teratogenic (4-yn-VPA) or nonteratogenic (IE-VPA) analogs of VPA, trichostatin A (TSA: a histone deacetylase inhibitor), or saline (vehicle control). After a 2-hour exposure period, the embryos were removed from the uterine horn, frozen and serially sectioned. Rhombencephalon tissue was isolated by laser-capture microdissection from the sectioned embryos. Gene-expression profiles were determined by hybridizing cDNA synthesized from each specimen to Affymetrix rat expression arrays (RAE230). Changes in gene expression were determined by comparing the profile seen in the saline-treated embryos to those of the other treatments.

Results: Our results demonstrate that exposure to the nonteratogenic treatments (i.e., saline and IE-VPA) had similar expression profiles for some of the genes examined and these profiles differed from those resulting from exposure to the teratogenic agents. Analysis of these genes indicated that some have already been investigated as candidate genes for autism and others are located near autism-susceptibility loci.

Conclusions: These data suggest that exposures to some teratogens may result in autism through epigenetic mechanisms.

Supported by the Mae Stone Goode Foundation and NIH 5U19HD035466, a Collaborative Program for Excellence in Autism.

PS1.73

ANIMAL MODEL OF AUTISM USING SODIUM VALPROATE Carrie Yochum, Rutgers University

Background: Previous studies have demonstrated disruption in maturation of critical behaviors following 400mg/kg of sodium valproate (VPA) on P14 of mouse pup life.

Objectives: Create a histopathological correlate for the behavioral deficits seen in mice treated with VPA on P14. Accordingly we looked at the time course of VPA-induced apoptosis over several sections of sagitally sliced brain tissue.

Methods: Mice were examined from P5 through P40 using a developmental battery consisting of motor, cognitive and social tests. Motor tests included surface righting, mid-air righting, negative geotaxis, hanging wire, and rotorod. Cognitive tasks included both visible and hidden platform water maze tests. Social tests included open field analysis of play behavior with a novel same age and sex pup. Both VPA and saline injected mice were sacrificed at several time points following P14 treatment. Brains were paraffin embedded and analyzed for apoptosis using a TUNEL stain.

Results: Tissue samples and behavioral data for both the VPA and saline injected mice were determined by comparing the profile seen in the same age and sex pup. Both VPA and saline injected mice were sacrificed at several time points following P14 treatment. Brains were paraffin embedded and analyzed for apoptosis using a TUNEL stain.

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**Governor’s Council on Autism, Johnson & Johnson, Busch Biomedical Research Grant**

**PSI.74**  
**BETA-2 ADRENERGIC RECEPTOR ACTIVATION: AN ANIMAL MODEL FOR NEUROINFLAMMATION IN AUTISM**  
Maria C Zerrate, Eileen Kasda, Susan Connors, Diana L Vargas, Mikhail V Pletnikov, Carlos A Pardo, Theodore Slotkin, Andrew W Zimmerman, Johns Hopkins University School of Medicine, Department of Neurology, Neuroimmunopathology Laboratory  
**BACKGROUND:** Prenatal overstimulation of the beta-2 adrenergic receptor (B2AR) by terbutaline in humans has been associated with autism. Terbutaline, administered to newborn rats on postnatal days (PN) 2-5, causes astrogliosis, cortical abnormalities, and reduced numbers of cerebellar Purkinje cells, analogous to pathology in autism. Neuroglial activation has been demonstrated in postmortem autism brain, and neuroinflammation may affect pathogenesis in autism.  
**OBJECTIVE:** We studied the effects of overstimulation of the B2AR on neuroglial activation in different brain regions, and the behavioral outcome in developing rats.  
**METHODS:** Fischer344 rats were administered either saline or terbutaline on PN 2-5, the neurodevelopmental equivalent of mid-to-late second trimester in humans. Antibody Iba1 was used to detect activated microglia in different brain regions (cortex, cerebellum; white vs gray matter). Stereological assessment was carried out to quantify neuroglial activation on PN 6 and 30. Treated rats and controls underwent behavioral testing on PN 30, using open field activity and the acoustic startle response with/without prepulse inhibition.  
**RESULTS:** Terbutaline administration significantly increased microglial activation on PN 30, but not PN 6, across all measurements (p<0.03). Results were more significant when separate regions or gray and white matter were compared. Females showed an increase in acoustic startle; prepulse inhibition was unaffected by terbutaline. Male and female terbutaline-treated animals were hyperactive in the open field.  
**CONCLUSION:** Overstimulation of the B2AR on PN 2-5 in rats may prove useful as an animal model for autism, to study physiological changes that lead to neuroglial activation and behavioral abnormalities.  
Supported in part by Cure Autism Now (CAN) and The Fetal Physiology Foundation  

**PSI.75**  
**THE ANTICONVULSANT VALPROIC ACID (VPA) STIMULATES FOREBRAIN NEUROGENESIS THROUGH CELL CYCLE MECHANISMS.**  
**Background:** Recent studies suggest VPA exposure during gestation may increase the risk of autism symptoms. Furthermore, in culture models, VPA either inhibits or stimulates cell proliferation, effects that may potentially contribute to forebrain enlargement noted in some children with ASD.  
**Objective:** To define the effects of VPA on forebrain neurogenesis using cerebral cortical precursors.  
**Methods:** Precursor cultures from embryonic day 14.5 rat cerebral cortex were exposed to VPA for 8, 24 and 48h in defined media. DNA synthesis was assessed using cell cycle marker [3H] thymidine and BrdU through scintillation spectroscopy and immunocytochemistry. VPA effects on neurite outgrowth were analyzed using phase microscopy of live cells, whereas second messenger and cell cycle mechanisms were assayed using Western blotting.  
**Results:** VPA had a bimodal effect on DNA synthesis, increasing incorporation by 60% at 1mM, with progressive reductions to -70% at 3mM. At 1mM, there was a 57% increase in BrdU (+) cells indicating that more cells entered S phase. Conversely, this mitogenic dose elicited reduced neurite outgrowth, decreasing process-bearing cells by ~50%. To define mediating pathways we assessed second messengers and found VPA increased levels of acetylated histone H3, but not levels of activated ERK, AKT, GSK3 or PKC. Further, VPA stimulated cell cycle regulators increasing both cyclin D3 (not D1) and cyclin E at 8 and 24h, suggesting that VPA rapidly alters cell cycle mechanisms to enhance neurogenesis.  
**Conclusion:** VPA exposure maintains forebrain precursors in the cell cycle and reduces neuronal differentiation. VPA acts via histone acetylation and cyclins D3 and E to promote forebrain neurogenesis, effects which may be relevant to brain enlargement should similar effects occur in the developing animal.  
Support: NS048649-01, ES11256; USEPA-R829391; NJ Gov Coun Autism
PS2.1
DECREASED GABA-A RECEPTOR DENSITY IN THE ANTERIOR CINGULATE CORTEX IN AUTISM
Gene J Blatt, Sandy Thevarkunnel, Eleni Antzoulatos, Gillian Van Sluytman, Margaret L Bauman, Thomas L Kemper, Boston University School of Medicine

Background: Disturbances in 5-HT1a and 5-HT2a receptors have been previously found in the autistic brain in the anterior cingulate cortex (ACC; Antzoulatos et al., IMFAR, 2004), a cortical area that contributes to many higher order cerebral cortical functions, including socio-emotional behavior. The present study was undertaken to determine if the GABA-A receptor, demonstrated to be abnormal in the autistic cerebellum (Yip et al, IMFAR 2006) and hippocampus (Blatt et al., JADD 31:537-543, 2001), is also altered in the ACC.

Objective: To determine whether GABA-A receptors are altered in the ACC in the autistic brain and whether such changes are lamina specific.

Methods: Ligand binding autoradiography was performed measuring 3[H]muscimol labeled GABA-A receptors on fresh frozen sections in adult autistic and control brains. Optical densities were measured off Kodak-MR film in superficial, middle and deep regions using the Inquiry program. Two tailed student t-tests were used to compare the different layers by group.

Results: There was a significant decrease (p = 0.047) in GABA-A receptor density in the middle region (layer III) and a trend for significance (p = 0.075) in the deep region (layers V/VI).

Conclusion: This novel finding means that multiple neurotransmitter systems are altered in the ACC in autism and that layer III is primarily targeted for both GABA-A and 5-HT2a receptors. These suggest alterations in information processing for higher order cortical functions that are implicated in autistic behaviors.

Tissue was provided by the Harvard Brain Tissue Resource Center and the Autism Tissue Program. Supported by NIH STAART Center Grant U54 MH66398-03 and NINDS NS38975-01A1.

PS2.2
DENSITY OF PARVALBUMIN, CALBINDIN-D28K AND CALRETININ IMMUNOREACTIVE INTERNEURONS IN THE HIPPOCAMPUS IN AUTISM
Yuri A Lawrence, Thomas L Kemper, Margaret L Bauman, Gene J Blatt, Boston University School of Medicine

Neuropathological studies in autism have noted cellular abnormalities in various limbic system structures including increased packing density in the CA and subicular subfields of the hippocampal formation. It is not yet known whether the GABAergic interneurons in these subfields are also affected.

Objective: The purpose of this study is to conduct a quantitative stereologic analysis of the parvalbumin, calbindin, and calretinin-positive subpopulations of GABAergic interneurons in the dentate gyrus, CA, prosubicular and subicular subfields.

Design/Methods: 5 autistic and 5 control brains, age and sex matched were used for this study. Serial sections through the anterior hippocampal body were incubated with mouse polyclonal antibodies (Swant, Bellinoza, Switzerland) against parvalbumin (PV; 1:750), against calbindin (CB; 1:1000) and rabbit polyclonal antibody against calretinin (CR;1:500) and visualized with an avidin biotin complex immuno peroxidase enhancement system using 3 3-diaminobenzidine as the chromagen.

Stereological probes were conducted via Stereoinvestigator.

Results: In the autistic hippocampus there is a statistically significant increase in the density of calbindin immunoreactive interneurons in the dentate gyrus, of the calretinin immunoreactive interneurons in the CA1 subfield, and of parvalbumin immunoreactive interneurons in the CA1 and CA3 subfields.

Conclusion: There is a selective increase in density of the calbindin, calretinin and parvalbumin GABAergic interneurons suggesting that they are vulnerable targets in the autistic brain. Current studies are investigating whether the calcium-binding protein subpopulations of interneurons are altered in other limbic cortical areas or represent a unique feature in the autistic hippocampus.

Tissue provided by the Harvard Brain Tissue Resource Center, the Autism issue Program via the M.I.N.D. Institute (Dr. D. Amaral, Research Director), and the Miami Brain Bank. Supported by NINDS NS38975-01A1.

PS2.3
EXPRESSION ANALYSIS OF AUTISM CANDIDATE GENES IN SUBGROUPS OF CENTRAL NEURONS ISOLATED FROM POST-MORTEM BRAIN SAMPLES
Nicolas Ramoz, Gilles Maussion, Aude-Marie Lepagnol-Bestel, Jean-Marie Moalic, Philip Gorwood, Joseph Buxbaum, Michel Simonneau, U675 INSERM

Background: Several genes have been found associated with autism but their expression levels remain unknown in autistic brain.

Objective: Compare the level of expression of autism candidate genes in post-mortem brain samples between...
controls and patients.
Method: Post-mortem brain samples (prefrontal cortex, BA46, and cerebellum, lobe 6) were provided by the Autism Tissue Program, from 7 subjects with autism and 6 matched controls. As there are reports for a decrease in Purkinje cells in autism, Purkinje and granule cells of the cerebellum were captured by assisted-laser microdissection to characterize cell-specific expression. Reverse transcription was performed on mRNAs extracted from these different neurons and brain areas. The expression level was currently analyzed by quantitative Taqman® PCR detected with the Opticon® 2 fluorescence detection system.
Results: Different levels of transcription for SLC25A12/AGC1, EN2 and Nr-CAM genes are observed in the granule cells. However, these preliminary results are revealed no difference of expression between patients and controls.
Conclusion: We are currently measuring the expression of the SLC25A12/AGC1, EN2 and Nr-CAM transcripts and additional candidate genes in the BA46 area, Purkinje and granule cells, in order to relate genetic findings to functional biology in the neurobiology of autism.
Sponsor: Autism Tissue Program and France Telecom-Fondation Autisme

PS2.4
NEURONAL CELL PACKING DENSITY AND CELL SIZE IN THE ANTERIOR CINGULATE CORTEX IN THE AUTISTIC BRAIN
Marissa Leigh Simms, Hilary B Kaplan, Thomas L Kemper, Margaret L Bauman, Gene J Blatt, Boston University School of Medicine
Background: Numerous studies have reported limbic system abnormalities in the autistic brain. Within the limbic system, the anterior cingulate cortex (BA24) has shown alterations in multiple neurotransmitter systems (Blatt et al., IMFAR 2006) and in glucose metabolism (Haznedar et al., 1997).
Objective: To assess possible additional abnormalities in cell packing density and cell size in the three subdivisions of BA24 in the autistic brain, areas 24A, B & C.
Methods: Nissl stained, serial 80µm thick frozen sections were obtained from the midpart of BA24 from 4 control and 9 autistic brains that were matched for sex and age. Using the optical fractionator, neuronal density was determined in a 1 mm wide sample area centered on each cytoarchitectonic area. Separate measurements were made for the supra- and infragranular layers. The vertical nucleator was used to measured neuronal area and volume. Group differences were assessed using two tailed student t-tests assuming equal variances.
Results: In the autistic brain, a decreased cell packing density was noted in infragranular cell layer of area 24C (p = 0.025) and a decreased cell size noted in the supragranular cell layer of area 24B (p = 0.01).
Conclusions: In concert with studies mentioned in the background, abnormalities were also found in BA24 autism cases. These changes were selective and involved two of the three cytoarchitectonic areas.
Tissue was provided by the Harvard Brain Bank Tissue Resource Center and the Autism Tissue Program. Supported by NIH STAART U54 MH66398-03 and NINDS NS38975-01A1.

PS2.5
ALTERED GABA-A RECEPTOR BINDING IN THE POSTEROLATERAL CEREBELLAR HEMISPHERE IN AUTISM
S. Thevarkunnel, E. Antzoulatos, T.T. Gibbs, R.G. Marcon, M.L. Bauman, T.L. Kemper, G.J. Blatt, Boston University School of Medicine
Background: Recent GAD67 mRNA studies by Yip et al., (IMFAR 2006) have revealed abnormalities in the functional state of the cerebellar circuitry with its upregulation in GABAergic basket cells and its downregulation in GABAergic Purkinje cells. These findings prompted this study of two key GABA-A receptors in the cerebellar cortex.
Objectives: Determine whether GABA-A receptor binding is altered in the cerebellar hemisphere in the autistic brain.
Methods: Multiple concentration autoradiographic radioligand binding experiments were completed for 3[H]-flunitrazepam and 3[H]-muscimol on fresh frozen sections from the posterolateral cerebellar hemisphere in adult autism and control brains. Optical densities were measured off Kodak-MR film in the molecular, Purkinje cell and granule cell layers using the Inquiry program. Student t-tests were used to compare Bmax and Kd values for the different layers by group.
Results: The 3[H]-flunitrazepam binding studies yielded a significant decrease in the number of benzodiazepine binding sites (Bmax) in the molecular layer of the autism group as compared to controls. In the 3[H]-muscimol binding studies, the number of GABA-A receptors (Bmax) and their binding affinity (Kd) were significantly different for the Purkinje cell layer, while the difference in both parameters approached significance for the molecular layer.
Conclusion: These results indicate that key aspects of the GABA-A receptor system are downregulated in the cerebellar cortex in autism and may provide useful markers for the increased GABA released by basket cells onto Purkinje cells. The net result appears to be alterations in the functional state of remaining Purkinje cells which could in turn affect its target innervation to the cerebellar nuclei and thus to higher order association areas.
Tissue was provided by the Harvard Brain Tissue Resource Center and the Autism Tissue Program. Supported by NICHD HD39459-04 and the Hussman Foundation

PS2.6
OXIDATIVE STRESS IN BRAIN TISSUES FROM AUTISTIC PATIENTS: INCREASED CONCENTRATION OF ISOPROSTANES
Diana L Vargas, Veera Bandaru, Maria C Zerrate, Andrew W Zimmerman, Norman Haughey, Carlos A Pardo, Johns Hopkins University School of Medicine, Department of
Studies in brain tissues from autistic patients have demonstrated that neuroinflammation may play a role in the pathogenesis of autism. Inflammation may induce oxidative stress, a pathological process involved in neuronal dysfunction by lipid peroxidation, protein and DNA oxidation.

**OBJECTIVE**

To determine whether oxidative stress reactions are involved in neuropathogenic mechanisms in autism.

**METHODS**

We studied the presence of markers of oxidative stress in brain tissues from 7 autistic patients (age range 8-40yrs) and 10 controls (age range 5-35 years). Protein analysis by immunoblotting and lipidomics techniques [electrospray ionization tandem mass spectrometry (ESI/MS/MS)] were used to analyze cerebral cortex and white matter of the frontal, temporal, occipital lobes and cerebellum.

**RESULTS**

Lipidomic studies found significant increased levels of 8-iso-13,14-dihydro-15-keto Prostaglandin F2± (8-iso-PGF2±), an isoprostane, in both midfrontal gyrus and cerebellum of autistic patients as compared with control tissues. Interestingly, the increase of 8-iso-PGF2± was mostly seen in the white matter as compared with the cerebral cortex. In cerebellum, the cerebellar folia showed a marked increase of 8-iso-PGF2± as compared with the cerebellar white matter. Other markers of oxidative stress such as iNOS, the inducible form of nitric oxide synthase, and 4-hydroxynonenal (4-HNE) were seen predominantly in the midfrontal region as compared with the occipital and cerebellum but their expression was less prominent as compared with the control tissues.

**CONCLUSION**

The presence of elevated levels of 8-iso-PGF2± (a marker and mediator of oxidative stress) in the white matter of frontal cortex and cerebellum, suggests that oxidative stress pathways are activated in these selected areas of the brain in autistic patients as compared with other regions.

Supported in part by Cure Autism Now (CAN) and Baltimore s Autism Parents Support Groups.

**PS2.7**  
**AUTISM SPECTRUM DISORDER IN WILLIAMS SYNDROME: A CASE SERIES PERSPECTIVE USING THE ADI-R AND ADOS.**  
Michael S. Gaffrey, Bonnie P. Klein-Tasman, Carolyn B. Mervis, Shawn Thompson, Child Neurodevelopment Research Laboratory, University of Wisconsin - Milwaukee

**Background:** Children with Williams syndrome (WS) are typically described as prosocial, reflective, and demonstrating a connectedness with others. This is in stark contrast to the social aloofness and communicative deficits characteristic of autism spectrum disorders (ASD). As a result it would appear highly unlikely that behavioral overlap between the two conditions would occur. Nevertheless, reports of concomitant ASD in WS have surfaced in previous studies. The current study seeks to improve upon past case examinations by 1) having diagnosis of WS based on genetic testing rather than clinical impression; 2) using current diagnostic criteria for ASD, which have undergone change in the past decade; and 3) using empirically validated methods of arriving at a diagnosis.

**Objective:** To examine the presence of ASD in children with WS using the ADI-R, ADOS, and clinical impression.

**Methods:** Six children with WS (ages 3-6 years) who were referred for possible ASD, externalizing behavior disorder, or very low cognitive ability underwent diagnostic evaluation for ASD, including administration of the ADI-R and ADOS to identify behavioral symptoms characteristic of an ASD, as well as developmental testing.

**Results:** Four of the six children met the criteria necessary for a comorbid autism spectrum diagnosis based on ADOS, ADI-R, and clinical impression. Clinical and research implications will be discussed.

Supported by: NIH R03MH069400 to Bonnie Klein-Tasman and R37 HD29957 and R01 NS35102 to Carolyn B. Mervis.

**PS2.8**  
**ASSOCIATION STUDY OF THE GABA CLUSTER ON 15Q11-13 WITH AUTISM IN THE FRENCH CANADIAN POPULATION**  
Rob F Gillis, Jean-Baptiste Riviere, Julie Gauthier, Nathalie Girard, Eric Fombonne, Laurent Mottron, Ridha Joober, Guy A Rouleau, Center for the Study of Brain Diseases

**Background:** Chromosomal region 15q11-13 has been consistently implicated in autism through numerous avenues such as maternal duplications, breakpoints in the region, and presence of autism in patients with Prader-Willi and Angelman syndrome. Furthermore, linkage to GABRA3 within a cluster of GABA receptor subunit genes has been previously described and replicated in different autistic populations. The GABA cluster at 15q12 is also a good candidate region because of its connection with epilepsy and the comorbidity of autism and epilepsy within a phenotypic subtype of patients with 15q11-13 anomalies.

**Objectives:** Determine if there is an association between the GABA cluster and autism in the French Canadian population. If association is discovered, identify potential mutations in the surrounding haplotype that may contribute to autism.

**Methods:** We have assembled 140 trios, with affected patients diagnosed according to DSM-IV criteria, administration of the ADI-R and/or ADOS-G. Genomic DNA was extracted from lymphocytes of patients, of which 75% are of French Canadian origin. 27 SNPs spanning 820Kb of the GABA cluster on 15q11-13 were selected from the dbSNP and Celera databases based on minor allele frequency >0.05, spacing and haplotype
structure. The association analysis is being examined using the transmission disequilibrium test (TDT).

Results: Preliminary data from 40 trios has been collected. The additional 100 trios are expected to provide the statistical power to determine if there is an association in the French Canadian population.

Sponsor: CIHR

PS2.9
A COMPARATIVE STUDY OF DELETION CLASSES IN CHILDREN WITH ANGELMAN SYNDROME USING MICROARRAY-BASED COMPARATIVE GENOMIC HYBRIDIZATION: FOCUS ON AUTISM AND ASSOCIATED FEATURES
Sarika U. Peters, Trilochan Sahoo, Lynne M. Bird, Rene Barriere-Welge, Terry J. Bichell, Arthur L. Beaudet, Carlos A Bacino, Baylor College of Medicine

Background: Angelman Syndrome (AS) is a neurodevelopmental disorder characterized by mental retardation, dysmorphic features, ataxia, seizures and behavioral problems. AS is caused by maternal deficiency of UBE3A (E6-associated protein ubiquitin-protein ligase gene), located in an imprinted region on chromosome 15q11-q13. Intersitial deletions of the 15q11-q13 region account for approximately 70% of the AS patients. These deletions are usually detected by fluorescence in situ hybridization (FISH) studies. The deletions can also be sub-classified based on their size into Class I and Class II with the former being larger.

Objectives: To compare symptoms of autism and associated developmental domains across deletion classes of children with AS.

Methods: A microarray-based comparative genomic hybridization (CGH) assay was used to study 29 children with AS. Patients were assessed with the ADI-R and ADOS-G, the Bayley Scales of Infant Development-II, the Vineland Adaptive Behavior Scales, and the Preschool Language Scale-3.

Results: Preliminary data from 40 trios has been collected. The additional 100 trios are expected to provide the statistical power to determine if there is an association in the French Canadian population.

Sponsor: CIHR

PS2.10
GENETIC DISORDERS (RETT, FRAGILE X, TS, ETC.)
Susan E. Swanberg, Janine M. LaSalle, University of California Davis School of Medicine

Background: Rett syndrome is an X-linked pervasive developmental disorder caused by MECP2 mutations. Rett patients suffer from deficiencies in their respiratory rhythm oscillator. The early growth gene 2 (Egr2) plays a role in the transient formation of hindbrain developmental compartments, called rhombomeres, from which central rhythmogenic neuronal networks develop.

Objectives: To determine whether Egr2 expression is altered in a mouse model of Rett syndrome.

Methods: Expression of Egr2 was examined by immunofluorescence and laser scanning cytometry (LSC) in Mecp2-null and wild-type mice at six developmental time-points. MAR-Wiz, a bioinformatics tool which analyzes DNA sequences for the presence of matrix attachment regions (MARs) was used to search for MARs which might contain MeCP2 binding sites. Chromatin immunoprecipitation (ChIP) was utilized to determine whether MeCP2 binds within Egr2.

Results: A significant decrease in Egr2 expression was observed in Mecp2-null mouse cortical samples (p=0.032 by t-test). MAR-Wiz predicted the presence of a MAR in the 3' end of Egr2. This putative MAR contains several CpG sites near A/T runs, potential binding sites for MeCP2. ChIP results demonstrated that this Egr2 MAR sequence was enriched in the MeCP2 precipitated fraction compared to input control.

Conclusion: Preliminary findings suggest decreased expression of Egr2 in a mouse model of Rett syndrome and autism. Egr2 expression in the wild-type mouse may be induced by MeCP2 binding to the Egr2 MAR.

Sponsor: NIH NRSA Postdoctoral Fellowship

PS2.11
AUTISM SPECTRUM DISORDERS IN MALES WITH SEX CHROMOSOME ANEUPLOIDY, Nicole Renee Tartaglia, Susan Bacalman, Beth Goodlin-Jones, Lesley Deprey, David Hessl, Michele Ono, Stephanie Tsang, Shanlee Davis, Robin Hansen, Ann Reynolds, Randi Hagerman, University of California Davis MIND Institute

Autism Spectrum Disorders (ASD) are frequently observed in neurodevelopmental disorders with a known genetic etiology. Sex Chromosome Aneuploidy (SCA), an abnormal number of X or Y chromosomes, is often identified in genetic screenings of children with ASD, however the prevalence of ASD in the SCA population is unknown. In this study 50 males age 3-25 were recruited from national SCA organizations for a study on health and development in XXX, XYY, and XXY Syndromes. These subjects were screened for autism using the Social Communication Questionnaire (SCQ). Results showed that 17/50 (34%) of males with SCA had scores of 15 or higher suggesting a high probability an ASD diagnosis [XXX 2/13 (15%); XYY 2/2 (100%); XXY 13/35 (37%)]. Because of this high positive screen rate, we completed a multidisciplinary assessment for ASD on the subsequent 20 SCA males using the ADOS-G, ADI-R, cognitive testing, and medical evaluation. Results to date show that 0/5 (0%) XXX, 3/8 (37%) XYY, and 3/7 (42%)
XXYY males met criteria for Autistic Disorder (AUT) or PDD-NOS [XXY 0; XYY 1/3 AUT, 2/3 PDD-NOS; XYYY 2/3 AUT, 1/3 PDD-NOS]. Males with Y chromosome aneuploidy were more likely to show features of ASD than males with XXY. These results suggest that males with SCA have an increased risk for ASD and should be evaluated for ASD. Ongoing ASD evaluation in larger sample sizes will provide more information about the prevalence of ASD in SCA males. Cytogenetic testing is routinely recommended in the medical work-up for autism to identify chromosomal abnormalities such as SCA. Further research on the Y chromosome and its role in ASD is needed.

**PS2.12**
**FEATURES OF AUTISM IN KLINEFELTER’S SYNDROME (XXY) AND THEIR ASSOCIATION WITH NEUROPSYCHOLOGICAL FUNCTIONING**

Child Psychiatry Branch, National Institute of Mental Health, NIH

**Background:** Previous studies have associated X chromosome abnormalities with autism spectrum disorders (ASD). Some individuals with Klinefelter’s syndrome (XXY) show behavioral features similar to those found in ASD, including impaired language, social, and executive functions.

**Objective:** Determine whether ASD features are present in XXY and their potential relation to performance on neuropsychological tests.

**Methods:** 27 non-mentally retarded children and adolescents with XXY were recruited for a study of sex chromosome aneuploidies. ASD features were assessed via parent report using the Social Communication Questionnaire (SCQ). Neuropsychological functioning was assessed using an IQ measure, memory and executive functioning components of the Cambridge Neuropsychological Test Automated Battery (CANTAB), and measures of verbal fluency.

**Results:** 6 of the 27 individuals with XXY (22%) met screening criteria for an ASD and all 27 exhibited some features of ASD. In the XXY population as a whole, the number of ASD-like repetitive behaviors and restricted interests from the SCQ was positively correlated with cognitive inflexibility and verbal dysfluency during neuropsychological assessment.

**Conclusion:** Features of ASD were present in XXY to a significantly greater extent than population base rates. ASD features, particularly repetitive behaviors and restricted interests, were correlated with degree of executive dysfunction. The presence of overlapping clinical features in ASD and in individuals with a supernumerary X chromosome is suggestive of common pathogenic features and supports further examination of regions of the X chromosome that may contribute to dysfunction in both disorders.

Sponsor: NIMH IRP

**PS2.13**

**MISREGULATION OF THE AUTISM CANDIDATE GENE ATP10C AND ITS ANTISENSE TRANSCRIPT IN THE Mecp2-KNOCKOUT MOUSE**

Laura B Herzing, Nelson Garay, Kelly Barry, Northwestern University

ATP10C is a maternally expressed, imprinted gene within the autism candidate region 15q12-q13. We have demonstrated that its expression patterns overlap those of the Angelman syndrome (AS) gene, UBE3A. Imprinted ATP10C and UBE3A expression is similarly affected in cell lines carrying AS-imprinting center (IC) deletions, and in cortex from male and female Rett Syndrome (RS) patients, who carry a mutation in the MeCP2 gene. UBE3A expression may be regulated by an imprinted antisense transcript arising from the IC, which may in turn be affected by loss of MeCP2.

**Objective:** To determine whether an antisense transcript overlaps ATP10C/Atpt10c, and whether expression of this transcript is affected by loss of MeCP2.

**Methods:** Antisense transcripts were identified using EST database searches and by strand-specific RT-PCR. Relative gene expression between Meep2-deletion animals/ littermate controls was quantitated using Real-Time RT-PCR (sense) or semi-quantitative strand-specific RT-PCR. Allele-specific expression was determined using sequencing and RFLP analysis on animals carrying polymorphisms of known parental origin.

**Results:** Preferential paternal antisense transcription occurs over both the human and mouse ATP10C locus. In both human and mouse cortex, loss of MeCP2 is coordinate with a decrease in maternal ATP10C expression, with an increase in total antisense expression and in the relative proportion of maternal antisense expression.

**Conclusions:** We provide further evidence that regulation of chromosome 15 imprinted gene expression by the IC extends through ATP10C, and that loss of MeCP2 disrupts regulation of autism-candidate genes controlled by the AS-IC. Aberrant expression of these genes may contribute to the overlap between RS, AS and autism.

Sponsors: IRSA, CMH

**PS2.14**

**22q11.2 DUPLICATION SYNDROME and AUTISM**

Nahimotavalli Mukaddes, Sabri Herguner, Istanbul Medical Faculty, Istanbul University

**Background:** Although several reports have described the co-occurrence of autism in subjects with chromosome 22 abnormalities including trisomy 22, deletion at 22q11.2 and ring chromosome 22, there is no report on autism in cases with duplication of 22q11.2.

**Method:** Case description: Here, we report a 9-year old female patient referred to our department due to the lack of communication, delay in language development and repetitive behaviors. She received the diagnosis of Autistic Disorder according to DSM-IV criteria. Because of her dysmorphic characteristics comprising synophrys, depressed nasal bridge, narrow forehead, narrow face, mandibular prognathism, low medial arcus in her feet, positional abnormalities in her
toes, alternating exotropia and reported cleft palate operation, she had gone under cytogenetic analysis. The karyotype 46XX ish dup 22(q11.2-11.2) (D22S75 ++, N85A3+) was identified utilizing interphase fluorescence in situ hybridization (FISH). In addition, reviewing her family history proved the presence of autism in her maternal uncle and epilepsy in her cousins.

Conclusion: Although the present case was ascertained because of some overlapping features with VCF/DG, the duplication of 22 q11.2 was detected. Previous reports on psychiatric aspects of 22q11.2 duplication showed the existence of cognitive deficit and hyperactivity but autism. The phenotypic outcome in this case might be determined by the combination of chromosomal abnormality and positive family history. Moreover, the lack of report in co-occurrence of autism and 22q11.2 duplication may be related to paucity of reports on 22q11.2 duplication as a result of technical problems.

PS2.15
AUTISM-RELATED, ADAPTIVE AND CHALLENGING BEHAVIOR IN CORNELIA DE LANGE SYNDROME

Ina van Berckelaer-Onnes, Gijs van Duijn, Ilse Noens, Raoul Hennekam, Leiden University, The Netherlands

Background: Cornelia de Lange Syndrome (CdLS) is a multiple anomaly syndrome characterized by a distinctive facial appearance, prenatal and postnatal growth deficiency, psychomotor delay, behavioral problems, and malformations of the upper extremities; the phenotypic expression is variable. Recently, NIPBL gene mutations have been identified in 30-50% of the CdLS-cases.

Method: In the present study 36 Dutch CdLS clients were evaluated. Mutations in the NIPBL gene were found in 56% of the cases, which is slightly higher than the frequency reported in other studies. Each of the 36 clients was assessed on adaptive behavior using the Vineland Adaptive Behavior Scales Expanded Form (VABS) (Sparrow et al., 1984), on challenging behavior using the Developmental Behavior Checklist (DBC) (Einfeld & Tonghe, 1994), and on autism-related behavior using the Diagnostic Interview for Social and Communication Disorders-10 (DISCO, 10th ed.) (Wing, 1999) and the autism-algorithm of the DBC (Brereton et al., 2002).

Results and conclusions: The results generally indicate that the level of adaptive functioning decreases as the chronological age increases. Autism-related symptoms mainly occur in low-functioning individuals with CdLS. Of the 19 individuals with a profound adaptive retardation, 17 meet ASD criteria using the DISCO. The study further confirms that individuals with CdLS have a considerable risk of developing severe challenging behavior. The severity is highly correlated with the level of adaptive functioning and the presence of autism-related symptoms.

PS2.16
AUTISM LINKAGE EVIDENCE ON CHROMOSOME 3Q13.31 IN A UTAH EXTENDED PEDIGREE

Kristina Allen-Brady, Hilary Coon, Judy Miller, Janet Lainhart, William McMahon, Utah Autism Research Program, University of Utah

We have performed a whole genome scan for a large Utah extended autism pedigree (7 affected cases and 24 other relatives) using the 10K Affymetrix SNP chip. Not accounting for linkage disequilibrium (LD) between SNPs, we found preliminary evidence for linkage on chromosome 3q13.31 using SimWalk2 (NPL=3.53, 123.38 cM, p=0.0003). The current objective was to determine if the linkage peak would remain after accounting for LD. Selecting a subset of 50 SNPs spanning the region of interest, we compared Affymetrix SNPs to unrelated CEPH parental genotype data from HapMap, and were able to match 45/50 SNPs. Pairwise linkage disequilibrium was assessed using the 45 SNPs from HapMap; all pairs with a D' > 0.7 and within 2 million basepairs of each other were considered to be in high linkage disequilibrium. Using a principal components analysis method, we selected a subset of the high LD SNPs that best captured the underlying genetic variation but avoided markers in strong LD. Repeating the linkage analysis using MCLINK, our linkage peak remained (NPL=2.99, 123.38 cM, p=0.0014). Two candidate genes (GAP43 and LSAMP) lie in this region and warrant further study.

Sponsor: R01 MH06359 and NICHD 5 U19 HD 035476

PS2.17
BROAD INVESTIGATION OF ISODICENTRIC CHROMOSOME 15 CELL LINES USING AGILENT ARRAY-CGH ARRAYS, EXPRESSION MICROARRAYS, AND FUNCTIONAL PROFILING

Colin Andrew Baron, Ryan R Davis, Condie Carmack, Clifford G Tepper, Stephenie Y Liu, Nicholas J Wang, Carolyn Schanen, Jeff P Gregg, UC Davis MIND Institute

Background: Isodicentric chromosome 15 (Idic15) is a cytogenetically common event that has been shown to be strongly correlated with autism. It is currently unknown what contribution the presence of additional gene content on chr15 has in the etiology of this disorder.

Objective: Evaluate the efficacy of Agilent CGH arrays to detect chromosomal copy number alterations in a known population with Idic15. Examine potential downstream effects of genomic alteration including its whole-genome transcriptional profile.

Methods: Peripheral blood lymphocyte cell lines were obtained from the Alfred I. duPont Hospital for Children and from the AGRE database and cultured for experimentation. Idic15 and control samples were processed on Agilent 60-mer CGH arrays followed by gene expression profiling using Affymetrix U133 2.0 Plus. Targets obtained from these analyses were further pursued for functional abnormalities.

Results: Array-based CGH detected chromosomal gains in all samples with previously described duplications. The detection resolution of these arrays enabled the differentiation of subtypes of Idic15 duplications with negligible false-positives. Differential expression of key genes within the region of interest, as well as potential downstream candidates was observed by FDR-corrected t-
test (112 probesets, p-value < 0.05) in samples with chr15 duplications. Further analysis of the affected cell lines potentially point to deficiencies in Ubiquitin-Proteosome Pathway.

Conclusion: Array-CGH is a robust alternative to traditional cytogenetics in the characterization of Idic15. Preliminary findings indicate that a cohort of relevant genes within the chr15 contig respond to gene dosage in this lymphoblast model and these genes may play a role in the observed functional deficiencies.

PS2.18
GENOTYPE-PHENOTYPE CORRELATIONS IN INDIVIDUALS WITH LARGE SUPERNUMERARY MARKER 15 CHROMOSOMES Patrick F Bolton, Russell J Thompson, Ellen E Craig, Marijcke MW Veltman, Nick R Dennis, Sian E Roberts, Simon Thomas, Sarah R Curran, Child & Adolescent Psychiatry Department & MRC Social, Genetic & Developmental Psychiatry Centre, Institute of Psychiatry, Kings College London, UK

Objective: To investigate genetic factors influencing the phenotype associated with large supernumerary marker chromosomes derived from chromosome 15 [SMC(15)].

Methods: Participants included 32 carriers of large SMC(15) (mean age 13 years 6 months) and a control group of 27 individuals with Down Syndrome (DS; mean age 11 years 8 months). Cognitive and behavioural phenotypes were assessed using age appropriate measures of intellectual ability, the Vineland Adaptive Behaviour Scales, the Autism Diagnostic Interview (ADI), and the Autism Diagnostic Observation Schedule (ADOS).

Results: A significantly higher proportion of SMC(15) carriers than DS controls met both ADI and ADOS criteria for autism (65% vs 7.5%). Comparisons between genetically defined subgroups of SMC(15) patients showed that mosaic cases had significantly higher levels of intellectual ability and adaptive behaviour than non-mosaic cases. Cases with only 1 additional copy of the Prader-Willi Angelman Critical Region (PWACR) showed a significantly lower incidence of epilepsy and a replication sample of 999 individuals with ASD spanning the MET locus were genotyped in an original sample of 231 individuals with ASD from 204 pedigrees and a replication sample of 999 individuals with ASD from 503 pedigrees. A subset of 299 individuals from 182 AGRE pedigrees was diagnosed with autism by both the ADI-R and the ADOS. Family-Based Association Test (FBAT) analyses were performed to determine association.

Objectives: To identify functional genetic variants within the MET receptor tyrosine kinase gene associated with autism spectrum disorder (ASD).

Methods: Seven single nucleotide polymorphisms (SNPs) spanning the MET locus were genotyped in an original sample of 231 individuals with ASD from 204 pedigrees and a replication sample of 999 individuals with ASD from 503 pedigrees. A subset of 299 individuals from 182 AGRE pedigrees was diagnosed with autism by both the ADI-R and the ADOS. Family-Based Association Test (FBAT) analyses were performed to determine association.

Results: FBAT analyses indicated over-transmission of the C allele of rs1858830 in samples with chr15 duplications. Further analysis of the affected cell lines potentially point to deficiencies in Ubiquitin-Proteosome Pathway.

Conclusion: Array-CGH is a robust alternative to traditional cytogenetics in the characterization of Idic15. Preliminary findings indicate that a cohort of relevant genes within the chr15 contig respond to gene dosage in this lymphoblast model and these genes may play a role in the observed functional deficiencies.
with ASD in both the original and replication samples (combined \( P=0.00001 \)). A functional assay indicated a 2.5-fold decrease in transcription from promoter constructs with the rs1858830 C allele compared to the G allele.

Conclusion: These data provide strong evidence for MET being an autism susceptibility gene. Disruption of MET signaling is consistent with neuropathological findings and reported medical complications in many children with ASD.

Sponsors: NIMH MH65299; NICHD HD15052

**PS2.21**

**NEURAL NETWORK ANALYSIS OF MAOA, SEROTONIN TRANSPORTER, AND SEROTONIN RECEPTOR (HTR1B) POLYMORPHISMS AND THE BEHAVIORS OF CHILDREN ON THE AUTISM SPECTRUM**

**METHOD:**
- **Source of Funding:** March of Dimes, Canadian Institutes of Health Research, Ontario Mental Health Foundation.

**PS2.22**

**PERIPHERAL BLOOD MONONUCLEAR CELL COLLECTION AND RNA EXTRACTION METHODOLOGY FROM ASD AFFECTED CHILDREN AND NORMAL CONTROLS**

Iris Eisenberg, Michal Galdzicki, Alal Eran, Isaac Kohane, Ingrid Holm, Louis Kunkel, Children’s Hospital Boston

Attainment of quality and sufficient quantity of RNA from children presents several technical challenges. It is imperative to collect the minimum amount of blood needed as drawing the blood from children who have ASD may be physically challenging as the child is restless, potentially afraid and uncooperative as also any child may be. Moreover, there is no need to collect more blood if the processing protocols can be sufficiently optimized for minimal amounts of blood.

We have examined several traditional and commercially available protocols for the extraction of microarray quality RNA. We interrogated the Paxgene (PreAnalytiX) system, the RiboPure Kit (Ambion), RNeoasy Mini Kit (Qiagen), and Trizol Extraction. Also, we tested stabilization with RNA Later (Ambion), and mononuclear cell separation with CPT tubes (BD), and Accuspin with Histopaque (Sigma). Ease of collection, timing of RNA stabilization, quality and quantity of RNA extracted are factors examined. Further processing in preparation for hybridization will depend on the microarray platform chosen for the expression study.

**SPONSOR:** Nancy Lurie Marks Family Foundation

**PS2.23**

**DIAGNOSTIC MARKERS AND ETHICAL DILEMMAS: BYPRODUCTS OF THE CHILDREN’S HOSPITAL BOSTON AUTISM STUDY**

Alal Eran, Stephanie Jo Brewster, Michal Galdzicki, Iris Eisenberg, Heather Peters, Louis Kunkel, Isaac S Kohane, Ingrid A Holm, Children’s Hospital Boston

During our gene expression study comparing autistic and control populations, we realized that transcriptome-scale profiling has the capability to detect diagnostic markers for diseases other than the one under study. Thus our study can potentially identify a patient, for example, as having a chromosomal rearrangement involved in cancer, or a similar diagnosis, that is unrelated to autism, but if confirmed, could make an important diagnosis (e.g. cancer). This raises both clinical diagnostic opportunities and ethical questions.

We use Affymetrix U133 Plus 2.0 microarrays to identify an autism expression signature in WBCs. In order to determine which of the array’s probe sets are potential markers diagnostic of a disease, we mapped the probe sets to proteins specifically involved in pathologic processes. We then classified the potential markers into two groups: transcripts whose actual presence or dysregulation are implicated in a disease and transcripts in which mutations have been described as associated with disease, and thus may alter the normal expression pattern. We identified...
287 probe sets that could potentially serve as direct diagnostic markers, and 1427 that map to disease-associated genes.

Although microarrays do not offer sufficient sensitivity and specificity required for clinical diagnostics, in our dual role as care providers, we decided that if the chip identified an imminent health threat to an individual, we could not ignore such information. Therefore, we are in the process of designing a protocol that addresses the detection of abnormal expression patterns among the 287 potentially direct diagnostic probe sets. An abnormality was defined according to previously reported expression data in affected populations. This protocol will include confirmatory testing in research and CLIA-laboratory settings and disclosure procedures to participants, in compliance with guidelines set by our institutional review board.

**PS2.24**

**EXPRESSION PROFILING OF WHITE BLOOD CELLS IN AUTISM**  
Michal Galidzicki, Alal Eran, Iris Eisenberg, Heather Peters, Stephanie Brewster, Rachel Hundley, Ellen Hanson, Janice Ware, Leonard Rappaport, Ingrid Holm, Louis Kunkel, Isaac Kohane,  
Children's Hospital Boston

As part of an integrative genomic approach to ASD, we profiled the gene expression pattern of pediatric patients who meet criteria for ASD on the ADOS/ADI-R. We searched for differentially expressed genes and pathways and an expression "signature" that could be used to classify ASD patients. Quantifying expression of mononuclear blood cells using Affymetrix U133 Plus 2.0 microarrays allows us to compare the ASD participants profiles to normal controls. The use of Peripheral Blood Mononuclear Cells (PBMCs) to investigate expression in ASD is based on the shared expression profile between different tissues. Thus we aim to find a set of genes that can be used to help diagnose ASD and further divide the ASD into subcategories based on experimentally quantifiable means. Furthermore, this analysis can identify individual genes and/or entire molecular pathways abnormally expressed in the affected population indicating possible pathological mechanisms. To date we have collected 12 samples in each of the affected and control groups. Despite the very small sample size the expression profiles of affected individuals fall into a separate cluster from normal controls. Because we expect the difference in expression to be a very subtle signal, our goal is to collect upwards of 1000 samples in each group. Increased sample size will allow us to sub classify ASD based on expression measures. In the future parental samples will be used to see where they classify among these subcategories.

**PS2.25**

THE DRD1 GENE AS A CANDIDATE LOCUS FOR AUTISM SPECTRUM DISORDERS  
Joe A Hettinger, Xudong Liu, Jeanette JA Holden, ASD-CARC, Queen's University

Background: Higher order functions in the central nervous system, such as cognition and social behaviour, are modulated by the neurotransmitter, dopamine (DA). Since impairments in executive functions and social cognition are features in individuals with Autism Spectrum Disorders (ASDs), DA is implicated in these disorders. The DRD1 receptor is integral to the neural circuitry mediating these processes. 

Objectives: The purpose of this study was to determine whether the DRD1 gene is associated with susceptibility to ASDs.

Methods: We genotyped 3 polymorphisms (D1P.6, D1.1 and D1.7) in the DRD1 gene in 185 affected sib-pair families. All families have two or more children with either autism or an ASD. The comparison group consisted of 445 anonymous individuals. FBAT, haplotype-FBAT (HBAT) and haplotype case-control analyses were performed.

Results: No significant FBAT or HBAT findings were observed in the complete family set. However, in families with two or more affected sons (MM), allele over-transmissions for two markers (D1P.6 and D1.1) were observed (P=0.041, P=0.047), with HBAT analysis showing over-transmission of a haplotype comprising all 3 markers (P=0.022). Haplotype case-control comparisons revealed an increase of this putative risk haplotype in affected individuals from MM families compared to controls (P=0.004).

Conclusion: Preferential haplotype transmissions of markers at the DRD1 locus and an increased frequency of a specific haplotype in MM families support DRD1 gene as a risk gene for ASD.

Funded by CIHR, NAAR and OMHF.

**PS2.26**

EFFECTS OF MATERNAL AND CHILD MAOA AND SEROTONIN TRANSPORTER POLYMORPHISMS ON THE BEHAVIOR PATTERNS OF CHILDREN ON THE AUTISM SPECTRUM  
Jeanette Jeltje Anne Holden, X Liu, SM E Lewis, AE Chudley, M Flory, EC Jenkins, WT Brown, M Gonzales, T Rovito-Gomez, ASD-CARC, IL Cohen, Queen's University

Background: MAOA metabolizes biogenic amines such as serotonin in the pre-synaptic neuron. We reported that a functional polymorphism in the MAOA promoter region was correlated with the behavioral and cognitive profile of a small sample of young males with autism (Cohen, et al., 2004). Since boys inherit the MAOA gene from their mothers, it was unclear whether our effects were related to the mother's or to the boy's genotypes. Since serotonin availability is also affected by the functional serotonin transporter gene promoter polymorphism (5-HTTLPR) (Heils, et al., 1996), this polymorphism was also studied.

Objectives: To examine the main and interactive correlations of MAOA-uVNTR and 5-HTTLPR polymorphisms with behavior patterns of boys and girls on the autism spectrum (n=216 to 278).

Method: Behavior patterns were assessed with the PDD
Behavior Inventory (PDDBI; Cohen and Sudhalter, 2005). The low or high activity allele status of all cases followed that suggested by Deckert, et al. (1999). MAOA analysis was done as described previously (Cohen, et al., 2004). 5-HTTLPR genotypes were characterized as short/short, short/long or long/long. All analyses were carried out using generalized estimating equations with age, sex, and source of data (Canada/USA) serving as covariates.

Results: There was evidence for gene-gene interactions for child and maternal genotypes. Children with the long/long 5-HTTLPR genotype had higher than average language skills if they had low activity MAOA alleles but relatively lower social communication skills if they had high activity MAOA alleles. Similarly, the association of sensory behaviors with the mother’s 5-HTTLPR genotype depended on her MAOA genotype.

Conclusion: These data point to the need to consider gene interactions in accounting for many of the behaviors shown by children with autism and may help to elucidate the role of these serotonin genes in this disorder.

FUNDING: CIHR, CHR-IHRT, OMHF, March of Dimes

PS2.28
SUPPORT FOR THE HOMEBOX TRANSCRIPTION FACTOR, ENGRAILED 2, AS AN AUTISM SPECTRUM DISORDER (ASD)

SUSCEPTIBILITY LOCUS Rym Benayed, Neda Gharani, Ian Rossman, Silky Kamdar, Gloria Lazar, Emanuel DiCicco-Bloom, Linda M Bzustowicz, James H Millonig UMDNJ-Robert Wood Johnson Medical School

Background: Our previous research using 167 nuclear families from the Autism Genetic Resource Exchange (AGRE I dataset) demonstrated that two intronic SNPs, rs1861972 and rs1861973, in the EN2 gene were significantly associated with ASD (Gharani et al., 2004).

Objective: In this study, we investigated whether association of these SNPs could be replicated in two additional datasets, an independent set of 222 AGRE (AGRE II dataset) families and a separate sample of 129 NIMH families.

Results: Significant replication of association was observed in both datasets individually (AGREII P=0.0016; NIMH P= P=0.0431) and in the combined sample of both AGRE datasets (389 families; P=0.0000033) and all three datasets (518 families; P=0.00000035). Population Attributable Risk (PAR) calculations for the associated haplotype using the entire sample of 518 families determined that the risk allele contributes to as much as 40% of ASD cases in the general population.

Conclusion: Together these data provide further genetic evidence that EN2 might act as an ASD susceptibility locus and suggest that a risk allele, which perturbs the spatial/temporal expression of EN2 could significantly alter normal brain development.

Sponsors: NIMH (1 R01 MH076624-01), NJ Governor’s Council on Autism, Whitehall Foundation (2001-12-54-APL) and National Alliance for Autism Research

PS2.29
SUPPORT FOR THE GLUTAMATE RECEPTOR 6 (GLUR6) GENE AS AN AUTISM SPECTRUM DISORDER SUSCEPTIBILITY LOCUS Xudong Liu, Jennifer Ng, Christine L Hall, Albert E Chudley, Suzanne ME Lewis, Jeanette JA Holden, ASD-CARC, Queen’s University

Background: GLUR6 (6q21) is a positional and functional candidate gene for Autism Spectrum Disorders (ASDs). Two recent studies have supported linkage and association of the GLUR6 gene with autism.

FUNDING: CIHR, CIHR-IHRT, OMHF, March of Dimes
Objectives: To carry out a replication study of two polymorphisms in the GLUR6 gene in a large number of affected sib-pair families with ASDs.

Methods: Three separate cohorts of families with two or more cases of ASD were studied (I: 45 families; II: 136 AGRE families; III: 97 families). We genotyped 2 intragenic SNPs in the GLUR6 gene, rs2227281(C/T) located in intron 14 and rs2227283 (G/A) located in exon 15. The FBAT program was used to perform transmission disequilibrium tests (TDT) for both single marker alleles and haplotypes under an additive model.

Results: There was significant preferential transmission of the C allele of rs2227281 and of the G allele of rs2227283 from parents to affected offspring in all three independent sets of families (P values <0.05). In the combined group of all three cohorts, the findings were highly significant: P = 0.0005 for rs2227281 and P=0.001 for rs2227283. The two markers are in moderately strong linkage disequilibrium. Haplotype FBAT identified a significant excess of transmission of the rs2227281C-rs2227283G haplotype (P=.0001) from parents to affected children.

Conclusion: The results of this study confirm the association between GluR6 and ASD susceptibility.

Source of Funding: Canadian Institutes of Health Research, Ontario Mental Health Foundation, and March of Dimes.

PS2.30 PHARMACOGENETIC TESTING IN CHILDREN WITH ASD Patty Manning-Courtney, Judy Reinhold, Tracy Glauer, Richard Wenstrup, Vinks Alexander, The Kelly O'Leary Center for Autism Spectrum Disorders, Cincinnati Children's Hospital Medical Center

Background: Pharmacogenetics examines the effect of an individual's genetic makeup on response to drug therapy. Children with ASD are frequently treated with medications metabolized by enzymes coded for by the polymorphic genes CYP2D6 and CYP2C19.

Objective: Evaluate CYP2D6 and CYP2C19 polymorphisms in a case series of children with ASD.

Methods: Children with ASD underwent CYP2D6 and CYP2C19 pharmacogenetic testing. Genotypes were determined after isolation of DNA from whole blood. Allelic variants were determined using customized Taq-Man reagents after real-time PCR on an ABI 7500 platform. In addition, some CYP2D6 duplication and deletions variants were detected by gel electrophoresis after long distance PCR.

Results: 29 children (3 girls) with autism/ASD underwent pharmacogenetic testing. 13 were extensive metabolizers (EM) for both CYP2C19 and CYP2D6. 6 were EM for CYP2C19 and intermediate metabolizers (IM) for CYP2D6. 5 were IM for CYP2C19 and EM for CYP2D6. The remaining 5 patients had genotype combinations of ultrarapid metabolizer (n=1), IM (n=2) and PM (n=2) for CYP2D6 with EM (n=2), IM (n=2) and PM (n=1) for CYP2C19. Poor metabolizers were more challenging with regards to medication management.

Conclusions: Pharmacogenetic testing in a sample of children with ASD reveals a range of findings similar to that seen in the general population. Information obtained may help guide medication management.

PS2.31 FUNCTIONAL STUDIES OF 3 CANDIDATE GENES SUGGESTS THAT ERRORS IN THE REGULATED SECRETION PATHWAY MAY UNDERLIE AUTISM Jean G Steyeart, John Creemers, Dries Castermans, Jean-Pierre Frijs, Koensraad Devriendt, Dept. Child Psychiatry Katholieke Universiteit Leuven, Belgium

Background: In some subjects, autism appears to be associated with single gene defects due to balanced chromosomal anomalies. These subjects are of particular interest as their autism is due to knock-out of a particular gene. This throw light on the possible effect of suboptimal alleles of this gene in autistic subject in whom polygenic mechanisms operate.

Objectives: Delineate candidate genes for autism in subjects with balanced chromosomal anomalies, and described the role of these genes through functional studies.

Methods: Karyotyping in a population of subjects clinically diagnosed with autism. Positional cloning of breakpoints in cases with balanced chromosomal anomalies. Perform biological functional studies on the thus found genes, in order to find which biological pathways are involved.

Results: Amongst approximately 500 subjects with autism, 4 unrelated subjects with intelligence in the normal range had chromosomal breakpoints. Through positional cloning deficiency of 5 different genes was described. One of these genes, neurobeachin, had been proposed as candidate gene for autism by other authors. Remarkably, three of the found genes participate in the same biological pathway: the intraneuronal regulated secretion pathway. Functional assays in mice support this hypothesis.

Discussion: The findings suggest that a dysfunction in the regulated pathway underlies autism in at least a subpopulation of subjects. The regulated secretion pathway plays a role in the neuronal secretion of neurotrophins.

Funding: Cure Autism Now; Flanders Fund for Scientific research.

PS2.32 X CHROMOSOME INACTIVATION AND CORRELATION WITH CLINICAL DATA IN FEMALES WITH AUTISM Zohreh Talebizadeh, Merlin G Butler, Children's Mercy Hospitals and Clinics

Background: An increased prevalence of autism in males suggests a role for the X chromosome. We previously studied X chromosome inactivation in 30 females with classical autism. A significantly higher (p=0.04) prevalence of X chromosome skewness was detected in autistic females (33%) compared with controls (11%). X chromosome skewness was also seen in 50% of the mothers with autistic daughters.

Objectives: 1) to perform additional X chromosome inactivation studies in females with autism, and 2) to analyze clinical features using the Autism Diagnostic Interview-Revised (ADI-R) from autistic females with
and without X inactivation skewness.

Methods: Autistic females were mainly ascertained from the Autism Genetics Resource Exchange (AGRE), a publicly available biomaterials repository for autism research. The diagnosis of autism was established with the use of the ADI-R and X inactivation status determined using the AR gene assay from genomic DNA. X chromosome skewness was classified into three groups: randomly, moderately and highly skewed using e 80:20% as a cut off (Talebzadeh et al., 2005).

Results: Currently, genetic data have been collected on 60 young autistic females and clinical analysis underway using ADI-R data.

Conclusions: Preliminary findings suggest a possible correlation with X chromosome inactivation and specific parameters (e.g., repetitive behavior) and, of interest, disturbances found in cDNA of two X-linked genes (NLGN3 and NLGN4) in two autistic females with skewness.

Sponsor: CAN Foundation

PS2.33 GENE EXPRESSION PROFILE IN AUTISM BY LASER CAPTURE MICRODISSECTION Flora Tassone, Marko Estrada, Christian C Leutenegger, Randi J Hagerman, Pul J Hagerman, Department of Biological Chemistry, University of California, Davis

Background: Gene expression studies using post-mortem brain tissue, obtained from individuals with autism, are needed for the development of hypotheses regarding the molecular underpinnings of neuronal development seen in autism.

Objective: Compare the gene expression pattern in brain of autistic and normally developing children. The genes included in the preliminary analysis were chosen because their relevant role in the development of the CNS, such as genes for proteins which signaling are required for the normal axonal outgrowth and guidance, dendritic branching and arborization or because their suggested involvement in autism from a number of reported studies.

Methods: Laser capture microdissection was used to isolate homogeneous cell populations, which allow a more precise definition of their expression profiles, without the confounding issue of tissue heterogeneity. We have initiated a pilot experiment to isolate cells from previously frozen cerebellar cortex from 3 individuals with autism and from normal controls. RNA isolated from 100 Purkinje cells, and 100 sections containing granular cells, was pre-amplified and the levels of expression of 25 target genes, including Gaba receptors, reelin, Serotonin, Rho GTPase, MeCP2, was determined by real-time TaqMan PCR.

Results: Preliminary findings suggest a differential gene expression levels between brain tissues derived from normal and individuals with autism. Specifically, differences appear to be cell type specific.

Conclusions: Preliminary data suggest a differential pattern of gene expression in autistic compare to control brain. This study will help to elucidate the relationships between altered expression profiles and the potential involvement or non-involvement of specific cell types and brain regions in the neuropathology of autism. Such a description represents an important starting point for a more detailed mechanistic study of the pathogenesis of this important neurodevelopmental disorder.

PS2.34 BLOOD GENOMICS OF THE CHARGE STUDY: THE EARLY RESULTS Jeff Gregg, Colin A Baron, Ryan R Davis, Rebecca Walker, Sally Ozonoff, Paula Krakowiak, Iri Hertz-Picciotto, Paul Ashwood, Judy VandeWater, Lisa Lit, Wynn Walker, Isaac N Pessah, Frank R Sharp, UC Davis MIND Institute

Background: Autism presents significant diagnostic and therapeutic challenges due to its clinical heterogeneity, lack of diagnostic markers, and its complex genetic architecture. Until recently, the identification of genes associated with autism has been based on linkage analysis to identify potential susceptibility regions. This systematic search for linked loci has not yielded definitively associated genes.

Objective: Blood genomics, the study of the transcriptome of whole blood, offers a unique and global approach to the identification of genes related to autism.

Methods: Gene expression profiles using Affymetrix U133 2.0 Plus arrays were conducted on peripheral blood from children enrolled in the CHARGE study at UC Davis. Children with autism (with and without regression), mental retardation/developmental delay (MR/DD), and age-matched typically developing children were analyzed and compared. The latter two groups were utilized as controls and all the children were from ages 3-5.

Results: Significance analysis was conducted between the groups using a stringent FDR corrected, unpaired t-test, filtering for genes showing significant differential gene expression (p-value 0.05). Differentially expressed genes that fit these criteria were identified, and these genes were able to differentiate autism (with and without regression) from typically-developing children and MR/DD children. A subset of these genes was confirmed with TaqMan quantitative RT-PCR.

Conclusion: This study demonstrates that a blood genomics approach has the potential for identifying genes that play a key role in autism. Prospectively, these genes may also be able to be utilized to sub-phenotype of autism, as well as serve as biomarkers for diagnosis and prediction.

PS2.35 PROSODIC SKILL DEVELOPMENT OVER TIME IN CHILDREN WITH HIGH-FUNCTIONING AUTISM. Lianne Carroll, Queen Margaret University College

Background: Difficulty with social communication is a core diagnostic feature of autism. One of the ways in which social communication competence is realised is through the understanding and use of prosody to serve grammatical, syntactic, and affective functions. Impairments in expressive prosody in individuals with
autism have been widely reported. However, little is known about their understanding of prosody (1). Further, there is no published research to date that has studied changes in receptive and expressive prosody skills over time.

Objectives/Methods: To longitudinally investigate prosody skills in 24 children (18 boys, 6 girls) aged 9 to 16 years with high-functioning autism (HFA). The participants were assessed twice approximately 2 ½ years apart using a computerised assessment of expressive and receptive prosody called Profiling-Elements-of-Prosodic-Systems-Children (PEPS-C).

Results: At Time-point 1 results of prosody skills were compared to typically developing peers matched on language age. The children with HFA performed significantly poorer (t-tests, p<0.01) than typical peers on seven of twelve subtests on the PEPS-C (2). Results for participants at Time-point 2 reveal that the children with HFA made significant gains on total PEPS-C scores (Wilcoxon signed ranks, p<0.01) and when compared to another group of typical peers matched on language age, the gap in the total score seen at Time-point 1 is no longer evident. However, a significant difference continues to exist in the subtest that assesses use of contrastive stress (Mann-Whitney U, z=-2.527, p=0.012).

Conclusions: This study found that children with HFA made significant gains in prosodic skills over time, indicating that most of the assessed prosody skills are delayed rather than deviant. Use of contrastive stress by children with HFA continues to be significantly below that of typical peers.

Sick Kids Friends Foundation, Edinburgh*

PS2.36 EARLY ACCELERATION OF HEAD CIRCUMFERENCE IN CHILDREN WITH FRAGILE X SYNDROME AND AUTISM Sufen Chiu, Jacob Wegelin, Jeremy Blank, Megan Jenkins, Josh Day, David Hessl, Flora Tassone, Randi Hagerman, University of California, Davis Department of Psychiatry and Behavioral Sciences and the M.I.N.D. Institute Background: Outside head circumference (OHC) growth is found to be accelerated in early childhood in both Fragile X syndrome (FXS) and Autism Spectrum Disorders (ASD).

Objective: To compare the rates of OHC growth between individuals with only FXS and those with FXS and comorbid ASD.

Methods: OHC measurements were available for 44 males with FXS in the first five years of their life, of whom 22 also had ASD. OHC percentiles were compared between the two groups (FXS-only and FXS+ASD) in two ways: by focusing on cross-sectional sub-samples and by fitting hierarchical linear models to the full sample.

Results: Neither group differed significantly from the norm in the first year of life (p>0.2). At 30 months, the FXS+ASD group had an average percentile at least 13 percentile points above the norm (p<0.0125) whereas the FXS-only group did not differ from the norm. At 60 months the situation was reversed, in that the FXS-only group was 21 points above the norm (p=0.029) whereas the FXS+ASD group did not differ from the norm. The FXS-only group exhibited an approximately linear trend of OHC increase from birth (p<0.01) whereas the FXS+ASD group exhibited a convex pattern (p=0.013), with average OHC percentile beginning near the national median at birth, rising to a maximum at about 2 ½ years of age and returning to the median by 5 years of age.

Conclusion: FXS-only and FXS+ASD groups exhibit different rates of OHC growth during the first five years of life.

Sponsor: All participants were recruited from the NIH funded IRB approved protocol Genotype-Phenotype Relationships in Fragile X Families (HD 36071).

Additional funding was provided by the MIND Institute and UC Davis Department of Psychiatry and Behavioral Sciences.

PS2.37 IQCJ-SCHIP1, A COMPLEX TRANSCRIPTIONAL UNIT ENCODING A CALMODULIN BINDING PROTEIN, AS A POTENTIAL CANDIDATE GENE FOR LANGUAGE DISORDERS. Dorota A Kwasnicka-Crawford, Andrew R Carson, Steve W Scherer, The Hospital for Sick Children Background: Language disorders are defined as failure to acquire normal language skills despite adequate intelligence and environmental stimulation. The molecular mechanisms underlying expressive and receptive deficits in language disorder are now being resolved and, in many cases, genetic factors are involved. Objectives: To map chromosomal loci for language disorders through the study of rare patients bearing chromosomal rearrangements. This approach is particularly useful in pinpointing chromosomal breakpoints containing potential candidate genes.

Methods: We describe a patient with significant impairment in both expressive and receptive language abilities carrying a paracentric inversion on chromosome 3q25-29 inherited from her father who was also language delayed. Fluorescent in situ hybridization (FISH) with locus-specific bacterial artificial chromosome clones (BACs) as probes was used to characterize the inverted chromosome 3.

Results: We isolate and characterize a novel schwannomin interacting protein 1 variant, containing a calmodulin binding IQ motif (named IQCJ-SCHIP1) highly expressed in the brain. The gene resides in close proximity to the 3q25 inversion breakpoint and its expression is reduced in lymphoblastoid lines carrying the inversion, presumably due to a position effect mutation caused by the chromosomal rearrangement. IQCJ-SCHIP1 is the longest isoform of a complex transcriptional unit that bridges two separate genes that encode distinct proteins, IQCJ, an IQ motif containing protein and SCHIP1, a schwannomin interacting protein. In our study, IQCJ-SCHIP1 localized to cytoplasm and actin-rich regions and in differentiated PC12 cells the protein was also seen in neurite extensions.

Conclusion: Our collective data suggests that the IQCJ1-
SCHIP1 transcriptional complex should be assessed as a candidate in other cases of language disorder.
Sponsor: Genome Canada/Ontario Genomics Institute and the Hospital for Sick Children Foundation.

**PS2.38**

**WHAT CAN WE LEARN ABOUT AUTISM FROM AUTOBIOGRAPHIES OF AUTISTIC PERSONS?**
Emmanuel Jaunay, Brigitte Chamak, David Cohen, B. Bonnau Department of Child and Adolescent Psychiatry, Université Pierre et Marie Curie, FRC CNRS «cognition et comportement», Hôpital Pitié-Salpêtrière, APHP
Background: Since the early 90s, the number of autobiographies written by autistic persons has increased, thus providing a useful database for a comprehensive analysis.
Objectives: Highlight the socio-demographic characteristics of autistic authors, their personal histories, their representations of autism, the way they see their different therapies; and compare their personal experiences with scientific and medical representations.
Methods: We analysed thirteen autobiographies of persons with autism or Asperger syndrome, which represent twenty books. By writing several books, some authors helped us underline their own evolution. We developed a three-page structured questionnaire allowing for a systematic screening of the autobiographies.
Results: The authors’ ages, countries and surroundings are diversified. Common troubles mentioned in these narratives deal with: different perception, difficulties in generalizing, fascination for spinning or shining objects, rules, habits and stereotypes to calm anxiety and to give impression of controlling the situation, fear of emotions, understanding and communication problems. These elements overlap clinical and cognitive sciences results, thus allowing us to integrate theories into a broader vision of autism. Moreover, this study stresses the function of cultural signifiers in constructing one’s representation of autism.
Conclusion: Autobiographies written by autistic persons provide an inside view of autism that can be useful for clinical practices, teaching professionals, as well as the fields of research and theories.

**PS2.40**

**THE ENHANCED SOCIAL INTERACTION PLAY SESSION (NSIPS): MEASURING SOCIAL ABILITIES IN CHILDREN WITH AUTISM SPECTRUM DISORDERS**
Mandy Steinman, Annette Estes, Geraldine Dawson, University of Washington
Background: Few experimental measures exist to assess social behavior and abilities in school-aged children with autism spectrum disorders (ASD).
Objectives: 1) Introduce the NSIPS as a measure designed to assess social abilities in children with ASD and 2) Investigate how school-aged children with ASD differ on social abilities assessed by the NSIPS, as compared to children with developmental delay (DD) and typical development (TD).
Method: Participants were assessed as part of a longitudinal study on the neurobiology of autism at the University of Washington. ASD was diagnosed using the ADI-R, ADOS, and DSM-IV criteria. Participants were assessed with the NSIPS - a new, semi-structured observation and play based measure. Measures of cognitive ability (DAS) and adaptive functioning (VABS) were also collected.
Results: Data were collected on 40 children with ASD, 17 children with DD, and 19 TD children aged 9 -10 years. Preliminary analyses indicate that children with ASD were less responsive to distress and less likely to initiate joint attention than the TD group. On scales of prosocial behavior and response to joint attention, the ASD group scored significantly lower than both DD and TD groups. No significant differences were found between TD and DD groups. Internal consistency of NSIPS scales was generally acceptable. Additional analyses will explore the relationship between the NSIPS and other clinically relevant research measures (i.e., ADOS, DAS, VABS)
Conclusion: Preliminary results suggest that scores on the NSIPS measure distinguish school age children with ASD from children with DD and TD on constructs related to social abilities.
Funding source: NICHD (U19 HD34565) and NIMH
Methods: Data were collected on 1662 metro-Atlanta backgrounds on the M-CHAT, and begin to investigate endorsed for children from lower and higher SES backgrounds should be targeted since they tend not to intervention time and prognosis. Children from lower SES backgrounds have a lower critical and total scores. Results remained consistent when analyses were conducted on a random sub-sample of age-matched children (M = 19 months, N=67 for both groups).

Conclusions: Preliminary investigation suggests that M-CHAT scoring may need to be adjusted for children from lower SES backgrounds. Previous research has found prevalence rates to be equivalent across SES; therefore, it is likely that higher M-CHAT scores in a lower SES sample indicate reduced specificity. Adequate specificity is necessary in order to minimize unnecessary parental concern and referrals for ASD evaluation.

Sponsor: GSU

PS2.43
STABILITY OF DSM-IV-TR SYMPTOMS IN YOUNG CHILDREN DIAGNOSED WITH AUTISM SPECTRUM DISORDERS Hilary C Boorstein, Emma L Esser, Leandra B Wilson, Pamela Ventola, Juhi Pandey, Jamie Kleinman, Saasha Sutera, Alyssa Verbalis, Michael Rosenthal, Marianne Barton, Sarah Hodgson, James Green, Thyde Dumont-Mathieu, Gail Marshia, Deborah A Fein, University of Connecticut

Background: Due to the increasing awareness of autism spectrum disorders (ASDs), children are being diagnosed at younger ages. However, there has been little research into the stability of diagnostic symptoms over early childhood.

Objective: To examine the stability of the 12 DSM-IV-TR symptoms of autism among young children first diagnosed with ASD at age 2

Methods: The participants were 35 children who were evaluated at 2 and 4 years of age. After each evaluation, the clinicians completed a symptom checklist using DSM-IV-TR criteria. All of the children were diagnosed with an ASD at the first evaluation.

Results: Paired sample T-tests revealed no significant difference in the mean number of total symptoms at each evaluation (6.40 at age 2 and 6.31 at age 4). While there were no significant differences between the mean number of symptoms in the domains of communication and stereotyped behaviors, there was a significant difference in social interaction, t(34)=2.400, p<.05. Children displayed fewer mean symptoms in this domain at age 4 (3.11 at 2 years vs. 2.63 at 4 years). The symptom with the greatest decrease was lack of pretend play (29% change), while inflexible adherence to nonfunctional routines showed the greatest increase (34% change).
Conclusion: Symptoms of ASD appear to be relatively stable during early childhood, confirming the reliability of early diagnosis. Specific symptoms tend to increase or decrease, but the overall number of symptoms displayed is stable. Further research is needed to examine if this stability extends to later ages.

**PS2.44**

EARLY SOCIAL COMMUNICATION SKILLS AND AUTISTIC SYMPTOMATOLOGY IN TODDLERS WITH AND WITHOUT AUTISM SPECTRUM DISORDERS

Lama K. Farran, Kimberly B. Oliver, Nicolle C. Angeli, Diana L. Robins, Georgia State University

Background: Brief experimental measures may be valuable in determining clinical risk for ASD.

Objective: To investigate whether early social communication skills, as measured by the Early Social Communication Scales (ESCS; Mundy et al., 1996), predict outcomes in language, social, and adaptive functioning in 16- to 27-month-old toddlers.

Method: Participants were recruited through pediatricians enrolled in a large metro-Atlanta screening study using the Modified Checklist for Autism in Toddlers (M-CHAT). Nine participants at risk for ASD (based on M-CHAT score) were administered the ESCS, and on a later day, the ADOS, Mullen Scales of Early Learning, CARS, Vineland Adaptive Behavior Scales-II, and ADI-R (mean age =22 months; age range = 16 to 27 months; diagnoses: 4 ASD, 2 broader autism phenotype, and 3 non-ASD delays).

Results: Strongest correlations were found between ESCS Initiating Behavioral Requests and ADOS Communication (r = -.88, p < .01), ESCS Responding to Joint Attention (RJA) and Vineland Socialization (r = .81, p < .05), and ESCS RJA and Mullen Expressive language (r = .86, p < .01). Although current results must be interpreted with caution in light of the modest sample size, these results will be used to guide multiple regression analyses in the near future as data collection continues.

Conclusion: Preliminary findings suggest that impairment in social communication on the ESCS is related to autistic symptomatology, language, and adaptive functioning in 16- to 27-month-old toddlers, thereby highlighting the potential utility of the ESCS in predicting clinical outcomes in toddlers with and without ASD.

**PS2.45**

SCREENING FOR AUTISM IN YOUNG CHILDREN WITH DEVELOPMENTAL DELAY: A FIELD TRIAL OF THE DBC-EARLY SCREEN

Kylie M Gray, Bruce J Tonge, Deborah J Sweeney, Stewart L Einfeld, Monash University, School of Psychology, Psychiatry & Psychological Medicine

Background: Research on the reliability of early diagnosis and the identification of early features of autism has paved the way for the development of autism screening tools. The availability and use of such tools has the potential to facilitate the early referral and diagnosis of young children with autism.

Objectives: This study aimed to assess the efficacy of the Developmental Behaviour Checklist (DBC) as a screening tool for autism in children with developmental delay aged 18 - 48 months.

Methods: Previous work reported on the development and preliminary efficacy of the DBC as a screening tool for autism in young children with developmental delay (Gray & Tonge, 2005), resulting in the development of the DBC-Early Screen. This paper will report on the results of a community field of this screening tool. Two hundred and ten children presenting with developmental problems were referred to a developmental assessment clinic. None of the children had been previously assessed. All received a comprehensive diagnostic assessment.

Results: Data will be presented on the sensitivity and specificity of the proposed screening tool, including examination of false positives and negatives.

Conclusion: Screening at risk children has the potential to assist in lowering the age at which autism is diagnosed, and facilitate the commencement of intervention and support. A number of screening tools have been developed, however it is essential that prospective evaluations of these tools be undertaken in order to fully assess their screening properties.

Sponsor: National Health and Medical Research Council of Australia (NHMRC)

**PS2.46**

THE EARLY SIGNS OF AUTISM IN TODDLERS. A HISTORICAL FOLLOW-UP STUDY

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Background: Studies on smaller groups have indicated that it is possible to identify the early signs of autism in children, before the age of two. There are only few studies of early signs in large groups.

Objectives: To study whether self-reported parent information during the first 1/2 years of life can predict the risk of the child receiving an autistic diagnosis later on.

Methods: This population based study will utilize data from the Danish National Birth Cohort where 70,296 mothers were interviewed 6 and 18 months after birth about their child’s development, behaviour and growth. In the Danish Psychiatric Central Research Register and the Danish National Patient Registry are all children in Denmark diagnosed with Autism Spectrum Disorder (ASD) or mental retardation (MR) registered. From this registers is it possible to get information about the children in the cohort with ASD or MR.

The plan is to compare the information from the interviews in tree different groups, namely the ASD group, the MR group and a control group of normal children. This will provide us with knowledge about the characteristics of children with autistic disorders before the age of two years.

Plan: The project starts in august 2006 and will be finished by the end of 2008. We have the necessary
permissions to obtain data for the project. The study will comprise from collaborations with two European Union member countries, where comparable studies are setup. Sponsor: The Danish Medical Research Council, Beatrice Surovell Haskell Foundation.

**PS2.47**

**EARLY DETECTION OF PERVERSIVE DEVELOPMENTAL DISORDERS USING A MODIFIED CHECKLIST FOR TODDLERS WITH AUTISM (M-CHAT) AT 18 MONTH CHECK-UP: A PRELIMINARY STUDY IN JAPAN**

**Naoko Inada, Kanako Takeshita, Yoko Kamio, Khushu University**

Background: Although the need for early detection of Pervasive Developmental Disorders (PDDs) has been widely recognized, it remains difficult to identify children with PDD without developmental delay at 18 months of age.

Objectives: The present study examined (1) whether the M-CHAT, a parent-administered 23 items questionnaire is useful for children at 18 months of age similarly as for children at 24 months of age, (2) whether the M-CHAT is applicable to Japanese parents whose childrearing culture may be different from western culture.

Methods: 659 children who visited 18-month health check-up were screened using the Japanese version of the M-CHAT together with a telephone follow-up one month later. Screen-positive children were evaluated at 2 years of age using DSM-c-TR, CARS-TV, the Tanaka-Binet Intelligence scale, the Enjoji’s Analytical Developmental Test.

Results: Among 15 children who received developmental evaluations, 11 were diagnosed as PDD and 4 were found to be non-PDD, resulting in a positive predictive power of 73.3%. 3 of 11 PDD children and all non-PDD children had within-average IQ. The items differentiating PDD children from the others covered varied behaviors: social interests, imitation, pretend play, joint attention, social reference and symbolic functions.

Conclusions: Preliminary findings of this study suggest that the M-CHAT is a promising screening tool for early detection of PDD in Japan.

Sponsor: RISTEX (Research Institute of Science and Technology for Society) (250 words)

**PS2.48**

**INFANT SIBLINGS OF CHILDREN WITH ASD DEMONSTRATE LESS EFFECTIVE WORKING MEMORY FOR SOCIAL STIMULI**

**Julia S Noland, Wendy L Stone, Tedra Walden, Elisabeth H Sheridan, J. Steven Reznick, Vanderbilt Kennedy Center, Vanderbilt University**

Background: Later born siblings of children with ASD have autism, and there is need for earlier (< 1 year) behavioral markers of risk. Reduced working memory and social awareness has been demonstrated at school-age by children with Autism and their older siblings without Autism.

Objectives: Compare infant siblings of children with ASD (sib-ASD) and without ASD (sib-TD) on a looking-

response assessment of working memory for social and non-social stimuli.

Methods: Sib-ASD and sib-TD infants (mean 7.5 months, range 6-9.5 months) were recruited in pairs (n=15) matched for gender and age. The delayed response task (a modified peek-a-boo game) was administered and coded for risk group. The target type was counterbalanced for blocks of social (experimenter) and non-social (toy) stimuli. Out of three possible locations, first looks to the location where the target had most recently disappeared were coded as correct.

Results: Sib-ASD infants had a significantly higher proportion of correct looks during the non-social trial block [sib-ASD, m=.53 (SD=.2) vs. sib-TD, m=.39 (SD=.18)]. The opposite was found with the block of social stimuli [sib-ASD, m=.37 (SD=.22) vs. sib-TD, m=.52 (SD=.25)].

Discussion: Sib-ASD infants are less successful in keeping track of the location of people but more successful in keeping track of the location of objects. Data collection is ongoing.

Sponsors: NAAR, NICHD

**PS2.49**

**AN UPDATE ON THE MODIFIED CHECKLIST FOR AUTISM IN TODDLERS (M-CHAT) SIBLING STUDY**


Research indicates that younger siblings of children with autism are at higher risk for the development of autism and other developmental disorders (Silverman, 2001.) While this higher rate of recurrence provides an opportunity to study the emergence of autism prospectively, it is not known whether siblings are representative of the larger autism population. The current study used the M-CHAT (Robins, et.al, 2001), a parent-report checklist, to detect Autism Spectrum Disorders in 16-30 month old younger siblings of ASD diagnosed children. Currently, 161 children have been screened (mean age = 19.5 months), of which 75 younger siblings failed the screening and 86 passed, resulting in an initial fail rate of 46.6%. 62 of the 75 children that failed the initial screen, also failed the telephone interview follow-up, and qualified for a developmental evaluation (mean age 22 months). 43 siblings have been diagnosed with ASD, 11 with language and other development delays, and 8 were found to be typically developing. These diagnoses suggest a positive predictive power of 69% for the MCHAT and a recurrence rate of 27% in our sample. With regards to severity of autism, our ASD sibling sample was similar to our general ASD sample. However, our ASD sibling sample was higher functioning than our general ASD sample in adaptive skills (Vineland daily living skills and socialization) and cognitive development (Mullen visual reception, fine motor, and expressive language.) These data will be presented in detail and
suggest that either autism in multiplex families is different from autism in singleton families, or that higher suspicion in parents of siblings results in diagnosis of more mildly affected children.

**PS2.50**

**MEASURING SOCIAL AND COMMUNICATIONAL BEHAVIORS IN TODDLERS AT RISK FOR AUTISM SPECTRUM DISORDERS**

Jennifer Richler, Rebecca Niehus, Catherine Lord, University of Michigan

**Background:** Researchers are beginning to focus on identifying early indicators of Autism Spectrum Disorders (ASD).

**Objective:** Measure social and communicative behaviors in toddlers at risk for ASD.

**Methods:** Participants undergo a battery of assessments, including a new module of the Autism Diagnostic Observation Schedule (ADOS) currently being piloted for use with very young children. Participants range from 6 months to 36 months upon entry into the study and are generally assessed every month or every 6 months subsequent to their initial evaluation.

**Results:** Data are available for 48 children (14 autism, 15 PDD-NOS, 14 non-spectrum developmental disorder, 5 typically developing; mean age at entry = 20.7 months). Because some children have been assessed repeatedly, data are available for 146 assessments. Preliminary analyses indicate that score distributions on many social-communicative items on the new module of the ADOS vary substantially with diagnosis. For some items, substantial differences exist between the autism and PDD-NOS and non-spectrum DD and TD groups. However, negligible group differences exist for some behaviors, particularly ones involving emotion regulation.

**Conclusions:** It is possible to detect early indicators of ASD in toddlers at risk for the disorder. Certain behaviors may distinguish children with autism from those with PDD-NOS and therefore may be predictive of autism severity.

**Sponsors:** Department of Education, NIMH

**PS2.51**

**PARENT REPORT OF GESTURES AT 12 MONTHS PREDICTS LANGUAGE AND DIAGNOSTIC STATUS OF INFANT SIBINGS OF CHILDREN WITH AUTISM AT 18 MONTHS**

Agata Rozga, Marian Sigman, Sally Rogers, Sally Ozonoff, University of California, Los Angeles

**Background:** Previous studies have documented a specific deficit in the use of nonverbal communicative behaviors among children with autism, and a link between the use of gestures and subsequent language development in this population.

**Objectives:** To examine the predictive relationship between parent-report of the child's use of gestures at 12 months of age, and language abilities and diagnostic status at 18 months in a group of toddlers at risk of autism.

**Methods:** 47 toddlers with an older sibling with autism were assessed at 18 months using the Mullen and the ADOS-G. Parent report of the child's use of early gestures was collected at 12 months using the MacArthur Communication Development Inventory (total number of items endorsed under "First Communicative Gestures").

**Results:** Significant correlations were obtained between parent report of gestures at 12 months and expressive language \((r = .37, p = .01)\) and receptive language \((r = .43, p = .003)\) at 18 months of age. Children who met criteria for autism/autism spectrum on the ADOS at 18 months \((n=13)\) used significantly fewer gestures, \(t(45) = -2.28, p = .028\), and exhibited lower receptive, \(t(45) = -2.28, p = .027\), and expressive, \(t(45) = -2.52, p = .015\), language abilities at 12 months compared to unaffected children.

**Conclusions:** Our findings suggest that early emerging deficits in the use of gestures along with language delays may be prospective indicators of autism.

**Funding:** STAART Center Grant MH068172

**PS2.52**

**AUTISM SPECTRUM DISORDER, DIAGNOSTIC DISAGREEMENT IN A DEVELOPMENTAL PERSPECTIVE**

Synnve Schjolberg, Sissel Berge Helveschou, Norwegian Institute of Public Health

Considerably attention has been devoted to developing standardized methods for diagnosing autism. Research instruments such as ADI-R and ADOS-G have contributed to our knowledge regarding behavioral characteristics in preschool children. Both tools are considered as gold standard in diagnosing autism. However, in specific instances the instruments are over or under diagnosing autism and for these reasons it is established that using clinical diagnosis takes precedence in cases of disagreement. However little research has explored the characteristics of children for whom there are diagnostic disagreement, either between clinicians or between different diagnostic measures of autism. There is still little information about inter-rater reliability for diagnosing autism in young children.

Forty-seven children (33 M:14 F) were recruited through the healthcare services in Oslo County. None had a diagnosis at the time of their assessment. 76.6% were first met at the primary health care level and had not been evaluated by specialists earlier. The mean chronological age for the total sample was 27.0 months \((sd=6.2)\), and the mean mental age \((MA)\) was 13.2 months \((sd=3.4)\). Data were collected during the children's evaluations and two clinicians made independent clinical diagnostic judgments of the children. The other clinician observed the administration of the ADOS and rated each child according to a checklist based on the DSM-IV criteria for Autism as well as scoring presence/absence of behaviors. The clinicians agreed in 88% of the children whether the child was within or outside the autism spectrum. The Corrected Kappa for expected value was 0.83 of 0.85 maximum possible. When comparing children within the autism spectrum, the clinicians agreed in 79.1% of the children concerning subgroups in the spectrum. The Corrected Kappa for expected value was 0.53 of maximum possible 0.89. The children with diagnostic
disagreement had specific characteristics.

**PS2.53**

VARIABILITY IN OUTCOME FOR CHILDREN DIAGNOSED WITH ASD AT AGE 2

Lauren M Turner, Wendy L Stone, University of North Carolina

Background: Few studies have examined the outcomes of children with ASD diagnosed at age 2. Additional research is needed to understand the children whose symptoms change over time.

Objectives: Objectives were to examine the behavioral outcomes of a carefully defined sample of 2-year-old children with ASD, and to identify child and environmental factors that contribute to variability in outcomes at age 4.

Methods: Forty-eight children diagnosed with autism or PDDNOS at age 2 were followed to age 4. Diagnostic measures included the ADOS-G, clinical diagnosis, and the CARS at ages 2 and 4, and the ADI-R at age 4.

Cognitive testing with the MSEL was performed at 2 and 4.

Results and Conclusions: Results replicated previous research revealing high agreement among diagnostic measures at ages 2 and 4. Diagnostic stability for an autism spectrum diagnosis (autism or PDDNOS) was 65%, and for an autism diagnosis was 71%, which is lower than previous estimates. Children whose diagnosis changed were more likely to: 1) be 30 months or younger at initial evaluation; 2) have milder symptoms of autism, particularly in the social domain; and 3) have higher cognitive scores at age 2. No differences between children who did and did not change diagnosis were found for amount of intervention services received. Implications and possible explanations for these findings will be discussed.

Sponsor: DOE Grant# H324C990039

**PS2.54**

COMPARISON OF A GENERAL DEVELOPMENTAL SCREENING TOOL AND AN AUTISM SPECIFIC SCREENING TOOL IN ASD ASSESSMENT

Lisa Young, Jennifer Pinto Martin, Anna Warszawa, Ellen Giarelli, Susan Levy, and the PACCADDRE team, University of Pennsylvania, School of Nursing, PA-Center of Autism and Developmental Disabilities Research and Epidemiology

Background: Concern regarding identifying Autistic Spectrum Disorders (ASD) at a young age has been on the rise. There is much discussion in the literature regarding best practices for screening and early identification. Some argue that at a young age, a general developmental screening tool is appropriate and as effective as an ASD specific tool.

Objective: Determine the utility of using a general developmental screening tool compared to an autism specific tool when screening for ASD.

Methods: An ongoing study to improve DD/ASD screening practices in a pediatric primary care center is currently underway. Data has been collected on a general developmental screening tool, the Parent Evaluation of Developmental Stages (PEDS) and on an autism-specific screening tool, the Modified Checklist for Autism in Toddlers (M-CHAT). Assessments are complete for 66 children (55% male, mean age 23 months, 41% African American, 30% Caucasian, 15% Biracial, 14% Asian). The sensitivity, specificity, and positive predictive value of the PEDS compared to the M-CHAT in screening for ASD were computed. While the sensitivity of the PEDS compared to the M-CHAT was 77.8%, the specificity was only 26.3% and the positive predictive value was just 14.3%.

Results: Preliminary analysis indicated that the PEDS is not a good substitute for the M-CHAT when screening for ASD in a general pediatric practice.

Conclusions: Specific red flag items for autism which are included on ASD screening tools are unique to these assessments and are not found in a general developmental screening tool.

Sponsor: Centers for Disease Control and Prevention

**PS2.55**

COMPARATIVE STUDY OF EARLY COMMUNICATION DEVELOPMENT IN YOUNG AUTISTIC AND MENTALLY RETARDED CHILDREN

Sonia De Martino, Marine Viellard, Anne-Marie Girardot, David Da Fonseca, Véronique Rey, François Poinso, Hôpital Sainte Margueritte

Background: Comparison of early communication development in young autistic and mentally retarded children.

Objectives: Observe a typical distortion of development of early communication skills in autistic children. Methods: 19 autistic children with mental retardation and 11 mentally retarded children were matched on developmental and chronological ages. Patients were recruited from « Centre de Ressources Autisme » of Child Psychiatric Unit of Hospital Ste Margueritte in Marseilles (France). Children’s parents were assessed with the ADI, resulting in a confirmed diagnosis of Autism. The developmental age was established with the PEP-R. The early communication skills were assessed with the Guidetti-Tourette scales (French adaptation of the Seibert-Hogan scales) which evaluate the levels of development of social interaction, of joint attention and of regulation activity.

Results: Preliminary analyses indicate significative between-group differences in the development of social interaction and joint attention. No difference was noted on regulation activity. However, the results exhibit the same communication profiles in social interaction and joint attention in young autistic children and mentally retarded children. These results confirm a more important deficit in early communication development in autistic children compared to mentally retarded children but also indicate the early communication development profile in ‘low-level’ autistic children is not so atypical.

Conclusion: Preliminary findings support the hypothesis of ‘slowing’ of early communication development in ‘low-level’ autistic children.

Sponsor: * Hôpital Ste Margueritte, Marseille, 13009,
PS2.56
EVALUATING COSMOBOT’S EFFICACY AS A TREATMENT APPROACH FOR CHILDREN WITH AUTISM SPECTRUM DISORDER (ASD)
Amy J Brishen, Carole Samango-Sprouse, Charlotte J Safos, Corinna E Lathan, AnthroTronix, Inc.
Background: CosmoBot(TM) is a robot developed as a treatment approach for children with disabilities -- children interact with the CosmoBot robot through body-movement, voice, joysticks or buttons. CosmoBot combines toy appeal with computer versatility, allowing for programmable tasks that are therapeutic and interactive. CosmoBot facilitates non-intrusive, direct clinician interaction with children with Autism Spectrum Disorder (ASD).
Objectives: To evaluate the engagement with CosmoBot and participation in structured tasks for children with ASD.
Methods: Patients were recruited from Dr. Samango-Sprouse’s practice, receiving early intervention services in various configurations. Diagnosis was confirmed using the Social Communication Questionnaire and DSM-IV criteria. CosmoBot was introduced to children in the familiar clinical setting in order to optimize their comfort level. Children interacted with CosmoBot in an unstructured manner for 15 minutes. Structured tasks were introduced: joint attention followed by motor commands and verbal imitation. Data were collected on 3 children--two boys, one girl--with ASD (mean age=3.7, range 3-7 years).
Results: All children engaged spontaneously with CosmoBot without any difficulty. All children followed 3 out of 5 motor commands but were more successful with the large motor movements in imitation than the smaller movements. Verbal imitation could not be elicited. Joint attention was variable and inconsistent. All children were attentive, engaging with CosmoBot for more than 15 minutes with pretend, interactive play.
Conclusion: CosmoBot has excellent potential as a therapeutic tool for children with ASD. Findings suggest that motor planning skills could be enhanced using CosmoBot. CosmoBot offers a distinctive prospect for children with ASD to promote neurodevelopmental progress and increase understanding of the relationship between brain and behavior.
Sponsor: CAN ITA Bridge Grant

PS2.57
THE RELATIONSHIP BETWEEN SENSORY REACTIVITY AND OTHER AREAS OF FUNCTIONING IN YOUNG CHILDREN WITH AUTISTIC SPECTRUM DISORDERS
Emma L Esser, Hilary C Boorstein, Leandra Wilson, Jamie Kleinman, Juhi Pandey, Michael Rosenthal, Saasha Sutera, Pamela Ventola, Alyssa Verbalis, Marianne Barton, Thye Dumont-Mathieu, James Green, Sarah Hodgson, Gail Marshia, Deborah Fein, University of Connecticut
Background: Children with autistic spectrum disorders (ASD) often exhibit unusual responses to sensory stimuli, but it is not clear how these responses are related to other areas of functioning.
Objective: To examine the relationship between sensory reactivity and cognitive functioning, adaptive functioning, and autism symptomatology in young children with ASDs.
Methods: Participants were 69 children (18 to 36 months old) who failed the Modified Checklist for Autism in Toddlers (M-CHAT; Robins et al., 2001) and were diagnosed with an ASD with ADOS, ADI, and clinician judgment. Instruments administered included the Vineland Adaptive Behavior Scales, Mullen Scales of Early Learning, and Childhood Autism Rating Scale (CARS), as a measure of symptom severity. Clinicians also completed a DSM-IV-TR checklist of symptoms. Parents completed the Sensory Profile (Dunn, 1999) and 45 additional sensory questions more specific to ASD (Liss, Saulnier, & Fein, 1999) that required parents to rate the frequency of sensory behaviors and reactions. Mean summary scores were calculated based on three factors: overreactivity, underreactivity, and sensory-seeking.
Results: Statistical analysis revealed significant correlations between sensory-seeking behaviors and poor adaptive functioning, sensory-seeking behaviors and increased autism severity, underreactivity and increased number of symptoms, underreactivity and increased symptom severity, overreactivity and increased symptom severity, and overreactivity and poor adaptive functioning. Cognitive functioning was not related to sensory behaviors. Data on behaviors most pathognomonic of ASD will be presented.
Conclusion: Sensory reactivity appears to be related to symptom severity but is not related to cognitive functioning in young children with ASD.
Sponsors: NIH and MCH

PS2.58
RESTRICTED ACTIVITIES AND EXPERIENCES IN PRESCHOOLERS WITH AUTISM SPECTRUM DISORDERS
Tia N. Holtzclaw, Kristen S.L. Lam, Lauren M. Turner, James W. Bodfish, UNC-Chapel Hill
In addition to abnormal repetitive behaviors such as stereotyped movements and ritualistic behaviors, children with autism may also display a restricted repertoire of adaptive activities. Restricted activities could conceivably lead to experiential deprivation and contribute to atypical experience-dependent brain and behavioral development in autism. The primary objective of this study was to compare young children with autism spectrum disorders (ASD) to young children with typical development (TYP) on measures of home / community activities and measures of autistic symptoms. Data was collected from 132 children, aged between 2-5 years (60 AUT, 72 TYP). Measures included the Social Communication Questionnaire (SCQ), the Repetitive Behavior Scale-Revised (RBS-R), and the Home and Community...
Activities Scale (HCAS). Results indicated that relative to typically developing children, children with autism participated in significantly fewer home and community activities, and significantly more isolated/alone activities. In the ASD group, restricted activity was significantly associated with the severity of their social deficits and not with their language or repetitive behavior deficits. Factor analysis of the HCAS resulted in discrete activity context factors that could be used to identify the specific contexts where children with autism are most restricted. These HCAS factors may be useful as a general guide for naturalistic interventions designed to boost experience-dependent behavioral development.

Supported by: RO1-MH73402-02; T32-HD40127

**PS2.59**

**A DEVELOPMENTAL STUDY OF SELF-REGULATION IN CHILDREN WITH AUTISM**

Asuka Maeda, Graduate School of Social Science, Ritsumeikan University

Background: Recent studies suggest children with autism have difficulty in self-regulation. There is concern about how their self-regulation developed during preschool years. Are there any differences in developmental processes between typical children and children with autism?

Objectives: This study examined the development of self-regulation in K (CA=5;2, DA=about 3 years old) and N (CA=8;9, DA=about 8 years old) who were confirmed diagnosis of Autistic Disorder and Asperger Disorder. They were recruited from the Ritsumeikan Counseling Center.

Methods: Refer from Luria’s theory (1961), go task and go/no-go task were administered to the participants. The experiment was controlled by a computer which could measure reaction time and error score, and measure of another their behavior during the experiment were collected from videotapes. Their self-regulation was analyzed in line with data on 69 typical developmental children (CA=2;9 to 6;1) which author had collected, and located in 3 levels of the self-regulation (Luria, 1961).

Results: K seemed to be at level 0 of the self-regulation, because he was hard to synchronize with stimulus and pushed the switch independently. N seemed to be at level 3, because he could direct their response either initiate or inhibit to different signals using private speech at times. Their levels of self-regulation matched with their developmental stages.

Conclusion: These results suggest that, at least on these tasks, self-regulation in children with autism would follow the same developmental process as typical developmental children, and sometimes would be disturbed by scattering of their attention.

Sponsor: science frontier project (2000-2004), open research center project (2005-); ministry of education, culture, sports, science and technology

**PS2.60**

**MATERNAL INTERACTION STYLE AND EARLY SOCIAL-COMMUNICATIVE ABILITIES IN CHILDREN WITH AUTISM SPECTRUM DISORDER**

Mieke Meirsschaert, Petra Warreyn, Mieke Dereu, Herbert Roeyers, Ghent University, Department of Experimental Clinical and Health Psychology, Research Group Developmental Disorders

Background: Later language and social-cognitive development of children with autism spectrum disorder (ASD) may be affected by their typical delay in social-communicative abilities, as well as by the caregivers’ interaction style.

Objectives: To investigate maternal interaction style, imitation and declarative joint attention in preschoolers with ASD and a group of children without signs of ASD.

Methods: For this study we recruited two groups of 19 children. The clinical group consisted of children with autism or PDD-NOS. They were matched on chronological age, IQ and language abilities with a control group. First, an ADOS-G and intelligence test were administered and the maternal interaction style was observed.

Second, imitation, joint attention, symbolic play, perspective taking and language abilities were tested.

Results: As expected, children with ASD experienced significantly more problems in symbolic and procedural imitation. Furthermore, children with ASD performed more poorly on tasks elicitating declarative joint attention. Regarding directing attention and behaviour, mothers of children with ASD were rated higher than mothers of control children, suggesting that mothers of children with ASD seem to adapt their interaction style to the special needs of their children.

Conclusions: The present study stresses the need for further exploration of the early social communication and interaction between a child with ASD and his or her mother.

Sponsor: Ghent University Research Fund

**PS2.61**

**POSITIVE AFFECT SHARING ACROSS SOCIAL-COMMUNICATIVE CONTEXTS**

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Background: Previous research has revealed that children with autism have deficits in their ability to make eye contact and share affect with others. However, these abilities may improve in certain structured social contexts.

Objectives: To examine the impact of social-communicative context on the frequency of eye contact and shared positive affect in children with autism compared to those with typical development.

Methods: Videotapes of the Screening Tool for Autism in Two-Year-Olds (STAT) were coded for 48 two- and three-year olds with ASD (mean CA=32.5 months, mean MA=17.7 months) and 48 children with typical development (TD) matched on MA (mean CA=16.7 months, mean MA=16.7 months). Frequency of eye contact and shared positive affect were coded for STAT items that varied in the level of adult-provided structure (high vs. low) and the social-communicative context (joint attention vs. requesting).
Results: The ASD group displayed the target behaviors less frequently than the TD group in all contexts except one; shared positive affect did not differ between groups during highly structured requesting items. Both groups shared more positive affect while engaged in joint attention than requesting, and used more eye contact and affect during the high structure (vs. low structure) joint attention contexts.

Conclusion: Young children with autism show increased eye contact and shared positive affect within more highly structured social situations.

Sponsor: NICHD Grant# T32 HD07226.

PS2.62
REGRESSION IN AUTISTIC DISORDER: PARENT PERCEPTION AND CLINICAL ASSESSMENT
Raun D Melmed, Sharman E Ober-Reynolds, Susan M Stephens, R Curt Bay, Janet E Kirwan, Josh J Jones, Theresa A Grebe, Southwest Autism Research and Resource Center

Context: Autistic Disorder (AD) is a complex developmental disability that typically appears during the first three years of life. Approximately 66% of children with AD develop symptoms during the first year of life and about a third of children appear to develop normally or near normally until the beginning of the second year of life. This is followed by a loss of verbal and non-verbal communication skills.

Objective: In this study we compared the identification of regression as reported by parents to that elicited during the course of a structured interview. Design: Parents of 114 children with AD confirmed by DSM-IV criteria and the ADOS and ADI-R completed the SARRC questionnaire regarding regression in their children. Regression was also ascertained through a structured clinical interview, the ADI-R.

Results: 30/114 reported the loss of a skill on the ADI-R (26.3%), while 73/114 (64%) reported the loss of a skill on the SARRC questionnaire (p<0.001).

Discussion: A statistically significant difference between parent reporting of regression and the number of children with regression evident on the ADI-R was obtained. Possible reasons for this discrepancy include parent perceptions being influenced by current popular theories, rigidity of the ADI-R scales for elicitation of this particular clinical finding or the way the questions were phrased. Objective tools are needed to delineate the precise nature of behavior prior to regression along with details of the regressive period itself.

PS2.63
PREDICTORS OF OPTIMAL OUTCOME IN TODDLERS DIAGNOSED WITH AN AUTISM SPECTRUM DISORDER

Background: It is important to gain a better understanding of what may predict various developmental trajectories of children with an ASD.

Objective: To determine which characteristics of children diagnosed with an autism spectrum disorder (ASD) at age 2 differentiate toddlers who retain the diagnosis at age 4 from those who do not.

Method: 101 children were evaluated after failing the Modified Checklist for Autism (M-CHAT: Robins, et al, 2001) at age 2 and re-evaluated at age 4. Of these, 74 were diagnosed with an ASD (using the ADOS and ADI) at their initial evaluation. At reevaluation, 12 of these 74 children no longer met criteria for ASD. Cognitive and adaptive skills were assessed at age 2 using the Bayley Scales or the Mullen Scales, and the Vineland Adaptive Behavior Scales. The Childhood Autism Rating Scale (CARS) was used as a measure of symptom severity.

Results: There were no differences between the outcome groups in symptom severity at age 2. The group of children who no longer met criteria for ASD at age 4 had higher Vineland Motor and Adaptive Behavior Composite scores and several trends toward higher cognitive scores at age 2.

Conclusion: Findings suggest that children who experience optimal outcome are difficult to differentiate at 2 years of age from children who will remain on the spectrum, with the exception of better motor development. Cognitive and symptom severity scores showed minimal differences. This lack of group differences at age 2 underscores the necessity of providing excellent intervention for all children, since it appears difficult to predict with any certainty which children will best be able to profit from the intervention.

Sponsors: NIH and MCH

PS2.64
THE POLYVAGAL THEORY: A NEW APPROACH TO AUTISM RESEARCH
Stephen W. Porges, Olga V. Bazhenova, J.W. Denver, E. Bal, K. Heilman, University of Illinois at Chicago

Background: The evolution of the autonomic nervous system provides an organizing principle to interpret the deficits in social engagement behaviors observed in individuals diagnosed with autism.

Objectives: Two intervention protocols, based on the Polyvagal Theory, were designed to recruit the anti-masking effects of the middle ear muscles and to stimulate social engagement behaviors.

Methods: In Experiment I, the intervention was delivered to young ASD children and consisted of vocal music computer altered to exercise the processing of voice. Behavior was measured by parent report and videotape. In Experiment II, laboratory measures of auditory processing, eye gaze, and cardiac vagal tone were measured prior to and following a protocol in which acoustic stimuli (i.e., music, stories) were lateralized. The intervention was delivered to verbal ASD adolescent participants.

Results: In Experiment I, the intervention improved listening, eye contact, and sharing behaviors. The effect occurred only in participants for whom the intervention
reduced auditory hypersensitivities. In Experiment II, the intervention had immediate effects on virtually all participants by increasing cardiac vagal tone and eye gaze to the upper face and improving auditory processing. Immediately following intervention, several participants performed in the range of typically developing adolescents. A follow-up 6 months post intervention demonstrated that the effects were transient.

Conclusion: The research demonstrates that an intervention strategy designed to recruit the neural circuit mediating social engagement behaviors can effectively and efficiently be stimulated. The findings demonstrate an immediate, although transient, positive influence on social engagement behaviors in children and adolescents with autistic spectrum disorders.

Sponsor: Unicorn Children’s Foundation, Cure Autism Now Foundation, and Nancy Lurie Marks Family Foundation*

**PS2.65**

**SEX DIFFERENCES IN TODDLERS WITH AUTISM SPECTRUM DISORDERS**


Background: Few studies have examined sex differences in autism. Several studies have shown that females with autism have lower IQs and that males with autism are more likely to show visual fascinations, stereotypic play, and decreased social skills

Objective: To compare the behavioral presentation of male and female toddlers diagnosed with Autism Spectrum Disorder (ASD).

Methods: 127 male children (mean age = 27 months) and 30 female children (mean age = 26 months) were diagnosed with an ASD after failing the Modified Checklist for Autism in Toddlers (MCHAT; Robins et al., 2001). These participants were compared on the MCHAT items, cognitive and adaptive measures, and diagnostic measures.

Results: The male participants failed significantly more items on the MCHAT, and failed two items related to pretend play and pointing to express interest significantly more often then females. No significant sex differences were found in IQ or adaptive functioning. While there was no overall difference between the sexes on the autism diagnostic measures, the males had significantly more abnormal scores on the ADOS play domain and on individual items on the Childhood Autism Rating Scale (CARS) related to listening response and intellectual consistency. Finally, trends show an interaction between diagnosis and sex on several scores, suggesting that females with AD have more severe symptoms then males, but males with PDD-NOS have more severe symptoms then females.

Conclusion: The data shown here replicates in toddlers previous findings for older children that female children with autism are more socially developed and have more appropriate play skills, but found no IQ difference. It is possible that at this age there is not enough variability in IQ scores to see a significant sex difference. These sex differences may be representative of the biological sex differences in typical children and may modify the disorder in females.

Sponsors: NIH and MCH

**PS2.66**

**COMPARATIVE STUDY WITH OBJECT SUBSTITUTION PRETENCE BETWEEN TYPICAL DEVELOPMENT CHILDREN AND CHILDREN WITH AUTISM**

Inoue Yohei, Ritsumeikan University

Background: There is concern about the role of object substitution pretence, especially by which stereotyped behavior would be gradually reduced or not.

Objectives: Investigate relation between stereotyped play and object substitution pretence to indicate developmental function of pretence for children with autism.

Methods: Participants were recruited from the Ritsumeikan Counseling Center. They were confirmed diagnosis of Autistic Disorder/ Asperger Disorder. Because of main complaint, obsession and localization of interest, they started to join interventional play program once a week based on constructive developmental theory.

Developmental stage was assessed with the use of Kyoto Scale of Psychological Development and others. An object substitution pretence task (Tomasello, M. et al, 1999), which asks children to choose an object represented by object substitution pretence, was used to identify level of understanding pretence.

Results: 101 typical development children was examined to grasp fundamental feature (CA=from 2; 6 to 5; 11). For example, in object substitution pretence task, two children with autism who are males (one child is CA=5; 2, DA=3 years old level and another child is CA=8; 9, DA=8 years old level) tend to be influenced by not reality but appearance depending on each developmental stage, and a repetitive play was modified through intervention if children understand object substitution pretence.

Conclusion: This study would indicate that repetitive play, which looks like stereotyped behavior, could be modified with acquisition of object substitution pretence.

Sponsor: Science frontier project (2000-2004), Open research center project (2005-); Ministry of education, culture, sports, science and technology

**THE ROLE OF STRESS TOLERANCE IN THE ETIOLOGY AND TREATMENT OF AUTISM**

Philip Roman Zelazo, Cheryl-Lynn Rogers, Caroline Reid, McGill University and Montreal Autism Centre

Background: Applied Behavior Analysis (ABA) approaches to the treatment of autism Spectrum Disorders (ASD) produce improvement in a number of domains of development (cf. S.J. Rogers, 1998) but, lack a precise developmental focus and offer little insight into the etiology of ASD. Developmental psychopathology offers a partial corrective. Our developmental-behavioral intervention (Zelazo, Kearsley, & Ungerer, 1984/2005) shapes compliance to task demands to encourage the
development of stress tolerance. Non-compliance to task demands and active avoidance (e.g., tantrums) arrest development pervasively, and preclude the development of stress tolerance and emotion regulation.

Objectives: Establish low stress tolerance in children with ASD and shape compliance to task demands and stress tolerance to facilitate development.

Methods: (1) Thirteen children with ASD (34 to 52 months), given 8 months of training and tested with easy, moderate, and difficult tasks, were compared with 32 typically developing children. (2) Two additional studies with 44 children (22 or 32 months) receiving 10 months of treatment and 36 children (22, 32, 36, or 42 months) receiving 24 months of treatment, examined domains of improved development.

Results: (1) Children with ASD showed less compliance and attention to moderate and difficult tasks relative to controls. (2) Developmental-behavioral intervention produced improvement across multiple areas including functional and symbolic play, expressive language, sustained attention, appropriate social behaviors, and conventional intelligence test scores.

Conclusion: These data support the role of stress tolerance to task demands as a core factor in the etiology and treatment of ASD and the effectiveness of intensive early intervention.

Sponsor: FQRSC*
Oral Session #4
Structural neuroimaging

Chair: Declan Murphy

Speakers:
Sarah Durston, Saskia JMC Palmen, Hilde Nederveen, Herman van Engeland, Rudolf Magnus Institute of Neuroscience, Dept. of Child and Adolescent Psychiatry, UMC Utrecht
Timothy A Keller, Rajesh K Kana, Nancy J Minshew, Marcel Adam Just, Carnegie Mellon University
Mitchel T Williams, Thomas J Eluvathingal, Michael E Behen, Diane C Chugani, Harry T Chugani, Departments of Pediatrics, Neurology and Radiology, Children's Hospital of Michigan, Wayne State University
Antonio Y Hardan, Rahul Bansal, Jeff Nutche, Matcheri S Keshavan, Nancy J Minshew, University of Pittsburgh

ABSTRACTS

NO EVIDENCE FOR PREFERENTIAL INVOLVEMENT OF MEDIAL TEMPORAL LOBE STRUCTURES IN HIGH-FUNCTIONING AUTISM
Sarah Durston, Saskia JMC Palmen, Hilde Nederveen, Herman van Engeland, Rudolf Magnus Institute of Neuroscience, Dept. of Child and Adolescent Psychiatry, UMC Utrecht

BACKGROUND: Autism is associated with slight increases in brain volume. There has been some suggestion that medial temporal lobe structures may be preferentially involved in this disorder, although results have not always been consistent. OBJECTIVE: Therefore, we investigated amygdala and hippocampus volumes in 42 high-functioning, medication-naive children and adolescents meeting DSM-IV criteria for autism or Asperger's syndrome and in 42 typically developing individuals matched for age, gender, IQ, height, weight, handedness, and parental education. Age ranged from 7 to 25 years. METHOD: Whole-brain MRI scans were acquired from all subjects. Medial temporal lobe structures were traced manually by a single experienced rater (HN), blind to subject identity. Measures of whole-brain and intracranial volume were also acquired. Intrarater reliability was assessed using intraclass correlation co-efficients and was 0.83 for left amygdala, 0.84 for right amygdala, 0.86 for left hippocampus and 0.91 for right hippocampus. RESULTS: Amygdala volume did not differ significantly between patients and controls (2.82 ± 0.56 for autistic subjects; 2.82 ± 0.50 for controls). Mean hippocampal volume was 6.87 (± 0.93) for the autistic subjects and 6.46 (± 0.75) for the control subjects (t= 2.21, p= 0.03). The increase in hippocampal volume was proportional to the increase in whole-brain volume and no longer significant after controlling for intracranial volume. CONCLUSIONS: These results argue against preferential involvement of medial temporal lobe structures in autism, at least in high-functioning medication-naive individuals.

REDUCED FRACTIONAL ANISOTROPY IN HIGH FUNCTIONING ADULTS WITH AUTISM LOCALIZES TO MEANINGFUL REGIONS OF WHITE MATTER
Timothy A Keller, Rajesh K Kana, Nancy J Minshew, Marcel Adam Just, Carnegie Mellon University

Background: Diffusion tensor imaging (DTI) allows in vivo quantification of the structural integrity of white matter. A previous study (Barnea-Goraly et al, 2004) has reported widespread reductions in fractional anisotropy (FA), a measure of the coherence of fiber orientation derived from DTI data, in children with autism. Objectives: Compare FA between high functioning adults with autism and normal controls. Method: Diffusion data were acquired for 20 high functioning adults with autism and 21 age- and IQ-matched control adults. Diffusion data were reduced to FA maps for each participant. These FA maps were spatially transformed to a standard space and voxelwise t-tests of the difference
between groups were conducted on the normalized FA data. Results: Control participants had higher FA values than participants with autism in an area the left corona radiata near the genu of the corpus callosum, in bilateral areas near the splenium of the corpus callosum, in two areas of left frontal white matter near Broca’s area (one in the unicate fasiculus and one in the anterior corona radiata), in posterior bilateral areas of the inferior fronto-occipital fasiculus, and in bilateral parietal areas of the superior longitudinal fasiculus. There were no areas where participants with autism had higher FA values than controls. Conclusions: White matter abnormalities in individuals with autism persist in adulthood, with a number of areas showing decreased coherence of fiber orientation. The locations of these abnormalities are consistent with a role cognitive and social deficits and with patterns of decreased functional connectivity reported in fMRI studies. Funding: This study was supported by an NICHD/NIDCD Collaborative Program of Excellence in Autism.

**ABNORMAL ASYMMETRY IN THE ARCUATE FASCICULUS OF AUTISTIC CHILDREN: A DTI STUDY**

*Mitchel T Williams, Thomas J Eluvathingal, Michael E Behen, Diane C Chugani, Harry T Chugani, Departments of Pediatrics, Neurology and Radiology, Children's Hospital of Michigan, Wayne State University*

**Background:** Although communication disorder is present in autism, disturbances in the connectivity of language pathways remain poorly understood.

**Objectives:** The arcuate fasciculus, a white matter pathway connecting language cortices, was assessed in autistic and typically developing children using diffusion tensor imaging (DTI).

**Methods:** Nineteen autistic children (14 boys, 5 girls; mean age 4.65+ 2.14; range = 2.16 to 8.75 years) and 15 control subjects (10 boys, 5 girls; mean age 4.62 + 2.44; range 1.84 to 10 years) underwent MRI with DTI at 3T. Fiber number, apparent diffusion coefficient (ADC), and fractional anisotropy (FA) for the temporo-frontal and parieto-frontal segments of the arcuate fasciculus, as well as for the corticospinal tracts, were determined for both groups.

**Results:** For children less than 3.5 years, ADC values were significantly higher for the autistic children compared to control children in the arcuate fasciculus. Both the temporo-parietal arcuate fasciculus and the corticospinal tract in the autistic group showed a significant age-related decrease in asymmetry, while the controls displayed an increase favoring the left hemisphere.

**Conclusion:** Preliminary findings of this study indicate a possible age-dependent effect on white matter development suggesting that there may be early left hemisphere dysfunction related to language impairments seen in autism.

**CORTICAL THICKNESS IN AUTISM: A LONGITUDINAL MRI STUDY**

*Antonio Y Hardan, Rahul Bansal, Jeff Nutche, Matcheri S Keshavan, Nancy J Minshew, University of Pittsburgh*

**Background:** Increase in several brain structures including total brain volume have consistently been reported in autism. Increase in grey matter volume has also been described but it remains unclear whether this enlargement is related to an increase of cortical thickness, surface area or both.

**Objectives:** The goal of this investigation is to examine in a longitudinal design cortical abnormalities including cortical thickness in children with autism

**Method:** Total and lobar cortical grey matter cortical thickness were measured using MRI scans acquired from 18 male children with autism and 22 age- and gender-matched normal healthy controls. Measurements of sulcal and gyral thickness were also obtained. Nineteen individuals (9 with autism and 10 controls) had, to date, their imaging studies repeated 30 months after their baseline scans and measurements were also conducted on this sample.

**Results:** Increased total cerebral gyral and sulcal thickness were observed in children with autism when compared with controls. Similar findings were found in the temporal, and parietal lobes but not in the frontal and occipital. Results remained unchanged after controlling for total brain volume. At follow-up, preliminary analysis indicates an increase in cortical thickness in the autistic group when compared to controls, but without reaching statistical significance.

**Conclusions:** While the exact pathophysiology and developmental trajectory of increased brain size in autism remains unclear, preliminary evidence from this study indicate that increased cortical thickness may contribute to the increased grey matter volume and total brain size observed in children with autism and may also underlie anomalies in cortical connectivity.
Oral Session #5
Neurophysiology

Chair: Chantal Kemner

Speakers:
Christianne Bolduc, Élyse Limoges, Élyse Chevrier, Laurent Mottron, Roger Godbout, Centre de recherche Fernand-Seguin & Neurodevelopmental Disorders Program, Hôpital Rivière-des-Prairies, and Dept. Psychiatry, Université de Montréal
Clifford D Saron, David M Horton, Sharon Coffey-Corina, Susan M Rivera, UC Davis Center for Mind and Brain
Raphael Bernier, Geraldine Dawson, Michael Murias, Audrey Quinn, Sara Webb, University of Washington Autism Center
Tuulia Lepistö, Marika Kajander, Raija Vanhala, Paavo Alku, Minna Huotilainen, Risto Näätänen, Teija Kujala, Cognitive Brain Research Unit, Department of Psychology, University of Helsinki, Finland

ABSTRACTS

EEG ACTIVITY DURING REM SLEEP IN AUTISM: PRIMARY VS NON-PRIMARY VISUAL AREAS

Christianne Bolduc, Élyse Limoges, Élyse Chevrier, Laurent Mottron, Roger Godbout, Centre de recherche Fernand-Seguin & Neurodevelopmental Disorders Program, Hôpital Rivière-des-Prairies, and Dept. Psychiatry, Université de Montréal

Introduction: Neuropsychological, EEG and brain imaging studies point toward enhanced low-level visual perception in High Functioning Autism (HFA), not Asperger Syndrome (AS). We compared the distribution of fast EEG activity across primary and non-primary visual areas in HFA and AS participants during REM sleep, a state during which the visual system is activated endogenously.

Methods: 10 HFA (9M, 1F; 20.8 ± 3.7 years), 8 AS (8M; 23 ± 3.1 years) and 16 control (15M, 1F; 21 ± 4.3 years) participants were recorded for two consecutive nights. Spectral analysis of REM sleep fast ("Beta") EEG activity (13.0 to 19.75 Hz) was performed on primary (O1, O2) and non-primary (T5, T6) visual areas. Left and right relative spectral amplitude was calculated using the formula 

\[ \text{Relative Spectral Amplitude} = \left( \frac{\text{primary electrode}}{\text{non-primary electrode}} \times 100 \right) \]

Results: In the three groups, Beta activity was consistently greater over primary areas (O1 and O2) than secondary areas (T5, T6). HFA and AS groups displayed less absolute spectral Beta amplitude for O1 and O2 electrodes than controls but T5 and T6 were not different. HFA participants showed lower O1/T5 ratio compared to controls (p<.04) and AS participants (p<.04).

Conclusions: There is a decreased contrast between activation of left primary and secondary visual areas in HFA, suggesting that an atypical EEG distribution over visual areas in REM sleep occur only in HFA. Further study should investigate if this correlates with the visual performance.

Supported by CIHR

SENSORIMOTOR AND MULTISENSORY DEFICITS OF INTEGRATION: A BEHAVIORAL AND ERP INVESTIGATION OF CHILDREN WITH AUTISM SPECTRUM DISORDERS

Clifford D Saron, David M Horton, Sharon Coffey-Corina, Susan M Rivera, UC Davis Center for Mind and Brain

There is now good empirical and theoretical support for the idea that deficits in multisensory integration (MSI), the combination of various senses to form a single integrated experience of the world, are widespread in autism spectrum disorders (ASD). We have developed a trisensory stimulator that produces robust single sensory and multisensory responses within nearly the same perceptual binding domain. The current study examined MSI in children (9-12 yrs.) with autism.
spectrum disorder (ASD) and typically developing (TD) children through analysis of dense-channel array event related potentials (ERPs) elicited in response to visual, auditory, and somatosensory stimuli delivered alone or in simultaneous combination. The task was the detection of all stimulus events in a simple reaction time (RT) paradigm. Differences between multisensory and the summed responses of unisensory stimuli were used as a measure of MSI. Participants with ASD did not consistently show reaction time facilitation in excess of that predicted by probability summation. Furthermore, analog recording of reaction time responses revealed that motor output from the children with ASD was highly variable, a factor which may be an important feature of sensorimotor organization in ASD such that even simple manual responses to transient environmental events are poorly programmed and fail to become automatized. Electrophysiological results suggest that early (50-80 ms) inhibitory interactions between sensory systems are diminished in ASD individuals compared with TD controls, results convergent and consistent with the RT findings.


EEG CORRELATES OF MIRROR NEURON ACTIVITY AND IMITATION IMPAIRMENTS IN AUTISM Raphael Bernier, Geraldine Dawson, Michael Murias, Audrey Quinn, Sara Webb, University of Washington Autism Center

BACKGROUND: Imitation ability has consistently been shown to be impaired in individuals with autism and a deficit in self-other mapping ability has been proposed (Williams, et al, 2004). Mirror neurons provide a possible neurological mechanism for self-other mapping. The EEG mu rhythm is believed to reflect underlying mirror neuron activity.

OBJECTIVE: The goal of this study is to further investigate evidence of mirror neuron dysfunction by studying EEG mu rhythm during the observation, execution, and imitation of movements and examining its relation to behaviorally assessed imitation ability. METHODS: Fifteen adults with autism and fifteen age, gender, and IQ matched controls participated in an EEG experiment with five conditions: observation (watching a hand grasp a block of wood); execution (grasping on verbal instruction); imitation (imitating the grasp); control (watching a hand on the screen); and resting. They were also administered the Mature Imitation Task (Rogers, Cook, Greiss-Hess) in which participants imitated single and sequenced hand gestures and facial expressions, complex gestures, hand movements, and actions on objects.

RESULTS: On the Mature Imitation Task, the adults with autism demonstrated significantly poorer performance compared to the typical controls in overall imitation ability (p<.02), number of errors made (p<.01), and imitation of style (p<.02). On the EEG task, typical individuals demonstrated significant attenuation of the mu rhythm during the observation condition. Analyses of the mu rhythm in the individuals with autism are currently being conducted. CONCLUSION: These preliminary results indicate that imitation impairments previously observed in children and adolescents persist into adulthood. Further analyses will examine the relation between imitation abilities and the EEG mu rhythm.

Funding source: NICHD (U19 HD34565) and NIMH (U54MH066399) and the National Alliance for Autism Research Foundation.

THE PROCESSING OF INVARIANT SPEECH FEATURES IN AUTISM Tuulia Lepistö, Marika Kajander, Raija Vanhala, Paavo Alku, Minna Huotilainen, Risto Näätänen, Teija Kujala, Cognitive Brain Research Unit, Department of Psychology, University of Helsinki, Finland

Background: The ability to identify phonemes despite their constantly varying acoustical features is fundamental for speech perception. Previous studies have indicated good pitch-discrimination abilities in autism, suggesting enhanced low-level feature processing in this disorder. This may have adverse effects on speech perception, for the enhanced processing of irrelevant acoustic cues may make it more difficult to extract the invariant, abstract features of the phonemes and to identify them.

Objectives: The ability to extract the invariant features of phonemes was investigated in autism using the Mismatch negativity (MMN), a brain event-related potential indexing sound-discrimination abilities.

Methods: MMN was recorded from children with autism and their controls to phonetic and pitch changes in two different conditions: while the stimulus background was kept constant, and while it was constantly varying.

Results: Children with autism had enhanced MMNs for pitch changes in both conditions. However, their MMNs for phonetic changes were enhanced only in the constant-feature condition, not in the varying-feature condition.
Conclusions: The enhanced ability of the children with autism to discriminate phonemes is abolished under conditions of high acoustic variance. The causes and significance of this finding are discussed.
Sponsor: Finnish Cultural Foundation
Oral Session #6
Repetitive Behavior

Chair: Margaret Bauman

Speakers:
James W. Bodfish, Kristen S.L. Lam, Mark H. Lewis, University of North Carolina at Chapel Hill
Sylvie Goldman, Miran Salgado, Nicole Florance, Cuiling Wang, Mimi Kim, Paul Greene, Isabelle Rapin, Saul R. Korey Department of Neurology and Rose F. Kennedy Center for Research in Mental Retardation and Human Development, Albert Einstein College of Medicine
Mark Henry Lewis, Yoko Tanimura University of Florida
Evdokia Anagnostou, Jin Fan, Latha Soorya, Danielle Halpern, Jonathan Osowsky, Eric Hollander, Mount Sinai School of Medicine

ABSTRACTS

EMPIRICALLY-DERIVED PHENOTYPES OF REPETITIVE BEHAVIOR IN AUTISM SPECTRUM DISORDERS James W. Bodfish, Kristen S.L. Lam, Mark H. Lewis, University of North Carolina at Chapel Hill
Our goals in this study were (a) to identify putative subtypes of repetitive behavior using multivariate phenotypic analyses, and (b) to determine if subtypes have unique patterns of association with genetic, neurologic, and behavioral markers. Repetitive behaviors were assessed using either the Repetitive Behavior Scale (RBS n = 498) or the Repetitive Behavior Scale Revised (RBS-R n = 583). Subsamples were separately analyzed with a factor analysis / cluster analysis algorithm designed to yield discrete subtypes of cases. Validity of derived subtypes was examined by analyses of the association of behavioral, neurological, and genetic factors with the derived subtypes of repetitive behaviors. Three discrete subtypes were found using the factor analysis / cluster analysis algorithm: (a) a ‘Subclinical RB’ subtype characterized by significantly lower scores on all RB factors, (b) a ‘Lower-order RB’ subtype characterized by elevated scores for the stereotypyed behavior and self-injurious behavior factors, and (c) a ‘Higher-order RB’ subtype characterized by elevated scores for the compulsion, routines, and need for sameness factors. Examinations of the association with developmental, genetic, behavioral, and neurological markers confirmed that the three empirically-derived RB subtypes had differential patterns of association with these markers. These results indicate that there is a significant degree of structure within the repetitive behavior domain in autism and suggest that empirically-derived subtypes of RB may be useful in studies of pathogenesis and treatment of autism. Supported by: NIH MH73402, NIH HD30615

LONGITUDINAL STUDY OF STEREOTYPIES IN PRESCHOOL, 7 AND 9 YEAR OLD AUTISTIC VERSUS NON-AUTISTIC DEVELOPMENTALLY DISABLED CHILDREN Sylvie Goldman, Miran Salgado, Nicole Florance, Cuiling Wang, Mimi Kim, Paul Greene, Isabelle Rapin, Saul R. Korey Department of Neurology and Rose F. Kennedy Center for Research in Mental Retardation and Human Development, Albert Einstein College of Medicine
Background: Stereotypies are frequent, troublesome, yet poorly studied in autistic and developmentally disabled children.
Objectives: To study the evolution of stereotypies, defined as purposeless patterned repetitive movements, at preschool, ages 7 and 9, comparing high/low IQ groups in autistic/nonautistic developmentally disabled children.
Method: We coded stereotypies in 554 videotaped 15 minutes standardized play sessions from 336 children, 278 seen at preschool, 153 at 7, and 123 at 9. At each age approximately half were autistic and half had NVIQs below 80. Fifty two children were observed at all three ages. We used
the generalized estimating equation method for analysis of the longitudinal data. 
Results: At preschool, stereotypies occurred in 68.2% of autistic versus 23.5% of non-autistic 
children (OR=6.99, p<.000); at age 7, 44.7% of autistic versus 7.8% of non-autistic children had 
stereotypies (OR=9.58, p<.000), and at age 9, 47.4% of autistic versus 10.6% of non-autistic 
children had stereotypies (OR=7.56, p<.000). Longitudinal analysis indicates that autistic children 
were consistently more likely to have stereotypies than non-autistic children (OR=5.98, p<.000), 
adjusting for cognitive level and time effects. Low cognitive level was also positively associated 
with stereotypies (OR 1.81 (p=0.03) at preschool, 10.92 (p<.000) at 7, and 6.58 (p<.000) at 9). 
Conclusion: Autistic children and children with low cognitive level are more likely to have 
stereotypies than non-autistic and cognitively unimpaired children at the ages studied. Stereotypies 
decrease with age in all groups. Data on types of stereotypies and correlations with social 
functioning, autism severity, and neurological examination will be presented. 
Sponsor: Supported by a grant from NAAR and NINDS program project #20489.

REPETITIVE MOTOR BEHAVIOR IN A MOUSE MODEL: ASSOCIATIONS WITH PROCEDURAL LEARNING AND COGNITIVE FLEXIBILITY Mark Henry Lewis, Yoko Tanimura University of Florida 
Repetitive behavior disorders (e.g., stereotypies, compulsions) in autism and related conditions 
have been linked to alterations in cortical-basal ganglia circuitry. Thus, learning and memory 
processes mediated by this circuitry (e.g., procedural learning, executive function) are likely 
impacted in individuals exhibiting high rates of repetitive behavior. Moreover, restricted, repetitive 
behavior has been hypothesized to be associated specifically with deficits in cognitive flexibility. 
Thus, we assessed both procedural learning and cognitive flexibility (reversal learning) using a T-
maze task. Mice reared in either standard laboratory cages or in larger more complex 
environments were assessed for their level of stereotyped behavior prior to cognitive testing. Mice 
reared in larger, more complex environments exhibited significantly less stereotypy and better 
procedural and reversal learning on the T-maze task versus standard cage mice. Rates of 
spontaneous repetitive motor behavior were not systematically related to procedural learning but 
high stereotypy mice exhibited poorer reversal learning than low stereotypy animals. This effect 
was largely due to mice exhibiting backward somersaulting which displayed the poorest 
performance on both the procedural and reversal phases of the task. In summary, early experience 
associated with the prevention/attenuation of stereotypy was also associated with better procedural 
and reversal learning. In addition, high rates of stereotypy were associated with deficits in cognitive 
flexibility. The finding that repetitive motor behavior is associated with cognitive inflexibility or 
perseverative behavior significantly expands the range of restricted repetitive behavior associated 
with our model.

FMRI OF RESPONSE INHIBITION IN AUTISM Evdokia Anagnostou, Jin Fan, Latha Soorya, Danielle Halpern, Jonathan Osowsky, Eric Hollander, Mount Sinai School of Medicine 
Background: Repetitive behaviors constitute the third symptom domain in autism. There is limited 
data on the neuro-anatomical and functional abnormalities associated with this domain. On a 
previous study, we showed volumetric abnormalities in the basal ganglia associated with higher 
order repetitive behaviors in autism. 
Objective: The goal of this study was to explore functional abnormalities in the frontostriatal 
system in autism using a response inhibition task 
Methods: We recruited adult subjects age 18-45 with high functioning autism or Asperger 
syndrome and compared them to a group of healthy volunteers matched for age and IQ on a task 
of response inhibition (Go, NoGo). The subjects were shown a series of faces with happy or sad 
expressions in random order and asked to press the button when they identify one emotion but not 
the other. The BOLD imaging was performed using a gradient echoplanar (GE-EPI) sequence on a 
Siemens 3T Allegra system. 
Results: Subjects with ASD demonstrate statistically significant decrease in activation in the 
anterior cingulate cortex (ACC) and prefrontal cortex, for the NoGO-GO comparison, indicating a 
relative deficiency in inhibiting an already initiated action. 
Conclusions: Preliminary data supports the hypothesis of dysfunction of the frontostriatal circuitry 
related to the presence of repetitive behaviors in autism. 
Sponsor: Seaver Foundation
Imitation difficulties in autism: findings and potential mechanisms

Sally Rogers, University of California Davis Medical Center

A host of studies concerning imitative difficulties of people with autism, across the spectrum of age and severity of disability, have been published over the past 20+ years. However, until recently imitative difficulties have not figured prominently in theories or models of autism. This presentation will review the main findings from behavioral and neuroscience studies of imitation in autism. It will then describe evidence supporting hypotheses concerning several mechanisms that have been posited to underlie imitation problems in autism. Recent findings on imitative performance in early autism will be presented, and potential implications for treatment discussed.
Invited Educational Symposium #3
A primer on neuroimaging studies of autism: key concepts and state-of-the-art findings

Speakers:
Kevin Pelphrey, Duke University
Susan Bookheimer, University of California, Los Angeles
Heather Hazlett, UNC, Chapel Hill
Marcel Just, Carnegie Mellon University

ABSTRACTS

KEY CONCEPTS AND STATE-OF-THE-ART FINDINGS Susan Bookheimer, University of California, Los Angeles
The advent of noninvasive functional neuroimaging techniques, particularly functional magnetic resonance imaging (fMRI), has accelerated our ability to understand the neural basis of complex developmental disorders such as autism. This talk will cover fMRI basics including the basis of the MRI signal, neurovascular coupling, and the nature of blood oxygen level dependent (BOLD) contrast, and will explore the kinds of questions one can answer with functional neuroimaging. Different experimental designs for between group comparisons will be presented including blocked vs. event related designs, designing control conditions that are appropriate for the study population, and how to take into account potentially confounding variables such as subjects ability, performance deficits, and differences in brain structure. As an example we will present our recent work on functional imaging on the mirror neuron system in autism.

Mirror neurons, first identified in monkey single unit recording studies, respond during the execution of actions and during observation of others performing the same actions. These neurons primarily lie in the inferior frontal gyrus (IFG, area 44 in humans), and via the insula, affect brain regions involved in emotional experience including fear and reward circuits. A mirror neuron deficit in autism might explain many of its core symptoms including deficits in social cognition, understanding the intentions and affective states of others (theory of mind and empathy, respectively), as well as repetitive behaviors. Recent studies of mirror neuron regions in children with autism show that despite a similar ability to imitate observed facial expressions, children with autism do not activate areas of the brain implicated in the mirror neuron system including the IFG and the circuits stimulated by fear and reward via the mirror neuron system including amygdala and ventral striatum. This example demonstrates how functional imaging can test a specific hypothesis about core deficits in autism and reveal deficient neural circuitry that may be critical to developing social communication.

A DEVELOPMENTAL PERSPECTIVE ON STRUCTURAL IMAGING IN AUTISM Heather Hazlett, UNC, Chapel Hill
This lecture will begin with an overview of Magnetic Resonance Imaging (MRI) and Diffusion Tensor Imaging (DTI), two imaging techniques that have been used to study the brain structure of individuals with autism. Core concepts of MRI and DTI will be presented, as well as important considerations for conducting these types of studies. Limitations of these methods related to working with pediatric populations and longitudinal studies will also be examined. Key structural brain imaging studies of individuals with autism will be summarized, with an emphasis on the most current findings in the field. Recent work by our research lab examining very early brain development in young children with autism will be discussed as well as future directions for this field.

CORTICAL UNDERCONNECTIVITY IN AUTISM Marcel Just, Carnegie Mellon University
A number of fMRI studies of cognitive processing in people who have autism and are high-functioning indicate some consistent differences in brain activation, compared to matched normal control subjects. Although the same or similar areas of the cortex become activated in autism as in controls, there are two indicators that the integration of information across cortical areas is lower
in the group with autism. The first indicator is the lower level of synchronization in the brain activation among the activated areas in people with autism, particularly between anterior (prefrontal) areas and other areas. The second indicator is that the amount of activation in certain areas differs between the groups, such that generally, the group with autism 1. tends to have less activation in areas that play an integrating role or that generate an abstract level of interpretation (such as theory of mind computations or non-literal interpretations of language) and 2. tends to have more activation in areas that are involved in sensory, perceptual, and imagery processing. For example, in sentence comprehension, the autism group shows less activation than the control group in Broca's (left inferior frontal gyrus) area, and more activation than the control group in Wernicke's (left laterosuperior temporal) area. In sentence comprehension, Broca's area may be more involved in integration at the syntactic and thematic levels, whereas Wernicke's area may be more involved in lexical-level processing. Such findings suggest that the neural infrastructure of cognition in autism entails a lower degree of information integration and synchronization across the large-scale cortical networks that are assembled for each task.

Invited Educational Symposium #4
Psychopharmacology in autism: research considerations, current findings & future directions

Speakers:
Michael Aman, Ohio State University
Lawrence Scahill, Yale University Child Study Center
Eric Hollander, Mount Sinai School of Medicine

ABSTRACTS

MEDICATION USE IN AUTISM VERSUS EVIDENCE Michael Aman, Ohio State University
Medications from several classes have been used for the treatment of autism, though supportive evidence is variable. Community surveys show that the most commonly used classes of medications in autism are the selective serotonin reuptake inhibitors (SSRIs) (e.g., fluoxetine), atypical antipsychotics (e.g., risperidone) and stimulants (e.g., methylphenidate). This presentation reviews data from recent studies to show the efficacy and safety of these medications in children with autism.

Although commonly used in practice, fluoxetine has been poorly studied in children with autism. One recent study showed that fluoxetine was superior to placebo, but the magnitude of effect was small. Use of low doses reduces the risk of behavioral activation. The short- and intermediate-term effects of risperidone were evaluated in 101 children with autism by the Research Unit on Pediatric Psychopharmacology (RUPP) Autism Network. This study showed that risperidone is effective for the treatment of tantrums, aggression, or self-injury. No serious drug-related adverse effects were reported, but weight gain and increased prolactin were observed. The RUPP Autism Network also completed a placebo-controlled study of methylphenidate for the treatment of hyperactivity in 72 children with autism or PDD-NOS. Methylphenidate was superior to placebo, but the magnitude of effect ranged from small to medium. Taken together, these results indicate that effective medication treatment in children with autism follows from the identification of target symptoms. Appropriate expectations regarding the likelihood and magnitude of effect for medication treatment in children with autism is essential for clinical management.

RESEARCH CONSIDERATIONS Lawrence Scahill, Yale University Child Study Center
This presentation examines the evolution of psychopharmacological research in children with autism. Early research studies were conducted in single center environments. Most studies included small, inadequately described samples with poorly articulated treatment targets. The limitations of these studies hindered replication and provided inadequate guidance to clinical practice. More recent trials tend to be larger, multisite studies in which treatments are matched to target symptoms in well-described subjects.
This presentation reviews contemporary approaches to subject characterization and study design in autism. Careful matching of target symptoms and outcome measurement in combination with adequate subject characterization are essential prerequisites for study replication and application of study results in clinical practice. Using findings from recently published studies, the presentation illustrates the importance of clear entry criteria, the need for balancing homogeneity and heterogeneity in sample selection and the careful choice of a primary outcome measure. The pros and cons of different types of outcome measures (e.g., parent ratings, clinician ratings, and structured interviews) are examined. The presentation also highlights novel designs such as the combination of medication and behavioral treatment.

**FUTURE DIRECTIONS** *Eric Hollander, Mount Sinai School of Medicine*

To date, successful medication treatments in autism have focused on target symptoms. Although rational, this approach is somewhat limited. The focus on target symptoms has been driven by necessity as there have been few candidate treatments for the fundamental social and communication deficits in autism. Drug treatment in autism is poised to advance. Several potentially promising treatments based on plausible, though unproven, theories on the underlying neurobiology of autism have emerged in recent years. For example, intravenous immunoglobulin was examined in one small pilot study. Although this intervention showed only limited benefit, there is continued interest in immune-based therapies. Based on the possible dysfunction of the glutamate receptor complex, the partial agonist, D-cycloserine has been proposed as a treatment for autism. One small pilot study provides intriguing, but uncertain results. Neurobiological advances in other fields such as schizophrenia may also inform drug development programs in autism. This presentation reviews several recently completed pilot studies with various medications such as oxytocin, D-cycloserine, guanfacine, valproate among other compounds. In addition to the examination of specific drug candidates, this presentation also examines methods for developing medication treatments from pilot study to multisite trial. To achieve more rapid progress in the drug treatment of autism, a more systematic method of drug development is needed.
PS3.1
COPPER-MEDIATED MEMBRANE DAMAGE IN AUTISM
Ved Chauhan, Abha Chauhan, Ashfaq Sheikh, Ted Brown, Harish Chander, NYS Institute for Basic Research in Developmental Disabilities

Background: We have reported decreased levels of phosphatidylethanolamine (PE) in the erythrocyte membrane (Chauhan et al. (2004), Life Sci. 74, 1635-1643), and of ceruloplasmin, a copper-transport protein, in the serum (Chauhan et al. (2004) Life Sci. 75, 2539-2549) of children with autism as compared to their normal siblings. These results suggested that altered plasma copper levels may lead to increased lipid peroxidation in autism.

Objective: This study was conducted to investigate whether copper plays a role in altering the levels of membrane lipids in autism.

Methods: Mouse brain lipids were extracted, and liposomes containing 100 mg lipids were prepared by sonication of lipids for 15 minutes. The liposomes were incubated for 12 h in the presence of different metal cations [10 mM] namely copper (Cu2+), cadmium (Cd2+), calcium (Ca2+), iron (Fe3+) and zinc (Zn2+) at 37°C. The lipids were then extracted, phospholipids were measured. Cu2+-mediated oxidation of PE was also studied in autistic and control lymphoblasts.

Results: Among the metal cations studied, only copper was able to oxidize PE selectively while it did not have any effect on other lipids. Copper was found to decrease PE levels in concentration- and time-dependent manner, and it oxidized both plasmalogenic PE and non-plasmalogenic PE. Additional experiments showed that copper could induce the oxidation of PE in the lymphoblasts also. This effect of copper on PE oxidation was higher in autistic lymphoblasts as compared to control lymphoblasts.

Conclusion: These results suggest that copper may be a factor in inducing the membrane phospholipid abnormalities in autism.

Sponsor: NYS Office of Mental Retardation and Developmental Disabilities.

PS3.2
GRAY MATTER METABOLIC DEFICITS IN AUTISM ASSESSED BY PROTON SPECTROSCOPIC IMAGING
Tim J DeVito, Dick J Drost, Nagalingam Rajakumar, Peter C Williamson, Rob Nicolson*, Dept of Medical Biophysics, Dept of Psychiatry, University of Western Ontario

Background: Proton magnetic resonance spectroscopic imaging (1H-MRSI) allows for the non-invasive quantification of metabolite levels from many brain regions in a single experiment. The few autism studies to date using this methodology have reported disparate localized metabolic deficits, though findings have been rather inconsistent.

Objective: To characterize the global metabolic profile of gray and white matter in a sample of male children with autism using 1H-MRSI.

Methods: Thirty-three male patients with autism (aged 6-17) and 33 healthy males (aged 6-17) participated in this study. All images were acquired using a 3.0-tesla head-only MRI system. Localized proton spectra were acquired from two 9-mm thick oblique-axial slices using a spin-echo 1H-MRSI sequence (TE=135 ms). Spectra from each ~1-mL voxel (~500 voxels per participant) were analyzed, and regressed against gray matter fraction in that voxel to determine estimates of global gray and white matter metabolite levels.

Results: Linear mixed model repeated measures analysis revealed significant group differences in global gray matter metabolite profiles (p<0.0001). Post-hoc tests revealed significantly reduced levels of gray matter glutamate + glutamine (Glx, p<0.001) and NAA (p<0.01) in the patient group. No differences were observed in global white matter metabolite levels.

Conclusions: This is the first report of reduced global gray matter Glx levels in autistic patients, and may reflect widespread abnormalities in glutamatergic circuitry. Reduced NAA is consistent with previous studies and may reflect widespread neuronal dysfunction. Further parcellation of the present data into sub-regions, such as brain lobe and hemisphere will help localize the observed metabolic deficits.

Sponsors: Ontario Mental Health Foundation, Hospital for Sick Children Foundation, Autism Society Ontario, Child and Parent Resource Inst., NSERC.

PS3.3
BRAIN-DERIVED NEUROTROPHIC FACTOR mRNA LEVELS ARE NOT INCREASED IN FUSIFORM GYRUS OF SUBJECTS WITH AUTISM
Kristine LP Garcia, Guanhua Yu, Diego Garzon, Victor S Chiu, Jeremy Goldberg, Peter Szatmari, Margaret Fahnestock, McMaster University

Background: The neurobiological substrates of autism are unknown. Previous studies reported increased brain-derived neurotrophic factor (BDNF)-immunoreactive protein in autism. However, BDNF mRNA levels have not been previously studied.

Objectives: This study examined BDNF mRNA and protein in post mortem fusiform gyrus tissue from autism and control subjects.

Methods: Nine postmortem brain samples from subjects with autism and nine control brain samples were provided by the Autism Tissue Program (Princeton, NJ) via the Harvard Brain Bank (Cambridge, MA) and the University of Maryland Brain and Tissue Bank (Baltimore, MD).
Subjects with seizures were excluded from the study. BDNF mRNA was measured using real-time RT-PCR, and BDNF protein was measured using ELISA and Western blotting. Results: BDNF mRNA levels were unchanged in the autism group compared to controls. There was no statistically significant difference in levels of BDNF protein in autism samples compared to controls as measured by Western blotting. However, total brain-derived neurotrophic factor-like immunoreactive protein, as measured by ELISA, was increased in autism samples compared with controls, in agreement with previous studies.

Conclusion: Our data demonstrate that BDNF mRNA is not elevated in fusiform gyrus of autism patients compared to controls, and therefore any alterations in levels of BDNF-like immunoreactive protein are not transcriptionally driven. BDNF protein levels are unchanged in autism as measured by Western blotting; ELISA results demonstrating elevated BDNF protein levels are likely due to non-specific binding. Supported by: Ontario Mental Health Foundation and National Alliance for Autism Research.

PS3.4
GLYOXALASE I SNP MOUDLATE GENE EXPRESSION IN AUTISM
Mohammed A. Junaid, Salomon Kuizon, New York State Institute for Basic Research in Developmental Disabilities

We had earlier shown that an altered isoform of glyoxalase I (Glo1) is an autism susceptibility factor (Junaid et al., Am. J. Med. Genet. 131A:11-17, 2004). The GLO1 rs2736654 C419A SNP associated with autism results in reduced enzyme activity, causes storage of methylglyoxal and advanced glycation end products (AGE).

Objective: To study whether Glo1 isoforms mediate actions through receptor for advanced glycation end products (RAGE) that initiates a signal transduction culminating in modulation of gene expression.

Methods: Brain and lymphoid cell extracts from autism and controls were resolved by SDS-PAGE, proteins transferred onto nitrocellulose membranes and probed with antibodies against RAGE and transcription factor NF-kappaB.

Results: The accumulated AGE causes increased levels of RAGE in brain and lymphoid cells from autism individuals. The RAGE is an integral membrane bound phosphoprotein that upon binding of ligand initiates a secondary signaling mechanism. The signaling leads to modulation of transcription factor NF-kappaB expression. Western blot analyses showed decreased levels of NF-kappaB in brain and lymphoid cells from individuals with autism.

Conclusions: A majority of autism subjects are homozygous for the GLO1 rs2736654 C419A SNP. In agreement with our earlier observations, the RAGE levels are modulated in these samples that reduces the levels of NF-kappaB. NF-kappaB activation is earlier indicated in neurite outgrowth, thus a decrease expression during crucial neuronal development may be a contributing factor in the autism pathophysiology.

Grants support: NIH (NS 40691), NAAR and NYS OMRDD

PS3.5
URINARY EXCRETION OF 5-HYDROXYINDOLEACETIC ACID AND SEROTONIN IN NORMOSEROTONEMIC AND HYPERSONEROTONOMIC AUTISTIC INDIVIDUALS
Erik J Mulder, George M Anderson, Alida Oosterlou-Duinkerken, Ido P Kema, Ruud B Minderra, University Medical Center Groningen/Accare, University Center Child and Adolescent Psychiatry

Background: An elevation of serotonin (5-hydroxytryptamine, 5-HT) in platelets of individuals with autism is one of the most well replicated findings in neuropsychiatry. Although the elevation recently has been better characterized, the cause of the hyperserotonemia is still unknown.

Objectives: Compare urinary excretion of 5-hydroxyindoleacetic acid (5-HIAA) and of 5-HT in normoserotonemic and hyperserotonemic autistic individuals to examine the possible role of gut 5-HT production in the platelet hyperserotonemia.

Methods: Urinary excretion of 5-HIAA and 5-HT were compared across 10 normoserotonemic and 10 hyperserotonemic age-matched autistic individuals.

Results: No significant differences were found between the groups for urinary excretion of 5-HIAA or 5-HT. The urinary 5-HIAA/5-HT ratio was also similar in the two groups. However, when focusing on subjects with lowest and highest platelet 5-HT values, there were strong trends to higher 5-HIAA excretion in those subjects with the highest platelet 5-HT concentrations.

Conclusion: The results indicate that further careful study in large groups of biochemically and behaviourally well characterized subjects is necessary to elucidate definitively the potential contribution of altered gut production of 5-HT to the platelet hyperserotonemia of autism.

Support: Korczak Foundation for Autism Research

PS3.6
INCREASE IN PHOSPHOLIPASE A2 ACTIVITY AND CHOLESTEROL: PHOSPHOLIPID MOLAR RATIO IN THE LYMPHOBLASTS OF AUTISM
Ashfaq M Sheikh, Abha Chauhan, Harish Chander, Mazhar N Malik, Ted Brown, Ved Chauhan, NYS Institute for Basic Research in Developmental Disabilities

Background: We have recently reported increased oxidative stress (Chauhan et al. (2004) Life Sci. 75, 2539-2549), and abnormalities in aminoglycerophospholipids levels in autism (Chauhan et al. (2004), Life Sci. 74, 1635-1643). Others have reported decreased levels of polyunsaturated fatty acids in the erythrocyte membranes of autism as compared to normal subjects (Bell et al. (2000) Prostaglandins, Leukotrienes and Essential Fatty Acids 63, 21-25). Altered levels of polyunsaturated fatty acids in autism could be linked to abnormality in phospholipase A2 (PLA2) activity. Since chromosomal linkage studies in autism also points to a locus where
PLA2 gene is located, this enzyme may have an important role in the etiology of autism.

Objectives: To measure and compare the cytosolic PLA2 activity, and cholesterol / phospholipid molar ratio in the lymphoblasts of autism and controls.

Methods: Lymphoblasts from autism and controls were obtained from AGRE. 2 million lymphoblasts (autistic and control) in 100 ml PBS were probe-sonicated for 10 seconds on ice. The sample was centrifuged at 14,000 rpm for 10 minutes. The supernatant (35 ml) was used for measuring the cytosolic PLA2 activity by kit from Amersham Biosciences.

Results: Cytosolic PLA2 levels were observed to be significantly increased (P < 0.05) in the lymphoblasts of autism as compared to controls. Cholesterol: phospholipid molar ratio, an indicator of membrane rigidity, was also found to be increased in the lymphoblasts of autism as compared to control lymphoblasts.

Conclusion: These results suggest that autism is associated with membrane lipid alterations.

Sponsor: NYS Office of Mental Retardation and Developmental Disabilities.

PS3.7
PHYSIOLOGICAL RESPONSIVENESS TO AFFECTIVE STIMULI AMONG THOSE ON THE AUTISM SPECTRUM. Ashleigh Hillier, Allen Carpenter, Ryan M Smith, David Q Beversdorf, The Ohio State University

Background: Previous research has shown both typical and atypical physiological responses to affective stimuli among those on the autism spectrum.

Objective: To investigate physiological responsiveness to distress cues, threatening, aversive, positive, and neutral stimuli among those with autism spectrum disorders (ASD), and whether responsiveness will correspond to behavioral ratings of the stimuli.

Methods: Participants were presented with stimuli from the International Affective Picture System. Seven slides in each of five categories: distress, threat, aversive, positive, and neutral were presented for five seconds each during which skin conductance responses (SCR) were measured. Subsequently participants rated each picture for valence and arousal.

Results: Those in the comparison group demonstrated significantly larger SCRs to aversive stimuli compared to positive, distress, and neutral stimuli. In contrast, those with ASD did not show any significant differences in their responsiveness between the various stimuli categories. In addition, those in the comparison group showed a significant relationship between SCRs and subsequent arousal and valence ratings whereas those with ASD did not.

Conclusion: These findings suggest that those on the autism spectrum do not vary in physiological responses to a range of affective stimuli. In addition, their physiological responses may not be significantly related to their cognitive appraisals of affective stimuli.

This research was supported by the National Institute of Neurological Disorders and Stroke (NINDS) K23

PS3.8
PRE-SLEEP EEG IN HIGH FUNCTIONING AUTISTIC SPECTRUM DISORDERS Cathy Léveillé, Christianne Bolduc, Élyse Limoges, Élyse Chevrier, Laurent Mottron, Roger Godbout, Centre de recherche Fernand-Seguin & Neurodevelopmental Disorders Program, Hôpital Rivière-des-Prairies, and Dept. Psychiatry, Université de Montréal

Introduction: Persons with autism often report symptoms of sleep-onset insomnia, a condition characterized by hyperarousal. Spectral analysis of the EEG in idiopathic psychophysiological insomnia patients have shown high values in fast frequencies (Beta activity) and/or low values in slow frequencies (alpha, theta, delta). We analyzed the EEG of adults with autism at bedtime to verify whether typical insomnia-type patterns would be found.

Methods: Six men with high functioning (normal IQ) autism (21.8 ±3.9 years) and six male controls (22.7 ± 3.5 years) were recorded for two consecutive nights. On the evening of night 2, just before bedtime, we recorded five minutes of EEG with eyes closed using a 23-electrode montage. Spectral analysis was performed on 60 seconds of artefact-free EEG and spectral amplitude was extracted for Delta, Theta, Alpha, and Beta activity. Results were compared using Mann-Whitney U-tests.

Results: Compared to controls, the clinical group showed more Delta activity for Fp1 (p < .02), F7 (p < .06), T3 (p < .05), and T5 (p < .05). No significant differences were found for the other frequency bands or recording sites.

Conclusions: These results are in the opposite direction to what would have been observed in typical insomnia since persons with autism showed *more* slow activity than controls. Persons with high functioning autism also do not spontaneously complain of insomnia and they do not show abnormal cortisol levels (Limoges et al., Brain, 2005). We conclude that insomnia in high functioning autism is of an atypical type.

Supported by CIHR

PS3.9
EVIDENCE FOR THALAMOCORTICAL DYSRHYTHMIA IN AUTISTIC CHILDREN Katherine M. Martien, Frank Duffy, Massachusetts General Hospital LADDERS Clinic/Harvard Medical School

Background: Neurobehaviorally, autistics show abnormalities in central coherence, sensory processing and sleep. Neurophysiologically, they show abnormal sensory evoked potentials, sleep architecture and epileptiform EEGs, often with spike and wave (SW). At the neurobiological level, this pattern of abnormalities could result from an increased excitation/inhibition ratio (Rubenstein and Merzenich, 2003) affecting the thalamus, particularly the reticular nucleus (nRT) and associated thalamocortical circuits. Animal studies (Marini et al. 2002) have shown increased runs of temporal-parietal theta and spike waves on QEEG in behaving rats.
Following bi-rostral nRT GABAergic cell ablation.

Objective: To review QEEG records in autistics looking for evidence of increase theta activity and spike wave discharges in waking.

Methods: We reviewed waking (non-stage 1/2) QEEG records of 25 anticonvulsant-free autistic children (DSMIV criteria) ages 1.11 to 8.11 yrs (mean 4.2 yrs) for paroxysms of theta and epileptiform activity.

Results: 18/25 (72%) of autistics showed increased runs of theta of variable length, compared to normative age-matched data, in temporal (83%) and central-parietal (27%), but not in frontal or occipital regions. 12/25 (48%) showed epileptiform activity, 33% of which was SW.

Conclusions: Our data suggest that increased runs of temporal-parietal theta are common in autistic children often accompanied by SW epileptiform activity. These findings support the hypothesis that autistics have an increased excitation/inhibition ratio affecting the nucleus reticularis of the thalamus producing thalamocortical dysrhythmia, most likely via disinhibition. Further studies on the role of thalamic disinhibition in autism are warranted.

**PS3.10**

**FAMILIAR AND NOVEL FACE PROCESSING OF ADULTS WITH ASD IN AN ERP STUDY**

Kristen Merkle, Sara J Webb, Michael Murias, Elizabeth Aylward*, Geraldine Dawson*, University of Washington Study Objectives: Research indicates that adults with autism have a delayed ERP N170 to novel faces. Using fMRI, individuals with ASD recruit object-processing regions during processing of unfamiliar faces. However, individuals with ASD can recruit the same neural processing regions as typical individuals when shown pictures of familiar faces. To determine if familiar faces recruit more typical temporal processing capabilities, this study examined the ERP responses to a familiar face in adults with ASD and matched controls.

Methods: ERPs were collected to a familiar and unfamiliar face. The unfamiliar face was of the same ethnicity, age, and sex as the familiar face.

Results: Similar to prior reports, preliminary evidence suggests that the N170 to all faces was delayed in individuals with ASD as compared to controls. However, the ASD group did show a more negative and faster N170 to a familiar face than to targets (houses). At a later component, the control group but not the ASD group showed a greater response to the repeating unfamiliar face than the familiar face.

Conclusions: These results suggest that the temporal response to familiar faces is also slowed in adults with ASD. However, individuals with ASD did show preferential processing of a familiar face compared to objects and thus may have benefited from familiarity. Later stage ERP components linked to memory processes differed between individuals with ASD and controls. These results support fMRI findings suggesting that familiarity can recruit face-processing systems.

Funding source: NICHD (U19 HD34565) and NIMH

**PS3.11**

**DIPOLE SOURCE LOCALIZATION OF FACE PROCESSING IN AUTISM**

Neva Oskin, Kristen Merkle, Sara Webb, Todd Richards, Heracles Panagiotides, Elizabeth Aylward, Geri Dawson, Department of Radiology, University of Washington

Background: Studies of face processing in autism have demonstrated abnormal temporal characteristics of the face-sensitive ERP component (N170).

Study objectives: Dipole source localization of ERP recordings was used to determine whether the locations of the sources for the N170 component during face processing differ for individuals with autism and control subjects.

Methods: ERP data were acquired in a face stimulus experiment for the two groups of subjects, each composed of six individuals. Source analysis was performed on grand-averaged data for each group using the software BESA.

Results: For the control group, 95% of the variance of the ERP waveforms in the time range surrounding the N170 peak was accounted for by a model of two dipoles bilaterally located in the fusiform gyrus. In the autism group, source analysis localized 70% of the variance in the ERP signal around the N170 peak to two bilaterally symmetric sources superior to the fusiform gyrus, in the occipital lobe. Placement of additional dipoles did not appear to improve the solutions.

Conclusion: These preliminary findings indicate that the sources for the N170 in individuals with autism are located in different areas of the brain than in control individuals. The differences in unexplained variance indicate that the sources may be more diffuse in location and variable among individuals with autism.

Funding: NICHD (U19HD34565) and NIMH (U54MH066399)

**SENSORY DYSFUNCTION IN CHILDREN WITH AUTISM**

Roseann C Schaaf, Teal Benevides, Lucy Jane Miller, Thomas Jefferson University

Background: Approximately 85% of children with Autism experience atypical responses to sensory stimuli (sensory dysfunction/SD) that interfere with their ability to fully participate in activities. Although it is clear that SD is a significant factor in autism, its mechanisms are not well understood; nor its impact on adaptive behavior. As a result, data supporting interventions that address sensory dysfunction are sparse and lack evidence to support their efficacy.

Objectives: This study addresses this gap by examining SD in forty 5-8 year old children with autism in comparison to 20 typically developing controls using measures of autonomic nervous system (ANS) activity as markers of sensory dysfunction. The hypothesis is that children with autism demonstrate differential, atypical physiological reactivity to sensory stimuli that is significantly related to adaptive behaviors. To control for the inherent heterogeneity within the group of subjects...
with autism, they will be classified into hypo and hyper reactive ANS groups.

Methods: Subjects participate in the Sensory Challenge Protocol (SCP), a unique, controlled research protocol designed to measure ANS reactivity to sensation. The vagal tone index (VTi), the parasympathetic marker, and the mean number and magnitude of peaks of electrodermal activity (EDA), the sympathetic markers, will be compared for each group during each phase of the SCP: baseline, challenge and recovery phases. The Short Sensory Profile and the Vineland Adaptive Behavior Scales II is used to evaluate sensory related behaviors and adaptive behaviors respectively.

Results: Data indicates that children with autism demonstrate variable patterns of ANS activity but that children with low vagal tone have lowest adaptive behaviors.

Conclusions: Preliminary findings support further study of SD, ANS activity their relation to adaptive behavior, in particular the relation of parasympathetic regulation and adaptive behavior.

DOUBLE-BLIND PLACEBO CONTROLLED, CROSS-OVER TRIAL OF SUBCUTANEOUS METHYLCOBALAMIN ON BEHAVIORAL AND METABOLIC MEASURES IN CHILDREN WITH AUTISM: PRELIMINARY FINDINGS

Robert Hendren, Lesley J. Deprey, Norman Brule, Rita Rafidi, Sarvenaz Sepehri, UCDavis MIND Institute

Background: Subcutaneous injection with methyl B12 is a current treatment for children with autism that has anecdotal reports of remarkable clinical improvements and few side effects but no published studies to support its clinical benefit.

Objective: To demonstrate that methyl B12 injections will improve cognition, communication, and behavior in children with autism and will be associated with metabolic improvement in cellular methylation and glutathione-dependent antioxidant capacity with few side effects. Methods: This study is a 12-week, DBPC, cross-over clinical trial. Half of the subjects are randomized to 6 weeks of active treatment followed by 6 weeks of normal saline (Group A) and half to 6 weeks of normal saline followed by 6 weeks of active treatment (Group B).

Diagnosis of autism is confirmed using the ADOS, ADI R, Vineland and Mullen Scales. The primary outcome measure is the clinical global impression scale-improvement (CGI-I). Secondary outcome measures at each interval include the ABC, NEPSY subtests, SB:V subtests, CDI, and the PPVT. The Parent Designed Report Form, designed for methyl B12 studies is also administered at 6 and 12 weeks. Video segments are recorded in the clinic and raters blind to treatment arm view the video and rate improvement using the CGI. The Parent Interview for Autism-Clinical Version (PIA:CV) or the CARS is then completed. Results: Twenty subjects (ages 3-8 years) with autism are being evaluated as part of a longitudinal study. Preliminary examination of the outcome data from 4 completers demonstrate relative improvements in communication and behavior in 2 of the 4 subjects. It is anticipated that at the present rate of enrollment, all 16 of the 20 subjects will have completed by the IMFAR meeting. Final results are discussed in relation to our hypothesis. Conclusion: Initial findings present evidence supporting the use of methyl B12 injections as a beneficial treatment for some children with autism.

PS3.14
OPEN LABEL STUDY OF THE EFFECTS OF EQUILIB NUTRIENT ON BEHAVIORAL MEASURES IN CHILDREN WITH AUTISM

Sarvenaz Sepehri, Norman D Brule, Robert L Hendren, UC Davis M.I.N.D. Institute

Background: Multiple vitamins are frequently used for children with a wide range of mental and neurodevelopmental disorders, but to date there are very few controlled treatment studies published. Equilib, a combination of amino acids, amino acid chelated minerals, anti-oxidant/anti-inflammatory agents and vitamins, is a current non-prescription treatment for children with disorders such as autism, bipolar disorder and ADHD. It is anecdotally reported to benefit symptoms associated with autism spectrum disorder.

Objective: To determine if Equilib will improve parent completed behavioral ratings in children with autism and whether implementation of a double-blind, placebo-controlled study is supported.

Methods: This is an open label, non random study of 29 children diagnosed with autism between the ages of 3 and 16 years. Daily rating of emotional regulation, problem behavior, and socialization included such symptoms as hand-flapping, lack of social smile, temper tantrums, anxiety, and avoidance of eye contact. Daily ratings began 4 to 12 days prior to starting Equilib and continued for 4 to 26 weeks.

Results: A four-month treatment average showed steady improvement in daily scores with some reduction in response scores. The mean of the total parent behavioral rating decreased from 27.49 (SD 12.24) to 14.43 (SD 10.60).

Conclusion: Equilib treatment correlates with improvement in parent symptom ratings. Further study with well defined treatment groups, larger sample sizes, standardized ratings by clinicians as well as parents, and longer duration of treatment are necessary to determine the benefits of Equilib in the treatment of autism.

Sponsor: Evince International, LLD

PS3.15
CONTROVERSIAL TREATMENTS FOR AUTISM IN THE POPULAR MEDIA

Jennifer M Wick, Tristram Smith, University of Rochester

Background: Popular but controversial treatments for autism include gastrointestinal and dietary interventions, nutritional supplements, detoxification protocols, and some sensorimotor and relationship therapies.

Objective: Examine popular media reports on controversial treatments.

Methods: The media database Lexis/Nexis was searched...
for reports each year from 1991 to 2005 on Facilitated Communication, Auditory Integration, Sensory Integration, Gentle Teaching, Vitamin Therapy, Gluten-Free and Casein-Free (GfCf) Diet, Secretin, and Chelation. Each report was rated as positive, negative, or neutral toward the treatment, and the basis for a positive or negative reference (e.g., case reports or research findings) was analyzed.

Results: Overall, reports on controversial treatments were 29% positive, 44% neutral, and 27% negative. Auditory Integration, Sensory Integration, Vitamin Therapy, and GfCf Diet had few negative reports (0-7%). Positive reports outnumbered negative ones for Facilitated Communication (39% positive, 29% negative) and Secretin (29% positive, 23% negative). Negative reports predominated only for Chelation (48% negative) and Gentle Teaching (33%). Negative reports usually cited anecdotal evidence of adverse effects rather than scientific studies. Reports increased from year to year. From 1991 to 1998, sensorimotor and relationship therapies received more references than biomedical treatments, whereas the reverse was true subsequently.

Conclusion: Media reports were mostly positive or neutral and usually cited anecdotal evidence rather than research studies. They occurred with increasing frequency over time, with an increasing focus on biomedical treatments. Funding: U54 MH066397 (Genotype and Phenotype of Autism)

**PS3.16**

**DECREASED TRANSFORMING GROWTH FACTOR BETA1 IN AUTISM: A POTENTIAL LINK BETWEEN IMMUNE DYSREGULATION AND IMPAIRMENT IN SOCIAL INTERACTIONS.**

Paul Ashwood, Christina Kwong, Paula Krakowiak, Sally Ozonoff, Judy Van de Water, The M.I.N.D. Institute, UC Davis

There is growing evidence that an abnormal immune response may play a major role in neurodevelopment and in the etiology of autism spectrum disorders (ASD). Several studies have demonstrated the presence of an autoimmune response to ‘self’ proteins in the brain and CNS in ASD patients, which may be, in part, due to deficits or dysfunction in the regulation of the immune response. Arguably, one of the most important immune regulators able to effectively control aspects of the immune response is transforming growth factor beta1 (TGF). To better define the immune status of children with ASD, we sought to examine circulating active TGF levels in subjects enrolled in a large case-control population-based study. ELISA analysis of TGF was performed on the plasma of ASD (n=75), age matched typically developing general population controls (n=36), siblings of children with ASD (n=28), and children with other developmental disabilities (n=32). Significantly decreased TGF was noted in ASD children compared with typically developing controls and children with other developmental disabilities (p<0.01). There was also a trend for lower circulating TGF levels in siblings of ASD. Interestingly, in children with ASD, there was a positive correlation between circulating TGF levels and with measurements of impaired social interaction and socialization (p<0.02) suggesting that ongoing inflammatory responses may be linked to disturbances in social interactions. This study demonstrates a significant reduction in TGF in children with ASD. Such immune dysregulation may predispose for the development of autoimmunity and/or adverse neuroimmune interactions during critical windows in neurodevelopment.

Support: The Ted Lindsay Foundation, Visceral, NIEHS 1 PO1 ES11269-01

**PS3.17**

**B-CELLS FROM NON-VERBAL AUTISM PATIENTS HAVE ELEVATED LEVELS OF SPONTANEOUS APOPTOSIS COMPARED TO VERBAL AUTISM AND CONTROL PATIENTS**

David S Baskin, Candace L Minchew, Vladimir V Didenko, The Methodist Hospital Research Institute

Background: Genetic heterogeneity of autism poses a problem in identification and characterization of its etiologies.

Objectives: Compare levels of spontaneous apoptosis in autistic patients who are verbal with those that are non-verbal.

Methods: Rates of spontaneous apoptosis and cell proliferation were investigated in cell cultures of peripheral blood lymphocytes taken from 5 autistic patients who were verbal, 5 autistic patients who were non-verbal and 5 healthy donors. Initially, the lymphocytes were subjected to EBV treatment to obtain immortalized populations of B-cells.

Results: All cell cultures had similar levels of cell proliferation but differed in their propensity to undergo spontaneous apoptosis. B-cells from autistic donors who were non-verbal had higher rates of spontaneous apoptosis compared to controls and verbal autism patients, as evidenced by a 36% increase in the activation of caspase-3, as well as other measures.

Conclusion: These data highlight genetic heterogeneity of two phenotypic presentations of autism, and present intriguing clues as to etiologies.

Sponsors: NIH, AGRE, GAC, TAUB Foundation, TMHRI, MNI

**PS3.18**

**INCREASED HEAT SHOCK PROTEINS 90 AND 60 ANTIBODIES IN THE SERUM OF CHILDREN WITH AUTISM**

Harish Chander, Abha Chauhan, Iral Cohen, Ted Brown, Ashfaq Sheikh, Edmund Jenkins, Ved Chauhan, NYS Institute for Basic Research in Developmental Disabilities

Background: Heat shock proteins (HSPs) are expressed by every cell in response to stressful situations, which are critical for many physiological functions. HSPs protect the cell against different kind of insults, and provide a link between infection, immunoregulation and autoimmune disease. Recently, the role of autoantibodies against heat shock proteins in autism has been suggested.

Objective: To compare the reactivity of different HSPs...
antibodies in the sera of autistic children with that in the sera of non-autistic developmentally normal siblings.

Methods: Blood samples from eight children with autism and their eight developmentally normal siblings were taken for this study. The immunoreactivity of autistic and control sera with different HSPs (90, 70, 60, 40 and 27) was analyzed by Western Blotting and densitometric analysis.

Results: Western Blot analysis revealed a higher binding of HSPs 90 and 60 as compared to other HSPs (HSP 70, 40 and 27) with their antibodies in autistic sera. Densitometric analysis demonstrated that the binding of HSP 90 and HSP 60 was higher with autistic sera than with control sera.

Conclusion: The results suggest that autistic sera have elevated levels of HSPs 90 and 60 autoantibodies that may play a role in the pathogenesis of autism.

Sponsor: NYS Office of Mental Retardation and Developmental Disabilities

**PS3.19**

**INCREASED SERUM COMPLEMENT C3 / C4 AND ALPHA-1-ANTICHYMOTRYPsin LEVELS IN AUTISM**

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Background: The patients with autism are known to suffer from gastrointestinal disturbances and infections. Acute phase response involves alteration in concentration of serum proteins following inflammatory stimulus. Among these proteins are positive acute phase complement proteins and alpha-1-antichymotrypsin (ACT). C3 is the most abundant protein of complement system, and is central component of both classic and alternate complement pathways. C4 is essential for activation of the classical complement pathway. ACT is one of earliest responding positive acute phase protein, and acts as a proteinase inhibitor. Physiologically, its major function is the inhibition of cathepsin G. The levels of C3/C4 and ACT increase in presence of inflammation and bacterial infections.

Objectives: This study was done to compare serum complement C3 / C4 and ACT levels in the serum samples from children with autism and their developmentally normal siblings.

Methods: Complement C3 and C4 levels were determined nephelometrically in serum samples from children with autism, and their developmentally normal non-autistic siblings. ACT levels were measured by enzyme-linked immunosorbent assay.

Results: The levels of C3 and C4 complement proteins, as well as ACT were significantly higher in autistic subjects as compared to their normal siblings. A positive correlation was observed between increased complement levels and severity of autism.

Conclusion: C3/C4 and ACT are the positive acute phase proteins in blood that facilitate immunological and inflammatory responses. Their increased levels in autism suggest that inflammatory reactions may play a role in the pathogenesis of autism.

Sponsor: NYS Office of Mental Retardation and Developmental Disabilities

**PS3.20**

**PROTEOMIC MASS SPECTROMETRY ANALYSIS OF SERUM IN AUTISM: IDENTIFICATION OF IMMUNE-RELATED PROTEINS**

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Background: Proteomic approaches complement genome initiatives by elucidating the biological defects involved in complex neurodevelopmental disorders, such as autism. Objective: We conducted mass spectrometric analysis comparing serum samples from 70 4 to 6 year old children with high- and low-functioning autism and 35 typically developing children.

Methods: Serum samples were subjected to mass spectrometric analysis for differential expression of proteins. Samples were analyzed for low and high molecular weight components. Proprietary software was used to track and quantify molecules for their differential expression.

Findings: More than 100 proteins were differentially expressed. Among these, the four upregulated proteins that showed the largest effect size between those with and without autism were tumor necrosis factor-alpha converting enzyme (TACE), Complement Factor H Related Protein (FHR1), Fibronectin 1 isoform (FN1) and Complement C1q. TACE regulates TNF-alpha and has both neuroprotective and neurotoxic properties. Factor H and C1q are involved in the complement system participating in both innate and adaptive immunity. FN1 is involved in the degradation of C1q and is related to reelin, a candidate gene in autism. Further, C1q works in concert with C4 also implicated in autism.

Conclusions: The data strongly support previous studies showing abnormalities of circulating proteins in autism. Our findings are suggestive of specific abnormalities in the immune system involving the complement system.

*Funding by the M.I.N.D. Institute

**PS3.21**

**AUTISM AND THE OCCURRENCE OF SUBTHROMBOTIC ACTIVATION OF COAGULATION**

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Background: A hypercoagulable state characterized by subthrombotic activation of coagulation was previously reported in a cohort of autistic disorder (AD) patients and family members [Bradstreet, et al., 2000]. Interestingly, many family members in this early cross-sectional study reported symptoms consistent with CFS/Fibromyalgia or other chronic illnesses. To clarify whether the association of coagulation activation was with the autism, chronic inflammatory illness or both, we performed a case-controlled study of subthrombotic activation in a local
cohort of AD patients who did not manifest overt inflammatory illness.

Methods: We prospectively studied 25 patients in whom AD was established via DSM IV, ADI, and ADOS criteria, and 25 healthy age-matched controls. Whole blood was collected in 3.2% citrate anticoagulant and analyzed for plasma fibrinogen, prothrombin fragment 1+2, thrombin-antithrombin complexes, soluble fibrin monomer, and platelet surface P-selectin, before and after platelet activation with ADP. This sensitive ISAC (Immune System Activation of Coagulation) Panel is positive if two or more results are abnormal.

Results: Valid data were obtained for 23 patients and 24 controls, and were scored for qualitative positivity rates and means. ISAC panel positivity rate was 0.087 (2/23) for patients and 0.208 (5/24) for controls. There was no statistical increase in either qualitative or quantitative abnormalities for the patients.

Conclusions: The results show that in this AD cohort there is an essentially background level of coagulation activation, in contrast to the findings of the earlier study that included families with CFS/FM or other chronic illnesses. While our current findings do not exclude central or autoimmune inflammatory processes as contributing to AD, they demonstrate that a high prevalence of subthrombotic activation of coagulation is not a generalized phenomenon in AD.

Sponsors: Hemex, SARRC, and TGen

PS3.22
ELEVATED TH1/TH2 CYTOKINES WITHOUT A REGULATORY IL-10 RESPONSE IN CHILDREN WITH ASD
Cynthia A Molloy, Ardythe L Morrow, Jareen Meinzen-Derr, Krista Dienger, Patricia Manning-Courtney, Mekibib Altaye, Marsha Wills-Karp, Cincinnati Children's Hospital Medical Center
Background: There is emerging evidence that Autism Spectrum Disorder (ASD) is associated with immune dysregulation.
Objective: Compare measures of the adaptive immune response in children with ASD and matched controls.
Methods: Subjects: children age 3 -11yrs. Cases (n=20) with ASD were matched to neurotypical children on age, race, gender and date of visit. Peripheral blood mononuclear cells (PBMC) were isolated from whole blood and cultured in media alone, or media plus mitogen. Cytokines from supernatant were assayed by ELISA.
Levels of cytokines IL-2, (Th0); IFN-gamma (Th1); IL-4, IL-5, IL-13 (Th2); and IL-10 (regulatory) were measured. Mean case-control differences in cytokine levels were calculated and mean case-control differences compared.
Results: Mean age = 6.9 years; 17 boys per group. In media alone, PBMC from cases produced higher levels of all cytokines except IL-10. Significant differences were observed between matched pairs for all Th2 cytokines (p<0.03). The ratios IL-13/IL-10 and IFN-g/IL-10 were significantly higher in cases compared to controls (p<0.03). The Th1/Th2 ratio as measured by IFN-g /IL-13 did not differ between cases and controls.
Discussion: Higher Th1/Th2 cytokine levels at baseline indicate that children with ASD have a generally activated adaptive immune response without significant skewing toward one arm. Relative to increased Th1 and Th2 cytokines, the IL-10 response in cases was significantly decreased. This insufficient IL-10 regulatory response supports the hypothesis of immune dysregulation in ASD.
Sponsors: CAN Foundation. NIH M01 RR 08084 (GCRC)

PS3.23
IMMUNE GLOBULIN ORAL (HUMAN): IMPROVEMENT IN GASTROINTESTINAL DYSFUNCTION AND BEHAVIOR IN AUTISM
Cindy Schneider, Center for Autism Research and Education
Background: Gastrointestinal (GI) dysfunction is commonly reported in autism and may contribute to behavioral symptoms. Autistic GI dysfunction (AGID) may be associated with GI mucosal lining inflammation caused by mucosal immunity dysfunction. Immunoglobulin G has demonstrated benefit in a range of immune-mediated conditions.
Objectives: We investigated the potential of Immune Globulin oral (human) (IGOH) to improve AGID (primary end-point) and behavioral symptoms (secondary end-point) in autistic children.
Methods: Twelve children aged 3-7 years, diagnosed with autism, and with chronic AGID received IGOH daily (420 mg) for 8 weeks. AGID was assessed using the GI Severity Index (GSI), and behavior using three different assessment scales at weeks 4 and 8, and 30 days post study. Adverse events were reported using NCI Common Toxicity Criteria (version 2.0).
Results: Fifty percent (6/12) of children had a positive response to IGOH; 42% (5/12) experienced clinical remission of GI symptoms. AGID significantly improved throughout the study. Median GSI decreased from 10 (7-12) at baseline to 6 (1-11) at week 4 (p=0.0074), and further to 4.5 (1-9) at week 8 (p=0.0024). Behavior also significantly improved by week 8. Overall, IGOH was well tolerated.
Conclusions: IGOH could improve AGID and behavioral problems in autistic children. An ongoing Phase II, dose-response trial involving 120 subjects (2-18 years old) with AGID will investigate this further.

PS3.24
DETECTION OF AUTOANTIBODIES TO NEURAL CELLS IN THE PLASMA OF PATIENTS WITH AUTISM
Sharifia Wills, Paul Ashwood, Jeff Bennet, David Amaral, Judy Van de Water*, University of California, Davis
Autoantibodies directed to various 'self' neural proteins have been reported in a subgroup of subjects with autism spectrum disorders (ASD) and are proposed to contribute to abnormal neurodevelopment. Using a two-pronged approach, we sought to identify the presence of autoantibodies to adult human brain protein(s) in the
plasma of subjects with ASD enrolled in a population based case controlled study. Western blot analysis using human brain region-specific lysates was performed with plasma obtained from patients with ASD, typically developing age-matched controls, siblings of children with ASD, and children with other developmental disabilities. Immunohistochemical staining of coronal brain sections obtained from the macaque monkey (Macaca fascicularis) was performed to identify specific cellular targets against which the 'self' reactive antibodies are directed. By Western analysis, plasma autoantibodies to specific proteins were observed against regions of the limbic system as well as the cerebellum in the ASD group compared to the control groups. Immunohistochemical analysis has thus far been confined to the cerebellum. Strong and selective immunoreactivity was noted in the plasma from 42% of children with autism towards what appear morphologically to be Golgi cells in the granular layer of the cerebellum. Such staining was absent in plasma from both the typically developing and disease controls. Staining has also been observed in the neocortex and other brain regions; a more comprehensive analysis of the targets of this staining is underway. Identification of the brain-specific autoantigens will help illuminate which brain structures and/or neurodevelopmental processes may be affected in patients with ASD.

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PS3.25
FETAL TESTOSTERONE AND AUTISTIC TRAITS
Bonnie W Au yeung, Simon Baron-Cohen, Emma Chapman, Rebecca Knickmeyer, Kevin Taylor, Gerald Hackett, Autism Research Centre, Cambridge University

Background: Studies suggest that autism may be an extreme of certain sexually dimorphic traits, an "extreme male brain", defined psychometrically. Anamnestic endocrine studies suggest that fetal testosterone (FT) levels shape the brain as either a 'male brain type' or a 'female brain type', and several lines of evidence suggest that high levels of FT may be a risk factor for autism.

Objective: To investigate whether a relationship exists in a between FT and autistic traits, measured by the Childhood Asperger Syndrome Test (CAST).

Method: FT levels were measured in amniotic fluid, obtained from pregnant women following routine amniocentesis and who were consenting to participate in a longitudinal child development study. At follow-up, the CAST, a 31-item screening instrument for Autism Spectrum Conditions, was administered to n = 227 of these women to answer on behalf of their children (91 females, and 136 males). Children's ages ranged from 5.46 years to 9.39 years (M=7.54, SD=.96).

Results: Sex differences on the CAST were found, with males scoring higher than females. Higher levels of FT positively correlated with a higher score on the CAST, even when controlling for the effect of sex.

Conclusion: These findings support the fetal androgen theory (Baron-Cohen et al, 2005) that high levels of FT are a risk factor for autism.

Sponsor: Nancy Lurie Marks

PS3.26
NO EVIDENCE OF PERSISTING MEASLES VIRUS IN PERIPHERAL BLOOD MONONUCLEAR CELLS FROM CHILDREN WITH AUTISTIC SPECTRUM DISORDER
Yasmin L D'Souza, Eric Fombonne, Brian J Ward, Division of Infectious Diseases, McGill University Health Center (MUHC)

BACKGROUND: Claims of an association between measles, mumps and rubella vaccination (MMR) and the development of autism spectrum disorder (ASD) are based primarily on the identification of measles virus (MV) nucleic acids in tissues and body fluids by PCR. These data come almost exclusively from a single group of investigators, Uhlmann and colleagues (Mol Pathol 2002; 55: 84-90).

OBJECTIVES: We sought to replicate the PCR assays used by Uhlmann et al. to determine whether or not MV nucleic acids persist in children with ASD compared with non-ASD children.

METHODS: We recruited 54 children with ASD and 34 developmentally normal controls referred to the Montreal Children's Hospital. Peripheral blood mononuclear cells (PBMC) were isolated and up to three real-time reverse-transcriptase PCR (RT-PCR) assays were performed. These assays targeted the N, F and H genes of MV using the primer pairs published by Uhlmann et al., with detection by SYBR Green I. Amplicons from positive reactions were sequenced.

RESULTS: The Uhlmann primer-based assays gave rise to a large number of positive reactions in both groups. For example, a positive signal was observed in 93% of ASD samples and 100% of the control samples using the F gene assay. Almost all of the positive reactions in the assays were eliminated by melting curve analysis and amplicon band-size on agarose gels. The amplicons for the remaining positive reactions were cloned and sequenced. No sample from either ASD or control groups was found to contain nucleic acids from any MV gene.

CONCLUSION: There is no evidence of MV persistence in the PBMC of children with ASD.

PS3.27
ELEVATED RATES OF ANDROGEN-RELATED DISORDERS IN WOMEN WITH AUTISM SPECTRUM CONDITIONS
Erin Ingudomnukul, Simon Baron-Cohen, Sally Wheelwright, Rebecca Knickmeyer, Autism Research Centre, Department of Psychiatry, University of Cambridge

Background: Several lines of research suggest a link between testosterone and autism spectrum conditions (ASC), including the 4:1 male:female ratio in ASC, lower 2D:4D finger ratios in individuals with ASC and their parents, and correlations between fetal testosterone (FT) and the development of autism-related traits such as eye contact, language development, and social difficulties in childhood.

Objectives: To investigate whether women with autism have an increased rate of androgen-related medical
conditions, and to see whether mothers of children with autism show similar abnormalities as part of the 'broader autism phenotype'.

Methods: A medical questionnaire was completed by 54 women with ASC, 74 mothers of children with ASC, and a control group of 185 mothers of typically developing children.

Results: Compared to the control group, women with ASC reported more androgen-related symptoms and conditions, including polycystic ovary syndrome (PCOS), hirsutism, severe acne, irregular menstrual cycle, and unusually painful periods. Mothers of children with ASC reported increased family history of androgen-related medical conditions such as growths, tumours, or cancers of the breasts, ovaries, or uterus.

Conclusion: These preliminary results are consistent with previous studies linking ASC and autism-related traits to testosterone and suggest current hormone abnormalities in women with ASC that merit further investigation.

Sponsor: Nancy Lurie Marks Foundation and Medical Research Council

PS3.28
BODYMASS INDEX IN CHILDREN WITH AUTISM AND TYPICAL CONTROLS
Craig J Newschaffer, Li-Ching Lee, Center for Autism & Developmental Disabilities Epidemiology, Bloomberg School of Public Health, Johns Hopkins University

Background: Little data are available on body mass index (BMI) in children with autism.

Objective: Report on cross-sectional patterns in BMI from ages 3 to 17 in children with autism and typical controls selected from a national sample survey.

Methods: Subjects were selected from the National Survey of Children’s Health, a random probability sample of 102,353 US children (ages 0 to 17). All data, including height and weight, were self-reported by parents/guardians on telephone interviews. A total of 483 children were identified as having an autism diagnosis. Controls were 58,953 children without report of autism, ADHD/DD, learning disability, or other medical conditions. Regression models were fit to test for differences in BMI across autism/control groups and to assess whether this association was modified by gender or age.

Results: Median and inter-quartile range of BMI values for ages 3-5, 6-11, 12-17 in autism and the typical control group, respectively, were: 17.29 (15.25, 21.00) and 17.09 (15.25, 19.77); 19.38 (16.47, 23.04) and 18.20 (15.62, 21.42); 22.80 (19.37, 26.45) and 20.90 (18.88, 23.62). Differences between autism and typical controls were not statistically significant at the p<0.05 level, nor was there statistical evidence suggesting BMI differences depended on age or gender.

Discussion: BMI in children with autism might be expected to differ from that of typical controls because of dietary patterns, opportunities for physical activity, and metabolic factors. Although at older ages children with autism were slightly heavier than controls, the difference was not beyond what could be expected due to chance variation.

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PS3.29
SUPPLEMENTS FOR CHILDREN WITH AUTISM
Patricia Stewart, Emily Healy, Jennifer T Foley, Eileen Blakely, Robin Peck, Danielle D Morris, Susan L Hyman, University of Rochester, Department of Pediatrics

Background: Supplement use is common in young children and may be more common in children with autism spectrum disorders (ASDs) as complementary therapy or to prevent deficiencies due to selective food intake or restrictive diets (e.g. Gluten/Casein free).

Objectives: To examine the nutritional content of supplements for children with and without ASDs.

Methods: The nutrients in supplements marketed for children with or without ASDs (15 formulations each) were compared to the Dietary Reference Intake (DRI) and TUL (Tolerable Upper Limit - the highest daily nutrient intake without likelihood of risk of adverse effects.) for children ages 1-3 and 4-8 yrs and to NHANES and CSFII data.

Results: Children’s vitamins often exceeded both the DRI (Vitamins A, D, C, Bs, Fe, Mg, Mn, and Zn) and TUL (Vitamins A, C, Niacin, B6, Folic Acid, Mg, Mn, and Zn). Products specifically marketed for children with ASD exceeded the DRI and TUL more frequently and to a greater degree. Based on NHANES data, average dietary intake is sufficient to meet the DRI for key nutrients in young children without supplementation.

Conclusions: Children ages 1-3, when ASDs are first diagnosed, are particularly at risk for receiving excess vitamin/mineral intake. The values used in nutrient labeling are often reported as Daily Value based on a 2000 calorie diet. This exceeds the requirements of young children. Known side effects for nutrient intake beyond the TUL include changes in appetite, neurologic changes, and diarrhea. Pediatricians should inquire about supplement intake and caution families about potential adverse effects. Research on the effects of food fortification and supplements in children is needed.

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PS3.30
PERSISTENT ILEAL MEASLES VIRUS IN A LARGE COHORT OF REGRESSIVE AUTISTIC CHILDREN WITH ILEOCOLITIS AND LYMPHONODULAR HYPERPLASIA: REVISITATION OF AN EARLIER STUDY
Steve Walker, Karin Hepner, Jeffrey Segal, Arthur Krigsman, Wake Forest University School of Medicine

Background: Autistic enterocolitis, consisting of a nonspecific ileocolitis coupled with ileocolonic lymphonodular hyperplasia (LNH), was first introduced as a new, potentially virus-induced disease entity eight years ago in a group of ASD children with developmental regression.

Objectives: The primary objective of this study was to...
examine ileal biopsy tissue in a large cohort of pediatric patients who carry a diagnosis of regressive autism and whose chronic gastrointestinal symptoms warranted diagnostic endoscopic evaluation, for evidence of measles virus RNA.

Methods: Patients who had been diagnosed with autism and who were referred to a pediatric gastroenterologist for evaluation of chronic GI symptoms were eligible to participate in this IRB approved study. For each patient, medical histories, vaccination records, histopathology reports, and ileocolonoscopic biopsy tissue were available for evaluation. Terminal ileum (TI) biopsy tissue was assayed by RT-PCR for the presence of measles virus RNA and PCR-positive samples were sequenced.

Results: Medical and clinical data have been collected for >275 patients who fit the study inclusion criteria. PCR analysis on TI biopsy tissue from an initial 82 patients showed that 70 (85%) were positive for the F gene amplicon. Fourteen have been verified by DNA sequence and an additional 56 amplicons are being sequenced now. Work is ongoing to assay the remaining specimens (~200) and to identify and assay relevant control tissue samples.

Conclusions: Preliminary results from this large cohort of pediatric autistic patients with chronic GI symptoms confirm earlier findings of measles virus RNA in the terminal ileum and support an association between measles virus and ileocolitis /LNH.

Sponsors: ARI; NAA; individual donations

PS3.32
THE RELATIONSHIP OF EPILEPSY AND IQ IN AUTISM SPECTRUM DISORDERS AND NON-SPECTRUM DEVELOPMENTAL DELAY. Sarah J. Spence, Rochelle Caplan, Aimee N. Sullivan, Shanping K. Qui, Gotham O. Kuite, Catherine Lord, UCLA

Objective: Data regarding the presence of EPILEPSY in children with autism spectrum disorders (ASD) and non-spectrum developmental delays (DD) were analyzed to explore the relationship among epilepsy, IQ, and autistic behaviors.

Methods: We studied 197 subjects (ages 12-16) from a well-characterized longitudinal sample collected by Dr. Lord who were referred for either Autism Spectrum Disorders (ASD) or Developmental Delay (DD). Verbal and non-verbal IQ (VIQ and NVIQ) and autism diagnostic testing (ADI-R, ADOS) scores from age 8-12 were analyzed. Presence/absence of EPILEPSY (>1 unprovoked seizure) was determined by chart review confirmed with interview. ASD and DD subjects with and without EPILEPSY were compared on IQ and measures of autistic behavior.

Results: The prevalence of epilepsy was similar in the ASD and DD groups (13% vs 15%). Seventeen percent of the ASD patients with EPILEPSY had significant brain malformations. EPILEPSY was associated with lower VIQ and NVIQ in both the ASD and DD groups. EPILEPSY was not associated with more prevalent autistic behaviors in the ASD group, but a trend for increased autistic behaviors in the DD EPILEPSY group was seen. The only notable difference between the ASD and DD groups with EPILEPSY was that the number of ASD EPILEPSY patients with VIQ<50 (14/17) was non-significantly higher than the DD EPILEPSY group (3/6).

Conclusions: EPILEPSY is associated with lower IQ scores both in ASD and nonspectrum DD groups. However, the increased number of patients with low VIQ scores in the ASD group might suggest that epilepsy has more of an impact on verbal function in autism.

Sponsor: This work was performed at the University of Michigan Autism and Communication Disorders Center (UMACC) and supported by a grant from the NICHD as part of the CPEA.

PS3.33
EEG CORRELATES OF LOW DREAM EMOTIONS IN ADULTS WITH AUTISTIC SPECTRUM DISORDERS. Anne-Marie Daoust, Félix-Antoine Lasignan, Claude MJ Braun, Laurent Mottron, Roger Godbout, Centre de recherche Fernand-Seguin & Neurodevelopmental Disorders Program, Hôpital Rivière-des-Prairies, and Dept. Psychiatry, Université de Montréal

Introduction: Difficulties in identifying and/or describing emotions are part of the Autistic Spectrum Disorder. We compared high functioning adults with ASD and controls on dream reports collected from REM sleep awakenings as well as on REM sleep Alpha EEG activity, an electrophysiological correlate of dream content.

Methods: Twelve persons with ASD and normal IQ (11M, 1F, 21.2±1.3 years) and 11 controls (10M, 1F, aged 21.9 ± 0.9 years) spent three nights in a sleep laboratory. REM sleep EEG was recorded with a 22-electrode montage, and Alpha activity (8-12 Hz) was extracted by spectral analysis. Transcripts of dream narratives obtained following REM sleep awakenings were scored according to standard methods. Groups were compared with Mann-Whitney U-tests. Spearman’s rho tested the correlation between EEG and dream emotions.

Results: Compared to controls, dreams of ASD participants contained significantly fewer words, a lower frequency of emotional elements and ASD participants used less words than control to express emotional elements. Both groups of participants showed a positive correlation between dream emotion scores and Alpha activity over centro-posterior areas (rho = .002 to .04). ASD participants showed significantly lower Alpha activity over midline and parasagittal areas, and higher Alpha activity over more lateral areas compared to controls (p = .0004 to .04).

Conclusions: ASD participants report less emotional content in their dreams. The relationship with REM sleep centro-posterior Alpha EEG activity may provide a neurophysiological support for the differences in dream content between persons with ASD and typically developed individuals.

Supported by FRSQ and CIHR

PS3.34
CONDUCTING SUCCESSFUL POLYSOMNOGRAMS IN CHILDREN WITH
AUTISM SPECTRUM DISORDERS Lynnette Marie Henderson, Karen L Adkins, Peter J Howard, Mark L Harvey, Susan G McGrew, Wendy L. Stone, Beth A. Malow, Vanderbilt University

Background: The performance of overnight polysomnography (PSG) is a critical part of research on sleep in children with autism spectrum disorders (ASD). Researchers have been concerned whether children with ASD would comply with and assent to the completion of PSG.

Objective: Determine the percentage of children with ASD who would complete an overnight PSG and develop supports to promote their success.

Methods: Children between the ages of 4 and 10 years whose ADOS and PPVT-III assessment scores placed them on the autism spectrum with average or better cognitive skills were invited to participate in the home and inpatient PSG. The PSGs were augmented with data from sleep diaries and actigraphy, each of which was collected for 7 days. Experienced professionals with behavioral training worked with the parents to individualize the supports. Supports included tactile desensitization games, staff-created picture books using a ‘social story’ approach, and individualized reinforcements.

Results: 22 children (92%) who were seizure-free and medication-free have completed the home PSG and two nights of inpatient PSG. One child completed the home study but not the 2-night PSG and one child withdrew assent for night 2 of the PSG.

Conclusion: Children with autism can successfully complete PSG with the proper supports.

Sponsor: VUMC Discovery Grant & NAAR

PS3.35
ENVIRONMENTAL CHEMICALS AS A POSSIBLE CAUSE OF AUTISM AND OTHER DEVELOPMENTAL DISORDERS: MONKEY BEHAVIOR RESEARCH Yoichiro Kuroda, Takayuki Negishi, Takumi Takasuga, Takaaki Shoda, Junko Kimura-Kuroda, Tomoko Tashiro, Yasuhiro Yoshikawa, Tokyo Metropolitan Institute for Neuroscience

Background: Intake of polychlorinated biphenyls(PCBs) in Yu-Cheng accident caused cognitive and other deficits in children born to exposed mother. Low doses of PCB congeners were found in CSF comparing to PCBs. In eye contact test, there seemed to be no significant correlation between eye contact frequency and total PCBs level of mother. A male offspring born to mother contaminated the highest PCBs showed the lowest score in the finger maze learning test. Total analysis also showed a negative correlation between learning scores and total PCB level in mother blood, both in male and female. These results contrast to no learning deficit in offspring exposed to dioxin(Negishi et al: Toxicol Lett,160:233, 2006).

Conclusion: PCBs and OH-PCBs in the brain can cause cognitive deficit in monkey and human as Yu-Cheng accident. What occurs in other behavioral tests or by other chemicals?

PS3.36
A STUDY OF MERCURY LEVELS IN YOUNG CHILDREN WITH AUTISM USING LABORATORY ANALYSIS OF HAIR SAMPLES P.Gail Williams, Joseph Hersh, Lonnie L Sears, University of Louisville School of Medicine

Autism is a developmental disability characterized by severe, pervasive deficits in social interaction, communication and range of interests and activities. The neurobiologic basis of autism is well accepted, although the specific etiology is unknown. It has been theorized that autism may result from a combination of predisposing genes and environmental factors. While autism has a known association with some environmental factors such as rubella and valproic acid exposure in utero, other proposed environmental mechanisms such as mercury toxicity or other heavy metal exposure have limited research support. Despite this fact, interventions including oral chelation therapy are being used to treat autism after hair, blood or urine samples are analyzed by specialty laboratories. Controls and standards for these laboratories are often unclear with minimal data supporting differences in lab values for children with autism and typically developing children.

Hair samples were obtained from 14 children with autism and 16 controls between the ages of 2 and 6 years. These samples were then sent to Doctors Data Lab where mercury levels were reported. The autism and control groups did not differ significantly in age or gender distribution. Analysis of hair sample data by t-tests for equality of means and equal variance yielded no significant difference in mercury levels for the two groups. Despite the small sample size, results raise questions about the usefulness of evaluation for mercury exposure using hair samples, and about claims of mercury toxicity in children with autism.

Partial support for this study was provided by a
University of Louisville Pediatric Research Foundation grant to PGW

**PS3.37**
**YOUNG ADULT OUTCOME OF AUTISM SPECTRUM DISORDERS** Linda C. Eaves, Helena H. Ho, Sunny Hill Health Centre for Children
Background: Earlier reports indicated poor outcomes, however current young people with ASD had early identification and intervention as well as full inclusion in school and community, thus better results would be expected.
Objectives: To investigate the life of young adults with ASD (59% IQ>50) and to identify childhood factors related to outcome.
Methods: Families of children diagnosed as preschoolers and followed into adolescence were contacted by mail. Of 76 eligible, 48 (63%) participated in a telephone interview about the young person’s health, education and quality of life. Global outcome scores were assigned based on work, friendships and independence (adapted from Lotter, 1974).
Results: At mean age 24.2 (19-31), 23% had good/very good outcome, 31% fair and 46% poor. Parents rated quality of life 5.2 on a 1-10 scale. 69% had been in special school programs. 29% attended post secondary.
Conclusion: Despite far more opportunities, current outcome for young adults with ASD was similar to that traditionally reported. Although no specific beneficial interventions were identified, family attitudes were positive. In other studies, childhood level of functioning tended to predict outcome.

**PS3.38**
**EFFECTIVENESS OF INTENSIVE BEHAVIOURAL INTERVENTION IN A LARGE-SCALE COMMUNITY-BASED PROGRAM FOR CHILDREN WITH AUTISM** Nancy Lynn Freeman, Adrienne Perry, Toronto Preschool Autism Service, Surrey Place Centre
Background: The Ontario provincial government launched a province-wide early intensive behavioral intervention (IBI) initiative in 1999, one of the largest programs of its kind.
Objectives: The purpose of the present study was to examine the outcomes for children at the Toronto Preschool Autism Service, the largest of the 9 regional IBI programs in Ontario.
Method: An analysis was undertaken of the clinical files for all children (N=89) for whom intake and exit assessment data were available. Children were assessed using the Vineland Adaptive Behavior Scales (VABS), the Childhood Autism Rating Scale (CARS), and the developmentally appropriate cognitive measure was available for a subset of children.
Results: As a group following treatment, symptoms of autism were reduced significantly on the CARS. Children also gained significantly in developmental skills on the VABS, doubling the initial rate of learning that they had shown prior to IBI. There was a complex pattern of results, taking into account children’s initial functioning, age, and duration of treatment, such that there were 7 different outcome subgroups. For those children who were below age four at intake and moderate or above in developmental level, the outcomes were particularly impressive. This subgroup of children had a similar pattern of results to the model demonstration projects in the published literature, with a substantial proportion showing average cognitive and diagnostic profiles.
Conclusion: The results of this program evaluation are significant, as they demonstrate that intensive behavioural intervention can indeed be very effective in a community setting, under less than ideal conditions.

**PS3.39**
**ASSESSING PARENT-TRAINING INTERVENTION OUTCOMES USING PARENT-CHILD INTERACTION SAMPLES** Catherine Hambly, Francoise Brosseau-Lapré, Lee Tidmarsh, Eric Fombonne, Montreal Children’s Hospital
Background: Parent-child interactions based on toys and books have not been compared to interactions in songs and games without toys ('people' games)
Methods: Mother-child interactions were analysed for two dyads in a randomized controlled trial (RCT) of the Hanen Centre’s More Than Words program. The children were matched for autism diagnosis and age (34 months), and both had limited word use in initial interactions. Books and toys were provided, but songs and people games were parent-chosen. Three pre- and one post-treatment segments (four 2.5 minute activities each) covering a six month period were transcribed and coded using the CLAN program (Child Language Data Exchange System).
Results: Only songs and people games were associated with changes post-intervention. In songs, both parents (P1, P2) increased their use of the program’s verbal cloze strategies (P1: 0% to 18% of adult turns; P2: 5% to 42%) and hand-over-hand help (P1: 20% to 39%; P2: 27% to 43%); Child 1 increased his nonverbal responses (30% to 60%) and Child 2 increased his verbal responses (8% to 42%). In people games, one dyad showed post-intervention changes. No changes over time were evident in book or toy interactions.
Conclusion: Positive intervention effects were seen in songs and people games but not in toys and books. Further study of all RCT participants is planned.
 treatment director, treatment intensity and duration, age, and sex were examined in order to explain the variability in the composite effect sizes. Center-directed programs were more effective than parent-directed treatments in development of cognitive, language, and adaptive skills. The ABA approach was more effective than the Lovaas approach in development of cognitive and adaptive skills, but yielded comparable ES values to the Lovaas for language. The results for impact of developmental approaches on cognitive and language were inconclusive. The treatment lasted a minimum of 9-14 months for development of cognitive skills, 9-12 months for language development, and 2 years for development of adaptive skills. The intensity of treatment had to be at least 20 hrs/wk for development of cognitive skills, 25 hrs/wk for development of language skills, and over 30 hrs/wk for development of adaptive skills. While children younger than 3 and older than 4 years of age benefited most from instruction in cognitive skills, children made significant gain in language only up to age 4. They had to be at least 3 years of age before they made gains in adaptive skills.

**PS3.42**

**OCCURRENCE OF SPONTANEOUS SOCIAL INITIATIONS CORRELATES WITH FREQUENCY OF ERROR-FREE INTERACTIONS IN CHILDREN WITH AUTISM**

*Helena C.G. Huckabee, Tasha Aper, Erika L. Roths, Emerge, P.C./JFK Partners, UCDHSC*

**Background:** Children with autism generally have significant difficulty spontaneously communicating with others.

**Objectives:** Assess correlations between error-free and failed interactions with subsequent occurrence of spontaneous social initiations.

**Methods:** Initial participants were 13 preschool boys (age 2-5 years) who sought treatment for autism in a university or private setting. Children received intensive Neuropsychological Treatment for autism incorporating principles of Pivotal Response Therapy and Applied Behavior Analysis. Normalized rates of therapists pressing for social interaction and children spontaneously initiating were acquired during bi- or tri-weekly treatment sessions of 2-3 hours duration for approximately 4 months.

**Results:** Frequencies of error-free social interactions (successful response to press) and failed social interactions (absence of child response) were both significantly correlated with subsequent frequency of spontaneous social initiations ($r = 0.38, R^2 = 14\%$ and $r = -0.34, R^2 = 12\%$, respectively). Results suggest children with autism may require high rates of error-free interactions with trained persons to develop skills for initiating to other family members, adults, and peers. Acquisition of social initiation skills was compared with results on standardized assessments at time of diagnosis.

**Conclusion:** Early and intensive individualized treatment may be necessary for acquisition of social initiation skills. Group intervention may not achieve high rates of social interactions necessary to maximize progress.
PS3.43
A COMPARISON OF OPTIMAL OUTCOME CHILDREN WITH A HISTORY OF AUTISM TO HIGH-FUNCTIONING CHILDREN WITH AUTISM
Elizabeth Kelley, Letitia R Naigles, Deborah Fein, University of Connecticut
An earlier study documented continuing pragmatic and semantic difficulties in a group of 5-9-year-old optimal outcome (OO) children with histories of autism (Kelley et al., in press). The current study assessed whether these children had caught up to their typically developing (TD) peers. Fourteen OO children (aged 9-14) were compared to a group of TD peers and a group of children with high-functioning autism (HFA). All children with a history of autism were given the ADOS-G (Module 3) and the ADI-R. All three groups scored within the normal range on standardized tests of language, NVIQ, memory for faces, and executive planning, although there was a tendency for the OO and TD groups to score higher on these tasks than the HFA children. The OO children scored significantly lower than their TD peers on tests of pragmatic language, theory of mind, mental state verbs and categorical induction, although most of these differences disappeared when VIQ was covaried, and they scored higher on these tasks than the HFA group. In addition, none of the OO group and all of the HFA group met the criteria for ASD on both the ADOS and the ADI, while the children in the OO group met criteria for autism by history on the ADI.
Results confirm diagnostic assignment of the OO children, and suggest that they continue to close the gap with their TD peers while showing mild residual deficits in pragmatic and semantic functions.

PS3.44
AUTISM IN ADULTHOOD - PRELIMINARY DATA
Lara Stern, Linyan Meng, Katherine Moxness, Eric Fombonne, Department of Psychiatry, Montreal Children's Hospital
Background: There is a paucity of published studies of autism in the adult population and none in Quebec to date. Objectives: To describe the current situations and developmental pathways of adults with autism in our community and to ascertain predictors of outcome among these individuals.
Methods: Adults over 20 years of age with a diagnosis in the autism spectrum are recruited from 2 of the rehabilitation centres in the Montreal area. Descriptive and historical information is obtained through record review, questionnaires, and informant (parent and caregiver) interview. Measures of current functioning include the Vineland Adaptive Behaviour Scale, Aberrant Behaviour Checklist, and Social Reciprocity Scale.
Results: Data have been collected on 35 subjects (mean age = 33.5 years; range = 21 to 58 years), 27 (77.1%) with Autistic Disorder and the remainder with PDDNOS.
74.3% of the sample is male. 48.6% have a history of epilepsy, 47% have received a comorbid psychiatric diagnosis, and 83% are currently on psychiatric medication. Preliminary analyses indicate a low level of adaptive functioning (mean Vineland Composite age equivalent = 3.02 years; SD = 2.45). Only 6% of the subjects have fluent speech and 40% are without language. Most (65.7%) have moderate or severe mental retardation. The level of current adaptive functioning was found to be significantly lower in those adults who had no language by age 5 years and in those with severe or profound mental retardation as well as in those with a history of epilepsy.
Conclusion: Preliminary findings indicate a relatively low level of functioning in this group of adults. Subject recruitment and data collection is ongoing and will provide further descriptive data for future analyses of correlations and predictors of outcome.

PS3.45
USE OF THE ADOS AMONG CLINICAL AND SCHOOL PSYCHOLOGISTS
Natacha Akshoomoff, Christina Corsello, University of California, San Diego
Background: The ADOS is currently widely available, but little is known about who is using the ADOS, training practices, and how it is used.
Objectives: Examine the reported use of the ADOS and other standardized measures in clinical and school settings.
Methods: The majority of the survey respondents were recruited through the mailing list of individuals who had purchased and ADOS or ADI-R kit or training materials from Western Psychological Services. The survey included questions about ADOS training and use, the use of other standardized diagnostic measures, and demographic information.
Results: Data were collected on 44 clinical and 44 school psychologists. There were no significant differences between the two groups in the types of standardized measures used in assessment or frequency of ADOS use. School psychologists spent significantly more time on an evaluation, were more likely to include a school observation and teacher input, and saw significantly fewer children with autistic spectrum disorders per year than clinical psychologists. The majority of psychologists in both groups had attended clinical training on the ADOS, but very few had attended research training. Qualitative analyses of questions regarding advantages and disadvantages of the ADOS will be presented.
Conclusion: Among this select sample, ADOS training and use appears to be similar between the two groups. Implications for training and accuracy of classification in clinical settings will be discussed.
Sponsor: NIMH K23MH071796

PS3.46
DECISION MAKING PATTERNS OF MOTHERS OF CHILDREN WITH AUTISM
Kara Hume, Indiana University
Professional and popular literature offers parents recommendations when evaluating interventions and making treatment decisions, in an effort to create the most appropriate program. There is little information in the current literature, however, that investigates the efficacy of these recommendations, or the frequency of their usage
by families. Objectives: The purpose of this qualitative research was to describe the process of how mothers make decisions and why mothers select specific interventions, as well as explore the similarities and differences of the decision making process across income level. Two research questions were addressed: (1) How do mothers of children with autism make decisions about treatments and interventions to use with their/for their child? and (2) How is the decision making process similar or different across socio-economic standing?

Methods: Eight mothers of children with autism, of varying economic status, were interviewed about what treatments they have used and are currently using, what information is used to make decisions about interventions, and how they decide when to start or stop a specific intervention.

Results: The results indicated that mothers of higher income make a larger number of decisions about treatments for their children, and that those decisions follow a pattern as children age. Parents of all income levels cited a variety of information sources when considering treatment, and reported that they start/stop interventions in a subjective manner. Disparities between the mothers of high income and the mothers of low income emerged, related to the decision making process, number of decisions made, and the sources of information used.

PS3.47 AUTISMCONNECTS: A VIRTUAL COMMUNITY OF AUTISM STAKEHOLDERS M Frank Huntley, Margaret Spoelstra, M.Suzanne Lewis, Hymie Anisman, Kim Matheson, Jeanette J Holden, ASD-CARC, Frank Huntley/Kingston Software Factory Background: Families affected by Autism are often isolated in their struggle to find support, leading to ineffective service allocation, fewer research opportunities and reduced dissemination of research-based strategies. The virtual community AutismConnects enables families to share their stories, concerns, and opinions more easily, and improves knowledge translation among Autism Community stakeholders (i.e. families, service providers and researchers). It also provides a framework for electronic tools identified by stakeholders as meeting their needs.

Objectives: To examine the longitudinal impact of virtual community participation and tools, and the capacity of the AutismConnects framework to evolve in response to stakeholder feedback.

Methods: We are assessing the system’s outcomes and its flexibility and ability to evolve. Specific longitudinal metrics of stakeholder activities include counts of unique web-site visits and registrations; questionnaire response rates; and measures of unsolicited feedback and structured discussion. Questionnaire data will be used to examine family history, how people cope with stressful events, social support, personality factors, and psychological well-being. Measures of new tools, information sharing opportunities and technology-facilitated partnerships, both with umbrella organizations such as Autism Society Ontario and with individual stakeholders, including families and researchers, will provide estimates of system expandability.

Results and Conclusions: A staggered launch of a series of components began January 5th 2006. We will present results of the first 5 months of AutismConnects, illustrating its impact in areas such as connections among stakeholders, coping strategies, new research questions, especially those informed by the actual daily experience of dealing with autism, and suggestions for how to apply and adapt the ever-emerging new generations of web-based technologies.

FUNDDED BY: CIHR, SSHRC, CFI

PS3.48 INCLUDING STUDENTS WITH AUTISM IN THE GENERAL EDUCATION SETTING: PROGRAM DEVELOPMENT & EVALUATION Caroline Ilona Magyar, Vincent Pandolfi, University of Rochester Background: Increasingly children with autism are participating in general education, requiring school districts to identify effective programs of support. Objective: Evaluate an inclusion program developed to support elementary students with autism.

Methods: Technical assistance was used to develop an inclusion program for 5 students. Program evaluation assessed student and personnel performance, program integrity, and social validity. Student performance was measured at pre-post across several domains using curriculum-based, standardized and criterion-referenced instruments. Repeated measurement was obtained on personnel performance, and post-test ratings on program integrity, quality, and social validity. Descriptive analyses of change scores were examined for student change. Visual inspection of change and absolute scores were used to examine personnel performance, and program integrity and quality.

Results: Student outcome was variable with largest gains noted in adaptive behavior. 4 of 5 students showed progress on IEP goals and several improved on standardized academic testing. One student was removed for significant aggression. Consultant team maintained high performance standards; minimal improvement noted for general education teachers. Program was implemented with good integrity and rated high on quality indicators. Personnel and parents reported high satisfaction.

Conclusion: Quality inclusive programming can be provided to students with autism in general education; however, student outcomes were variable suggesting some students may require additional supports or a modified educational program.

Sponsor: NIH

PS3.49 THE INTEGRATION OF CHILDREN WITH AUTISM IN REGULAR SETTINGS FOLLOWING AN ABA PROGRAM: RESULTS FROM AN OUTCOME MONITORING STUDY Katherine Moxness, Céline Mercier, Nancy Cusson, Myriam
Elia Jimenez, University of California, Los Angeles
Siller, Marian
Sigman, Amanda Chinchilla, Ted Hutman,

PARENT-TRAINING INTERVENTION
EFFECTIVENESS OF AN EXPERIMENTAL
IN AUTISM: A PILOT STUDY TESTING THE
FACILITATING PARENT-CHILD INTERACTION

PS3.50

FACILITATING PARENT-CHILD INTERACTION
IN AUTISM: A PILOT STUDY TESTING THE
EFFECTIVENESS OF AN EXPERIMENTAL
PARENT-TRAINING INTERVENTION

Michael Siller, Marian Sigman, Amanda Chinchilla, Ted Hutman,
Elia Jimenez, University of California, Los Angeles

Background: Previous longitudinal research has shown that the success of the parent-child dyad to manage a shared interest in objects/ events during play reliably predicts the language development of children with autism (Siller & Sigman, 2002).

Objectives: To evaluate whether mother-child interaction can be modified using an experimental intervention.

Methods: Eleven children with autism (CA=60 months; LA=15.5 months) and their mothers were invited to participate in a manualized experimental parent-training intervention that included 12 in-home training sessions. Prior to each session, 9 minutes of mother-child interaction were videotaped and coded for the duration of joint engagement (Bakeman & Adamson, 1984).

Children's language abilities were evaluated at intake, exit, and 12-month follow-up.

Results: To evaluate session-by-session change in joint engagement, we fit a simple multilevel model of change. Results indicate that the duration of joint engagement increased significantly from 264 seconds (session 1) to 322 seconds (session 12), F=4.7, p<.05. In addition, findings indicate that the magnitude of improvements in joint engagement was associated with gains in language observed during the 12-month follow-up period.

Conclusions: This pilot study suggests that play interactions between children with autism and their mothers can be effectively modified; further, improvements in joint engagement were associated with subsequent gains in language.

Funding: CPEA Grant HD-DCD35470; M.I.N.D. Institute; STAART Grant U54-MH068172

PS3.52

FACTORS PREDICTING DELAY IN SEEKING
SERVICES AMONG EARLY INTERVENTION
REFERRALS

Anna Marie Warszawa, Jennifer Pinto-Martin, Lisa Marie Young, Ellen Giarelli, Susan Levy, University of Pennsylvania School of Nursing, Center of Autism and Developmental Disabilities Research and Epidemiology

Background: There is some data to suggest that parents of children with ASD-like developmental concerns do not pursue early intervention (EI) referrals.

Objectives: To investigate factors predicting parent delay in follow up on EI referrals.

Methods: Demographic and newborn data was abstracted from 89 charts flagged for developmental concerns. The types of developmental concerns, their source, and physician referral were noted. The chart was then searched for evidence indicating whether the referral was pursued. Subsequent well-child visits were abstracted for data on persistence of developmental concerns and referral outcomes.

Results: Of the forty-nine children who were referred to EI, thirty parents did not pursue services. Parents of children who did not follow-up on physician referral were younger than those who did (22.5 versus 25.6). If there were no other children in the home, the parent was more likely to follow-up on EI referrals (50% versus 36.2%). Of those who did not follow-up when the concerns were first noted, only 25% eventually pursued EI.

Conclusion: Preliminary findings show that certain characteristics relate to delay in follow-up on EI referral. Compliance may improve with anticipatory guidance. Further data collection will allow for the assessment of the statistical significance of these findings.

Sponsor: Centers for Disease Control and Prevention*
Background: It is well documented that children with autism (CWA) have difficulty interpreting social cues. Our previous work has indicated similar difficulties making inferences using arbitrary cues.

Objectives: To investigate attention, memory, association and inference as possible factors contributing to difficulties in making inferences from cues.

Methods: Four tasks were completed by each child. These are modifications of an Attention Network Task, a Corsi Span task, a Paired Associate Learning task and an inference task.

Results: Participants are 20 CWA, 20 typically developing children (TDC) and 20 children with moderate learning difficulties. Groups were matched for receptive verbal ability and non-verbal ability. Preliminary analyses of 20 CWA and 18 TDC indicates no significant difference in performance on the memory, associative learning and inference tasks. However, analysis reveals that fewer children with autism show an alerting effect than an orienting effect in the attentional task. Further analysis including the age and ability matched control group will reveal whether memory, associative learning and inference abilities are specifically delayed in autism. In addition the relationship between factors and their impact on inferential skills will be examined.

Conclusion: Preliminary findings of this study indicate some attentional deficits in autism. Further analysis will explore the relationship between autism and learning difficulties, and attention, memory, association and inference. Results will be discussed in terms of the impact that these abilities and deficits may have on the ability to make inferences from cues.

Sponsor: Medical Research Council

PS3.54
ADAPTABILITY AND COGNITIVE STYLE: TWO DIMENSIONS TO THE CHARACTERISATION OF CENTRAL COHERENCE IN TYPICAL DEVELOPMENT AND ASD
Rhonda Denise Lowsley Booth, Francesca G E Happé, Institute of Psychiatry, King's College London

Objective: To characterise individual performance on measures of central coherence that cross processing-level/modality and demands for local/global processing.

Methods: A battery of coherence tasks (high-level and low-level, spanning visuo-spatial and verbal/auditory modalities) was administered to a TD sample (N=204, aged 8-25), males with ASD and age- and IQ-matched controls (N=31 each group, aged 9-21).

Results: (1) There was evidence of greater detail-focus in ASD versus TD and controls overall, although local bias was not universal in ASD. (2) A characterisation of individual participants into four categories appeared to capture the data best: predominantly local responders, predominantly global responders, good adaptive (respond locally or globally according to which the task favours), and poor adaptive responders. Only the latter two styles were related to IQ in TD and controls, but not in ASD.

Conclusion: Relationships between coherence tasks in ASD were distinct from those in TD and control groups, and suggest that the predominant detail-focused processing style bears a different relationship to global processing in ASD. The implication for models of local/global processing suggest that distinct mechanisms may need to be found underlying individual differences in featural processing and individual differences in global processing, with the two mechanisms not operating in trade-off.

Sponsor: Medical Research Council (UK).

PS3.55
MEMORY INTERFERENCE IN ADULTS WITH ASPERGER’S SYNDROME
Dermot Bowler, John M Gardiner, Sebastian B Gaigg, City University, London

Background: Individuals from the Autism Spectrum consistently experience difficulties in spontaneously using relational information to aid free recall.

Objectives: To assess memory interference as a function of relational encoding and/or retrieval manipulations in adults with Asperger’s syndrome (AS).

Methods: Sixteen adults with AS and 16 matched typical controls participated in four conditions over two sessions. The four conditions differed in terms of whether participants received category cues at encoding, at retrieval, throughout the task or not at all. In each condition participants first studied one list of 24 words followed by a second list of 24 words. Each list contained 6 sets of 4 items taken from the same 6 categories. Interference was assessed by comparing free recall levels for the first and second list.

Results: The AS participants responded similarly to controls to the manipulations of encoding and retrieval instructions, with all groups exhibiting enhanced recall when category labels were available during encoding or throughout the whole task. However, AS individuals showed diminished learning over trials. This was especially marked during the second list of each session. AS individuals were also less likely to cluster words into their respective categories during recall.

Conclusions: Our results support earlier reports of impaired list learning and attenuated use of organising strategies during recall in Asperger’s syndrome. These findings alongside unimpaired and even prolonged interference effects may suggest that recall difficulties in AS are not simply due to a lack of encoding relational information but to a reduced ability to use such information to aid recall.

PS3.56
FOETAL TESTOSTERONE LEVELS PREDICT EMPATHY SKILLS IN CHILDREN
Emma Louise Chapman, Simon Baron-Cohen, Bonnie Auyeung, Rebecca Knickmeyer, Kevin Taylor, Gerald Hackett, Autism Research Centre, University of Cambridge

Background: Empathy is a key cognitive ability in understanding and responding to others and allows us to interact effectively in the social world. Evidence shows there to be empathy impairments in autism spectrum conditions (ASC). According to the Empathising-
Systemising (ES) theory, typical females on average perform better than typical males on measures of empathyising. This sex difference likely doesn’t merely reflect experiential or social factors, but also developmental differences in brain structure. Animal studies suggest differences in brain structure are influenced by early organisational effects of foetal testosterone (FT), and human studies have found FT is inversely correlated with social behaviours such as eye contact in infancy and peer relationships in preschoolers. Male foetuses are exposed to levels of FT 2.5 higher than female foetuses.

Objectives: The aim of this study was to investigate empathising abilities in children whose amniotic measures of FT are known, to see if empathising abilities are inversely correlated with levels of FT.

Methods: 196 children (101 males, 95 females) aged 6-8 years of age were tested on the Empathy Quotient-Child Version (EQ-C) and the 'Reading the Mind in the Eyes' Task-Child Version (Eyes-C).

Results: There was a significant negative correlation between FT and performance on both the EQ-C and the Eyes-C.

Conclusion: These results suggest that whilst empathy may be influenced by postnatal experience, prenatal biology also plays an important role, mediated by androgen receptors in the brain. This has implications for the causes of empathy disabilities, such as ASC, and may help explain increased rates of such conditions among males.

Sponsor: Lurie Marks Family Foundation

PS3.57
THE DETECTION OF HIGH BUT IMPERFECT ENVIRONMENTAL CONTINGENCIES IN CHILDREN WITH AUTISM Jamesie Coolican, Susan E. Bryson, Dalhousie University

Background: Gergely and Watson (1999) propose that an early shift in contingency preference (from perfect to imperfect contingencies) provides a mechanism by which infants become more flexible and able to handle the lack of contingency in the social world. By implication, a failure in the development of this mechanism may underlie the social impairments in autism (Gergely & Watson, 1999).

Objectives: To investigate the hypothesized preference for perfect (vs. high but imperfect) contingencies in young children with autism.

Methods: Boys with ASD (mean age=6.9 yrs; SD=1.7) and developmentally-matched typical controls completed 3 contingency learning tasks: non-contingent (NC), perfectly contingent (PC) and high but imperfectly contingent (HbIC; 80% contingent). Tasks consisted of 20 learning trials, followed by 4 test trials, in which sensitivity to the contingent relationship between visual stimuli was indexed via anticipatory eye movements.

Results: Overall rate of anticipatory eye movements did not differ between groups, although a repeated measures ANOVA yielded a significant interaction between Groups and Conditions (NC, PC, HbIC). Children with ASD exhibited more anticipations during the PC and HbIC tasks, which did not differ, compared to the NC task. In contrast, the typical controls exhibited the opposite pattern (i.e., more anticipations during the NC task).

Conclusion: We found no evidence that children with ASD have difficulty learning High but Imperfect Contingencies, or that they prefer Perfect Contingencies. However, unlike typical controls, who preferred the novelty of non-contingency, children with ASD showed a strong preference for highly contingent relationships, thus providing some support for Gergely and Watson’s (1999) claim.

Sponsor: National Institutes of Health and Nova Scotia Health Research Foundation

PS3.58
THEORY OF MIND AND SYMPTOMATOLOGY IN CHILDREN WITH AUTISM AND TYPICAL DEVELOPMENT Michelle K. DeRamus, Amanda Peltz, Laura Grofer Klinger, Mark R. Klinger, University of Alabama

Background: Children with Autism Spectrum Disorder (ASD) have theory of mind (ToM) impairments but limited research exists on the relation of ToM to symptomatology.

Objectives: This study explored the relation between ToM and ASD symptoms in children with ASD and in typically developing (TD) children. It was predicted that ToM would diminish, or mediate, the relation between diagnosis and symptomatology.

Methods: Participants were recruited from the University of Alabama and the University of North Carolina, Chapel Hill. The ADI-R and the ADOS-G were used to confirm diagnosis. Participants completed four tasks measuring 1st and 2nd order ToM and a measure of grammatical language understanding, the Test for the Reception of Grammar. Parents completed questionnaires measuring social skills and repetitive behavior.

Results: Data were collected on 47 high-functioning children with ASD (mean age=10.9 years; range=6.5 to 16.5 years) and 47 TD children (mean age=10.3 years; range=6.3 to 16.3 years). Analyses indicated ToM was related to grammatical language understanding and repetitive behavior for both groups. A trend was present for a relation between ToM and social impairment symptoms in both groups. ToM mediated the relation between diagnosis and language understanding, but not social impairment or repetitive behavior. This mediation suggested ToM ability, rather than diagnosis alone, influenced level of language understanding in ASD.

Conclusion: Both ToM and diagnosis made independent contributions to the social and repetitive behavior symptoms found in ASD. However, the relation between diagnosis and language understanding was partially explained by level of ToM ability.

Sponsor: NICHD* (R01HD037842)

PS3.59
SELF-AWARENESS IN AUTISM SPECTRUM DISORDER, PATTERN OF ACCURACY IN
MEMORY PERFORMANCE JUDGEMENTS Mette Elmose Eriksen, Francesca Happe, Department of Psychology, University of Aarhus

Background: Investigating metamemory has been suggested as a relevant way to understand self-awareness of persons with autism spectrum disorder (Farrant et al., 1999). One aspect of metamemory is a person’s ability to judge their own ability to remember.

Objectives: To compare accuracy in performance judgements in children with autism spectrum disorder, typically developing children and children with moderate learning difficulties.

Methods: Participants were children with ASD, typically developing children and children with moderate learning disabilities. Participants were presented with a sequence of 6 pictures shown one at a time. Following a short sorting task the participants were asked to select pictures to reconstruct the same sequence (from 6 stimuli and 6 distracters). Judgments of performance were collected before and after seeing the actual stimuli and after task completion. Certainty judgements for each stimulus chosen were collected. Four trials were given using either faces or buildings as visual stimuli. Background information on IQ and mentalising abilities was assessed.

Results: Group differences in recall and group differences in patterns of accuracy judgements will be presented and discussed.

Conclusions: The differences in accuracy judgements and in the application of available information in the task in making these judgements may suggest a difference in awareness of own abilities in ASD.

Funding: Part of PhD. grant.

PS3.60 WHAT AFFECTS OUR MEMORY OF PHOTOS? DO INDIVIDUALS WITH ASD REMEMBER PHOTOS DIFFERENTLY? Megan Freeth, Danielle Ropar, Peter Mitchell, Peter Chapman, University of Nottingham, UK

Background: Research into the importance and salience of eyes and sensitivity to their direction of gaze for individuals with ASD is currently inconclusive. Individuals with ASD display poor joint attention skills (e.g. Leekham et al. 2002) and unusual visual scanning patterns when viewing social interactions (Klin et al. 2002, 2003). However, evidence suggests that the reflexive attention response in relation to an eye-direction cue is similar to that of typical developers (Kylliainen & Hietanen, 2004).

Objective: The research aimed to test the hypothesis that the attention of typically developing individuals will be over-focussed on people in photos and their direction of gaze, thus producing systematic memory biases; in contrast, individuals with ASD are predicted to remember photos more accurately as a result of their attention not being over-focussed on such aspects.

Design/Methods: After being presented with a set of photos on a computer screen - each containing a person sitting on the right or left, either gazing out of the photo or at another object in the photo - sixteen adolescents with autism and sixteen matched control participants were asked to manipulate a second set of photos according to their memory of the originals.

Results: Preliminary findings indicate that typically developing individuals display a systematic memory bias, shifting people in photos to appear more centrally (F (1,7)=25.90, p=0.001). Data from individuals with ASD are still being collected.

Conclusion: memory of typically developing individuals is biased by social aspects of scenes. We anticipate that this effect will be attenuated in individuals with autism.

Sponsor: University of Nottingham, School of Psychology

PS3.61 THE EFFECT OF AROUSAL ON LEARNING AND MEMORY IN ASPERGER’S SYNDROME Sebastian B Gaigg, Dermot M Bowler, City University, London

Background: Although it is well established that individuals with ASD experience difficulties in processing emotional information within the social environment, little is known about how emotional factors impact on other areas of cognition in this disorder.

Objectives: To assess the impact of emotional arousal on learning and memory.

Methods: In Experiment 1, 14 individuals with Asperger’s syndrome and 14 matched typical controls were subjected to a differential fear conditioning paradigm. In this task individuals were presented with different colours of which one (CS) was eventually paired with a startling noise (UCS) while their skin conductance responses (SCR) were monitored. In Experiment 2, groups of 20 participants implicitly studied arousing and non-arousing words while SCR was measured. Memory for these words was tested immediately after presentation, following 1hr and again after one day in order to assess forgetting.

Results: Results from Experiment 1 revealed generally intact fear acquisition in Asperger’s syndrome accompanied by an abnormal pattern of differential acquisition and fear extinction. Experiment 2 revealed that although no group differences existed in terms of SCR or immediate memory, individuals with ASD forgot arousing but not non-arousing items to a greater extent than controls.

Conclusions: The results suggest abnormal modulation of learning and memory due to arousal in ASD, providing further evidence for atypical emotional modulation of behavioural development in this group.

Sponsor: Wellcome Trust

PS3.62 DO INDIVIDUALS WITH AUTISM PROCESS CATEGORIES DIFFERENTLY? THE EFFECT OF TYPICALITY ON THE DEVELOPMENT OF EXPERTISE Holly Gastgeb, Mark S Strauss, Nancy J Minshew, University of Pittsburgh

Background: Categorization is a critical cognitive ability that has received little attention in the autism literature. Studies suggest that individuals with autism can form
categories but do so in a different manner. One unexplored issue is the role of typicality. Typicality plays an important role in categorization from early in life, and reaction times are faster for typical items in verification tasks.

Objective: To look at the nature of the storage of real world category information in individuals with autism across development.

Methods: High functioning adults, adolescents and children with autism (N = 76) and matched controls (N = 70) were tested in a category verification task with common categories (cats, dogs, couches, and chairs) varying in typicality from typical to atypical. Reaction time was measured.

Results: The autism groups differed from the controls in the way that they categorized objects. By adolescence, individuals with autism processed typical and somewhat typical category exemplars as efficiently as controls. However, they experienced difficulty categorizing atypical stimuli across the lifespan evidenced by significantly slower reaction times.

Conclusion: Individuals with autism have difficulty categorizing atypical exemplars of categories and do not develop typical adult levels of expertise. This may relate to differences in processing global information and highlights the need to consider the role that non social cognitive processes may play in autism for future research.

Sponsors: NAAR, NICHD

PS3.63

CONFIRMATORY FACTOR ANALYSIS OF THE WECHSLER SCALES IN HIGH FUNCTIONING AUTISM Gerald Goldstein, D N Allen, Nancy Minshew, Diane Williams, Fred Volkmar, Ami Klin, Robert Schultz, University of Pittsburgh School of Medicine

Background: Child (WISC) and adult (WAIS) tests have been factor analyzed with a 3 factor solution reported in the actual data set were the major statistics used. The above work was supported by grants from: NARSAD, March of Dimes, and a gift from the Spafford and Kirk families.

Methods: Using the standardization samples as baselines, we tested various models for children and adults with HFA. The hypothesis was that the autism groups would demonstrate different goodness-of-fit indices (GFIs) from standardization samples. We employed 1, 2, 3, and variations of a social intelligence 4 factor models. CFA involves testing hypothesized statistical models against actual data sets. GFI between the hypothesized model and the actual data set were the major statistics used. The sample consisted of 137 children and 118 adults with autism, all with IQs of 70 or above.

Results: There wasn't a satisfactory GFI for the 1 or 2 factor models in the national sample or the autism group. For the 3 and 4 factor models, the national samples obtained AGFIs higher than the autism samples. GFIs for the autism subjects were lower for all models than when using the standardization samples even when we evaluated a 'social intelligence' factor.

Conclusion: Despite the existence of a clearly prototypic profile in individuals with autism, there is no indication of a particular model that has comparable GFIs to those obtained by normal individuals. We suggest that the structure of intelligence is significantly different from normal in autism.

PS3.64

IMITATION SKILLS CORRELATED WITH COGNITIVE & ADAPTIVE ABILITIES BUT NOT SYMPTOMS IN AUTISTIC DISORDER (AD) Dina E Hill, Brian R Lopez, Robert J Thoma, Jeffrey D Lewine, Center for Advanced Medical Technologies, University of Utah

Background: Imitation impairments have been proposed as a core deficit in Autistic Disorder (AD). Research has identified relationships between imitation and AD symptoms, play, and language skills.

Objectives: To examine the associations between imitation skills, cognitive functioning, and AD symptoms in a group of young children with AD.

Methods: Twenty nine children (25 boys; mean age=67 months, range: 41-130 months) with AD were recruited as part of a larger study. The diagnosis of AD was confirmed with the ADI-R and the ADOS-G. Children underwent cognitive (Mullen Scale of Early Learning), imitation (PEP-R imitation subscale: PEP-R:I), and adaptive assessment (Vineland Adaptive Behavior Scales) over multiple sessions.

Results: In a multiple regression, PEP-R:I was the dependent variable and the Vineland ABC, the MSEL: Visual Reception subtest, and the ADOS total scores were independent variables. The overall regression was significant (F(28)=29.14, p<.001). There were significant independent effects for both Vineland ABC (beta=.29, p=.02) and MSEL: Visual Reception (beta=.68, p<.001) scores. However, there was no relationship between PEP-R:I and ADOS-total scores (p=.69).

Conclusions: Imitation skills not related to the degree of autistic symptoms, but rather are highly related to level of cognitive and adaptive functioning.

The above work was supported by grants from: NARSAD, March of Dimes, and a gift from the Spafford and Kirk families.

PS3.65

SUBJECTIVE PERCEPTION DOES NOT MODULATE EARLY VISUAL PROCESSING OF AMBIGUOUS PICTURES IN HIGH FUNCTIONING AUTISTIC INDIVIDUALS Boutheina Jemel, Anthony Hosein, Jacob A Burack, Laurent Mottron, Centre de recherche Fernand-Seguin, Hôpital Rivière-des-Prairies, and Dept. Psychiatry, Université de Montréal

Background: Activity in high-order visual areas is not solely dependent on the retinal image but can be modulated by high-cognitive effects such as subjective perceptual experience and other cognitive factors.

Besides, there is now increasing evidence suggesting that
perception in autism is less influenced by such high cognitive factors.

Objectives: Investigate the extent to which subjective perception modulates brain responses to ambiguous figures in adults with High Functioning Autism (HFA) by using event-related potential measures.

Methods: Ten HFA subjects and ten IQ and age-matched controls were shown 1) Arcimboldo and Arcimboldo-like portraits (ambiguous figures made up of a variety of painted objects, composed to form a human likeness), 2) paintings depicting human faces, and 3) objects and still life paintings while recording their EEG activity (59-channels). Subjects were asked to report their first impression when seeing each painting by pressing a key-button to indicate whether they perceived a face or an object.

Results: Overall, paintings depicting faces only evoked a larger N170 component than paintings depicting objects only, in both typically developing participants and HFA subjects. Interestingly, the amplitude of the N170 component elicited by ambiguous figures (Arcimboldo portraits) was larger when the participants’ subjective perception was that of a face than that of an object. This modulation of the N170 component by subjective perception was observed in typically developing participants only and not in HFA subjects.

Conclusion: The absence of any effect of subjective perception on early brain responses in autism suggests that the N170 ERP response, and thus perception in autism is immune to high-order cognitive factors.

Sponsor: NAAR grant (BJ)

PS3.66
VISUAL GAZE IN EXOGENOUS ORIENTING IN ADOLESCENTS WITH AUTISM SPECTRUM DISORDER
Christopher Klein, Lisa Glover, Mark R Klinger, Laura G Klinger, University of Alabama

BACKGROUND: Persons with Autism Spectrum Disorders (ASD) have shown impairments in their ability to automatically shift attention to a peripheral (i.e., exogenous) cue. However, it is unknown if this is because persons with ASD are less likely to notice and orient to peripheral cues or whether they are simply slower to orient.

OBJECTIVES: Use eye-tracking to measure the orienting behavior of adolescents with ASD and typical development (TD) on an exogenous cueing task.

METHODS: Participants were recruited through the University of Alabama Pervasive Developmental Disorders Clinic. Diagnosis was confirmed with the ADI-R and ADOS-G. Participants’ visual orienting was recorded through eye-tracking while they completed an exogenous cueing task, where the cues were either valid or invalid. Percentages of shifts to cues and average time to shift were calculated for both individuals with ASD and TD.

RESULTS: Preliminary analyses indicate that TD adolescents (N=6) were more likely to shift their attention to the cue (97%) than the adolescents with ASD (N=6) (77%). Results also showed that when they shifted their attention, adolescents with ASD did so at a similar speed (315ms) to those with TD (305ms).

CONCLUSION: Preliminary findings show that individuals with ASD have difficulty shifting attention to peripheral cues, but do so at relatively typical speeds when the cues are detected.

PS3.67
AUTOMATIC AND CONTROLLED SEMANTIC PRIMING IN PERSONS WITH AUTISM SPECTRUM DISORDERS AND TYPICAL DEVELOPMENT
Mark R Klinger, Chris Klein, Laura Klinger, Xavier Sonnerat, University of Alabama

Background: Individuals with Autism Spectrum Disorders (ASD) seem to have atypical methods of organizing information about the world. However, there are few studies describing how their semantics processes differ.

Objective: This research used a common cognitive task, semantic priming during a lexical decision task, to measure automatic and controlled semantic activation processes in persons with ASD and typical development (TD).

Methods: Participants were recruited from the University of Alabama PDD Clinic. The ADI-R and the ADOS-G were used to confirm diagnoses. Participants reaction time to judge whether letter strings represented words or not was measured. Each target word was preceded by a semantically related or unrelated priming word.

Automatic priming processes were studied by using a short (Experiment 1: 250 ms) interval between the start of the prime and start of the target. Controlled priming processes were studied by using a long interval (Experiment 2: 2000 ms).

Results: Thus far, data have been collected on 21 high-functioning children with ASD and 21 TD children (range=11 to 20 years). Priming was measured as faster responding to related prime trials compared to unrelated trials. Participants with TD showed semantic priming at both the short and long interval conditions. However, participants with ASD only showed significant priming at the long delay. Additionally, the short interval priming was significantly greater for TD than ASD participants.

Conclusion: Participants with ASD seem to possess semantic knowledge linking words. However, these relationships do not seem to be automatically activated as they are for TD persons.

Sponsor: NICHID(R01HD037842)

PS3.68
HIGH FUNCTIONING INDIVIDUALS WITH AUTISM SHOW EXCESSIVE CONTINGENT ATTENTIONAL CAPTURE IN A VISUAL TASK
Emilie Leblanc, Laurent Mottron, Pierre Jolicoeur, Jacob A. Burack, CERNEC, Université de Montréal

Background: Autism is associated with deficits in visuospatial attention, involving impaired regulation of attentional focus (Minshew et al, 1999), and with enhanced low-level perceptual processing, generating high bottom-up salience of stimuli (Mottron et al, 2006).

Objective: Explore the interaction between attentional and
perceptual aspects of processing in adults with autism or Asperger syndrome with a contingent attentional capture paradigm.

Method: The participant groups included 10 HFA participants, 10 individuals with AS, and 10 TD individuals, all matched on IQ and age. The task involved reporting the identity of a target-coloured digit embedded in a central rapid visual presentation stream of nontarget-coloured digits. Attentional capture was induced by presenting two peripheral distractors before the target appeared. Three distractor conditions were used: two grey distractors, one grey and one nontarget-coloured distractor, and one grey and one target-coloured distractor.

Results: Both the AS and the TD groups exhibited the typical contingent capture pattern of intact performance on the grey and nontarget-colour distractor conditions, but impaired performance with target-coloured distractors. The HFA group displayed a similar pattern of performance as the other two groups in the grey distractor condition, however, the amplitude of the contingent capture effect was much larger, and an interference effect was found in the nontarget-colour distractor condition.

Conclusion: HFA individuals appear to show an attentional deficit that might involve either the interaction between top-down controls needed to filter items that are irrelevant in terms of both colour and location or excessive bottom-up processing of physical attributes of stimuli.

Sponsor: CIHR

**PS3.69**

**EPISODIC MEMORY, THEORY OF MIND AND SELF-AWARENESS IN AUTISTIC SPECTRUM DISORDER** Sophie Elizabeth Lind, Dermot M Bowler, City University

Background: Autistic Spectrum Disorders (ASDs) are associated with diminished episodic memory and relatively intact semantic and procedural memory. Episodic memory is thought to depend upon a number of underlying cognitive capacities including temporally extended self-awareness (autonoetic awareness) and metarepresentational ability.

Objectives: To establish the possible antecedents of episodic memory impairments in ASDs.

Methods: Seventy-six children with ASDs, aged between 5- and 16-years, took part in a battery of tests over four sessions. Language was assessed using the British Picture Vocabulary Scale and a measure of complement syntax. A series of four tests of mental state understanding were also used to assess understanding of the relationship between perception and knowledge, false-belief and deception. Temporally-extended self-awareness was measured using the delayed video self-recognition paradigm. Finally, episodic memory was assessed using a measure of source memory.

Results: Temporally extended self-awareness is correlated with episodic memory even when developmental language level and recognition memory are partialled out. Control data are currently being gathered from both typically developing children and children with intellectual disabilities.

Conclusion: Episodic memory impairments in ASDs may be due, at least in part, to impairments in temporally extended self-awareness.

Sponsor: City University, Department of Psychology.

**PS3.70**

**DISCREPANCY BETWEEN VERBAL AND NONVERBAL ABILITIES AND CURRENT SYMPTOM SEVERITY IN AUTISM SPECTRUM DISORDERS** Tom Loucas, Gillian Baird, Susie Chandler, Tony Charman, Emily Simonoff, Andrew Pickles, School of Psychology and Clinical Language Studies, University of Reading

Background: Greater social impairment is reported in autistic individuals with a nonverbal advantage.

Objectives: Investigate relationships between cognitive profiles and symptom severity in children with special educational needs with and without PDD.

Methods: A population representative sample of 255 nine to 14 year olds with SEN were given ICD-10 diagnoses (Autism, Other PDD and No PDD) using information from ADI-R, ADOS-G and other sources. ICD-10 symptom scores (0-12) were derived, providing a dimensional measure of current symptom severity. Use of the British Picture Vocabulary Scale (BPVS) and Raven's Progressive Matrices (RPM) allowed measurement of cognitive ability across the wide ability range of the sample. WISC-III was also used with children able to complete the assessment.

Results: Preliminary analyses, pooling data for the three diagnostic groups, showed a small negative correlation between verbal ability (BPVS) and ICD10 symptom scores (r=-0.13, p=0.04), no correlation between nonverbal ability (RPM) and ICD10, and a positive correlation between nonverbal/verbal discrepancy (RPM-BPVS) and ICD-10 (r=0.24; p=0.001). Further analyses will look at the relationships between cognitive profiles, defined using WISC-III in addition to BPVS and RPM, and symptomatology, defined both in terms of diagnostic categories and dimensionally, using ICD-10, ADI-R and ADOS-G scores. A dimensional approach will also be used to investigate cognitive profiles and the different domains of impairment in autism.

Conclusion: Initial results suggest greater total symptom severity correlates with poorer verbal ability and a nonverbal advantage in PDD. Further analyses will elucidate the relationships between cognition and symptom severity and whether there is evidence for PDD sub-groups, reflected in different cognitive profiles. These results from a whole population will address the limitations of other studies based on referred populations.

Sponsors: Wellcome Trust, DH

**PS3.71**

**SHORT-TERM MEMORY IN ASPERGER’S SYNDROME** Jonathan Steven Martin, Marie Poirier, Dermot M Bowler, Sebastian B Gaigg, City University,
Background: While short-term memory is typically thought to be unimpaired in autism, an evaluation of the relevant literature suggests that this conclusion may be premature, and that recent theoretical views would predict impaired performance in some contexts.

Objectives: To investigate the performance of participants with Asperger’s Syndrome (AS) and controls in a serial recall task.

Methods: In a pilot study, 16 participants with AS and 16 matched controls were presented with sequences of 7 digits, which they had to recall immediately in the order of presentation. In a second study, 20 participants with AS and 20 matched controls were shown 6 item sequences of individually presented unrelated words. Immediately following the presentation of each 6 word list, participants were required to write down these words in the order in which they were shown.

Results: Results from the pilot study showed that the AS group performed significantly worse than the control group, recalling 64% of the digits correctly, compared to 79% in the control group. Ongoing analysis of the data from the second study has revealed further differences in performance between AS participants and controls. AS participants recalled fewer words in their correct serial position, and made more order errors.

Conclusion: The data reported supports the assertion that significant differences in immediate serial recall performance can be observed in people with AS.

Sponsor: ESRC*

PS3.72
UNDERSTANDING THE SYMBOLIC NATURE OF PICTURES IN CHILDREN WITH AUTISM. Kristen Heather McFee, James Mark Bebko, Adam Wesley McCrimmon, York University and CIHR/NAAR STIHR Inter-Institute Autism Spectrum Disorders Training Program (PI: JJAH)

Background: DeLoache and colleagues (1987; 1991) demonstrated that typically developing children as young as 2.5 years of age are able to use pictures as symbols of where to find a toy hidden within a room. Symbolic processing deficits have long been associated with autism, but only one previous study has investigated the use of pictures as symbols, and with a much older sample than DeLoache’s. In our lab, McCrimmon (2006) adapted the DeLoache paradigm for use with children with autism by minimizing language content; results with typical children were comparable.

Objectives: Using the reduced language protocol, determine whether children with autism are able to use pictures as symbols. If not, are specific prerequisite symbolic skills absent?

Methods: Twenty children diagnosed with autism (ADI-R, CARS, and DSM-IV criteria), and matched to a typical sample using the Mullen Scales, complete six tasks progressing in difficulty from simple matching through tasks in which the child must find a hidden toy using a photograph depicting its hiding location.

Results: Findings from this study are compared to the McCrimmon (2006) data with typical children to examine the development of symbolic skills in autism. Data analysis is currently underway.

Conclusions: If the present findings indicate that children with autism are unable to use pictures as symbols, then a need for the development of alternative augmentative communicative systems that supplement or precede existing approaches that are picture-based will have been identified.

Sponsor: Partially funded by a CIHR: IHRT grant to ASD-CARC (www.autismresearch.ca)

PS3.73
USE OF A COMPARATIVE NEUROPSYCHOLOGICAL STRATEGY TO ASSESS COGNITIVE ABILITIES OF AUTISTIC SPECTRUM DISORDER SUBJECTS: WORKING MEMORY TASKS Norton William Milgram, Sherri Thiele, Christina deRivera, Sohail Khattak, Danielle Pigon, Joseph Araujo, Isabelle Boutet, University of Toronto at Scarborough

Background: Working memory deficits are considered a core symptom of ASD. Recent research with high functioning (HF) subjects fails to support this conclusion, and little is known about working memory deficits in low functioning (LF) subjects.

Objectives: (1) developing assessment tools for evaluation of cognitive ability of ASD based on a comparative neuropsychological strategy, (2) assessment of working memory ability in both HF and LF subjects.

Methods: Subjects were ASD children and age matched controls ranging in age from 5 to 13. Visuospatial working memory was assessed using a delayed non-matching to position task (DNMP). This required the subject to remember a location, and avoid responding to that location after a delay. Object recognition was assessed using a delayed non-matching to sample task (DNMS). This required the subject to remember an object, and avoid responding to that object at a later time. The testing apparatus and protocols was a modified version of an apparatus and protocol used in assessment of primates and canines.

Results: Compared to controls, ASD subjects, both LF and HF, showed no significant differences in learning; nor did their performance deteriorate with increasing memory demands. By contrast, latency to respond did significantly distinguish ASD and control subjects.

Conclusion: ASD children are not deficient in simple visuospatial or object recognition memory. Differences in latencies are suggestive of attentional deficits. More challenging tasks may be required to detect working memory deficits in ASD.

Sponsor: Cure Autism Now

PS3.74
CENTRAL COHERENCE THEORY AND MUSIC IN AUTISM SPECTRUM DISORDER Eve-Marie Quintin, Anjali Bhatara, Eric Fombonne, Daniel J Levitin, McGill University

Background: Weak central coherence theory of cognitive
processing states that individuals with autistic spectrum disorder (ASD) focus on the details of a stimulus (local processing) owing to an impaired ability to form a global, integrated, "perceptual whole" (Frith & Happé, 1994). Whereas individuals with ASD exhibit spared or enhanced perception of local musical elements such as absolute pitch (Heaton, et al., 1998), they can perceive contour, a global property of music (Foxton et al., 2003). Objectives: To test the specific hypothesis that individuals with ASD can attend to global musical structure by ordering local musical segments correctly to create a proper musical whole.

Method: Children 12 to 17 years old with ASD and typically developing normal controls were presented with a musical puzzle consisting of 5 plastic cubes, each playing a segment of a melody. Rearranging the cubes alters the piece's melody (global structure) while leaving local structure (groups of notes that constitute a phrase or motif) intact. Children were asked to reconstruct tunes after several listenings. This sets up a cognitive contrast between local and global organization of the stimuli and allows us to test central coherence theory. Full-scale, verbal, and nonverbal IQ were also assessed using the PPVT and the WISC-IV and the amount of time spent listening to, playing, and singing music were used as covariates in our analyses using the SAMMI (Levitin, et al. 2004).

Results: Data will be analyzed with ANCOVA to test for main and interaction effects of diagnosis group, type of music, and ability to reconstruct the melody. As of this submission, pilot studies have shown a clear trend in the expected direction. By conference date, we expect to have tested 15 participants with ASD and 15 mental and chronologically-aged matched controls.

Conclusion: This experiment will assess the ability of people with ASD to perceive structure in music, an aspect of musical knowledge.

Sponsor: NAAR*

PS3.75

TRAIT INFERENCE IN AUTISM Rajani Ramachandran, Danielle Ropar, Peter Mitchell, University of Nottingham

Research question: Does a deficit in theory of mind affect the social perception of individuals with autism in terms of their ability to infer traits?

Objectives: Can individuals with autism infer traits from descriptions of behaviour?

Method:

Study 1 - 12 adults with an official diagnosis of Asperger Syndrome and 12 control participants matched for chronological age and Verbal IQ participated. This study involved reading sentences that imply a trait (e.g. He smiled and said hello to everyone at the tea party,) and then choosing one word of a pair of words that best relates to the sentence. There were two categories of word pairs, trait versus distracter (friendly in the above example versus an unrelated word) and semantic versus distracter (cup in the above example versus an unrelated word). The reaction time with respect to choosing the correct word was analysed.

Study 2 - The second study followed a similar paradigm to the first. Neutral sentences (which do not lead to any trait inference) and a third word pair, namely, behaviour versus distracter (greeted for the sentence above versus an unrelated word) were introduced. Data from 14 teenagers with an official diagnosis of Asperger Syndrome have been collected so far.

Results:

Surprisingly, participants with autism were significantly faster with trait words than a semantic associate or behaviour words. Data collection from control participants is in progress, but early indications suggest similar trends to the participants with autism.

Conclusion: The findings from these two studies indicate that individuals with autism are processing the sentences for their global meaning and are able to make trait inferences from descriptions of behaviour.

Sponsor: Commonwealth Scholarship Commission

PS3.76

VISUAL AND MEMORY SCANNING IN CHILDREN WITH HFA: AN EVENT-RELATED POTENTIAL STUDY Ruth Raymaekers, Jan R Wiersema, Jaap J van der Meere, Herbert Roevers, Ghent University, Department of Experimental Clinical and Health Psychology, Research Group Developmental Disorders

Background: Information processing abnormalities in autism have been widely documented and experimental studies have found empirical support for nonsocial perceptual, attentional and memory deficits. Furthermore, it has been suggested that problems with state regulation are associated with autism.

Objectives: To investigate working memory and attentional processes in children with autism and test whether the disorder is associated with a deficit in state regulation (effort allocation). Event-related potentials (ERPs) and behavioral performance measures are assessed.

Methods: Normally intelligent children (9 to 12 years) with high-functioning autism (HFA) are compared with normally developing peers, using a visual search paradigm wherein load is varied. On each trial, a memory set of 1, 2 or 4 letters is presented, followed by a new set (4 letters) in which the target has to be identified. In 50% of the trials, the target is present.

Results: In general, results suggest that performance efficiency (Mean RT, Standard Deviation of RT, Errors) is the same in children with HFA and in the control group. However, ERPs (e.g. P300) seem to differentiate both groups.

Conclusions: On the behavioral level, children with HFA cannot be differentiated from control peers. However, the differing ERPs indicate that processes underlying the performance are not the same.

Sponsor: Research Board of the Ghent University

PS3.77
ASSESSMENT OF HIGHER-ORDER THEORY OF MIND ABILITIES IN ADOLESCENTS WITH HIGH-FUNCTIONING AUTISM

Elizabeth Gayle Smith, Laura B Silverman, Loisa Bennetto, University of Rochester

Objectives: Several tasks have recently been developed to assess higher-order theory of mind (ToM) abilities in individuals with high-functioning autism (HFA). We examined performance on two of these tasks to determine whether adolescents with HFA showed deficits and whether abilities on the two tasks were related.

Methods: Participants were 15 adolescents with HFA and 15 typically-developing controls, matched on age and VIQ. We examined performance on ‘Reading the Mind in the Eyes’ (Baron-Cohen et al., 2001) and the ‘Triangle Task’ (Abell, Happe, & Frith, 2000). Diagnoses were established or ruled out with ADOS and ADI-R.

Results: We found no evidence of an autism-specific deficit on ‘Reading the Mind in the Eyes.’ However, adolescents with autism showed significant difficulty appropriately describing cartoons in the Triangle Task (p=.04). In particular, they were worse than controls when describing cartoons with mentalising themes (e.g., surprising; p=.02), but not goal-directed (e.g., dancing) or random themes. Performance on the two ToM tasks was not significantly correlated for either group. However, performance on the mentalising tasks was related to ADOS social algorithm scores for the autism group.

Conclusions: These findings suggest that while adolescents with HFA perform differently than controls on the ‘Triangle task’, this difference may not extend to all higher-order ToM tasks, such as ‘Reading the Mind in the Eyes’. Results are discussed in terms of the differences between the abilities tapped by these two ToM tasks, and in terms of this particular sample of individuals.

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PS3.78
FACE PROCESSING ABILITIES IN VISUO-CONSTRUCTION TASK IN AUTISM.

Michael Thomas, Dagmara Annaz, Birkbeck, University of London

Background: Recognition of faces is one of the most important skills for the development of social communication. Individuals with autism have been often reported to have poor ability to recognise faces, but in contrast they typically perform well on tasks that require them to use visuo-constructive skills such as pattern construction.

Objectives: The aim of the current study was to explore the development of face processing abilities using a visuo-construction task which was designed to act as a comparison to visuo-perceptual face recognition task.

Methods: 25 typically-developing children and 33 children with autism took part. Children in autism group were divided into two groups: High-Functioning (n=16) and Low-Functioning (n=17) based on Childhood Autism Rating Scale (CARS). Verbal and non-verbal IQ was obtained for all children. Each child was required to build an image of a face to match an image of a target face by placing correct features such as eyes, mouth and nose on a blank face.

Results: Children in HFA group showed a delayed performance in comparison to TD group. Children in LFA group showed atypical profile and demonstrated an unusual pattern by placing the mouth feature in the middle of face.

Conclusion: Children in autism groups showed different developmental patterns. These findings suggest that children in LFA group are unable to use their good construction skills in a face task. This contradicts the weak central coherence theory and clearly shows that the social status of the stimuli affected performance of LFA group more than HFA group.

PS3.79
OBJECT IDENTIFICATION ON THE BASIS OF CONTOUR FRAGMENTS

Eline Cecile Verbeke, Kim Neyrinck, Patricia Bjittebier, Jean Steyaert, Johan Wagemans, KULeuven, BELGIUM

Background: According to the ‘weak central coherence’ (WCC) account, people with A.S.D. process information differently: They focus more on details, do not integrate them into a coherent whole, and do not interpret them making use of context. Here, we test to what extent these different components of WCC affect identification of pictures of everyday objects presented in different formats.

Methods: The clinical group consisted of 24 boys (6 to 8 years old) with high-functioning A.S.D., recruited from a specialized outpatient psychiatric clinic and from special education. The control group consisted of 24 boys matched on age and IQ, recruited from a regular school. The stimulus set consisted of 50 line drawings of everyday objects, in 5 possible formats. In addition to the complete line drawings, we used versions with the external contour only, which could be presented as complete or fragmented, with 25%, 20% or 15% of the contour visible. Children were asked to name the objects represented by the stimuli, in decreasing order of difficulty.

Results: Analysis of cumulative identification scores shows that children with A.S.D. have more difficulties with the fragmented contours than the control group, although they are equally good at identifying the complete contours and line drawings.

Conclusion: This finding suggests that the impairment of children with A.S.D. in this task is mainly perceptual: The contour fragments are insufficient to trigger a possible interpretation and they are not easily grouped into larger units. Once the contour is complete, activating a memory representation and a name is no problem.

PS3.80
HOW WELL DO CHILDREN WITH ASPERGER'S DISORDER UNDERSTAND THEMSELVES?

Liljana Valetic, The Ontario Institute for Studies in Education, University of Toronto
Background: Ability for self-understanding is suggested to be impaired in autism, however, this ability has not been well studied.

Objectives: To compare self-understanding of a twelve year-old autistic boy with the accounts of him by others who know him.

Methods: A twelve year-old boy diagnosed with Asperger's Disorder, his parents, and his former teaching assistant participated in this study. Both quantitative and qualitative methods were used. The autistic participant was administered the Self-Perception Profile for Children (Harter, 1985) and the Self-Understanding Interview (Damon & Hart, 1988). The main participant's parents and his former teaching assistant were administered Teacher's Rating Scale of Child's Actual Behavior (Harter, 1985). Qualitative methods included clinical interviews with all participants, casual conversations with the main participant, and the main participant's autobiographical essay.

Results: On the close-ended questionnaires, there were both similarities and differences in self and others' ratings. Data obtained using open-ended methods revealed that most differences came from the differences in the interpretation of the questions. The analysis of qualitative data indicates that the ratings are comparable.

Conclusion: The obtained results suggest that self-understanding of this autistic boy is fairly accurate. We discuss this finding in light of theoretical accounts suggesting an impairment of self-understanding in autism and in light of clinical suggestions of the importance of self-understanding for determining the life outcome of autistic individuals.

PS3.81
HIERARCHICAL PERCEPTION IN FREE- AND FORCED-CHOICE CONDITIONS IN PERSONS WITH AUTISM
Lixin Wang, Laurent Mottron, Beijing Normal University

Background: exposure duration may be implicated in the microgenesis of construction of hierarchically complex visual information (Kimchi, 2000)

Objectives: Our previous study (2004) established that autistics present with spontaneous orientation and superior detection speed for local targets of hierarchical stimuli encompassing different visual angles. We investigate now the same parameters at different exposure durations (80, 200, 500ms) and the interference effects between local and global levels of compound numerals.

Methods: 15 autistics (mean age = 14;7 yrs, mean FSIQ (WAIS-R) =67) and 15 non-autistics participated in the study. The participants were matched on RSPM score, CA, gender and manual laterality. They were asked to name a) local and global targets of compound numerals encompassing various exposure durations in free-choice task b) local and global targets of compound numerals at medium visual angle and medium exposure duration in forced choice task.

Results: In free-choice task, NTs were shorter for local targets in autistics, whereas controls exhibited an opposite, global advantage. The shorter the exposure duration was, the shorter the NT was in controls only. Relative naming choices for local vs. global targets were equally distributed in both groups, whatever exposure duration. In forced-choice tasks, the autistics showed a local to global interference. In contrast, the controls showed both global to local interference and local to global interference.

Conclusion: Local targets processing is the "default" option for autistics, whatever stimulus sizes and exposure durations in free- as well as forced-choice tasks. However, the autistics are able to process global targets. Superior performance for local targets supports the Enhanced Perceptual Functioning hypothesis in autism, which proposes that low-level, static visual information is processed at a higher level in autistics, together with intact processing of static global information.

PS3.82
ANOTHER'S GAZE-DIRECTION AS A GUIDE OR DISTRACTION DURING DURING A TARGET-TRACKING TASK: THE EFFECTS OF AUTISM.
Justin H G Williams, Toby Gilbertson, Mandy S Plumb, Wilson D Andrew, Mon-William sM Mark, University of Aberdeen

Background: Autism is strongly associated with joint-attention deficits, but children with autism can use gaze-direction as a cue to speed up reaction times. However, a previous fMRI study that children with autism might not use always gaze-direction in such an advantageous way.

Objectives: To explore the advantages and disadvantages that gaze-following could confer on a dynamic target-tracking task in individuals with and without autism across an age-range.

Methods: 40 control children (5-11 years), 10 children with normal IQ and autistic disorder or Asperger's syndrome (6-15 years), and 10 adults pointed a laser at circular targets back-projected on a large screen. Targets moved randomly between the four corners of the screen during a 90s video. Three conditions were explored: (i) a technician's still head was displayed in the middle of the screen (baseline); (ii) the head moved so that gaze direction was directed to, and congruent with, target movements; (iii) head movements were directed away from, and incongruent with, target movements. The video display was time-locked with optoelectronic recording equipment that allowed precise measurement of the time taken to prepare and execute movements.

Results: Individuals within control groups universally showed faster RT with congruent than incongruent head movement. However, for the group with ASD, RT for congruent was usually either slower or the same compared to incongruent head movement. A minority performed normally. The movement speed and accuracy between points was indistinguishable from the controls.

Conclusion: Our dynamic laboratory-based task may provide an accurate quantitative measure of joint-attention effects on performance for individuals. Children with autism may be less susceptible to gaze-direction as a cue and may not reflexively use it to reduce reaction-times.
They may also be undistracted by incongruent actions.

**PS3.83**

**PERCEPTUAL DISTORTION INDUCED BY DIMENSIONALITY CUES: AN ATTENUATED EFFECT IN AUTISM**

*Peter Mitchell, Laurent Mottron, Anthony Hosein, Danielle Ropar, Fenja Ziegler, University of Nottingham*

Background: Controversy surrounds the level of distortion experienced by individuals with autism when viewing perspective-related illusions.

Objective: We compared judgments about two versions of the Shepard illusion. One looked like two tables side-by-side in characteristic orientation with strong 3-D cues and the other was the same but with legs removed thus making a pair of parallelograms with weaker 3-D cues.

Method: High functioning participants with autism and comparison participants adjusted the horizontal and vertical dimensions of the right-hand stimulus so that it matched the left-hand stimulus, using the arrow keys on a computer. If they succumbed to the illusion, they would make the right-hand stimulus too long and thin.

Results: The dependent variable was the ratio of the two dimensions of stimuli adjusted by each participant. Participants generally made a more severe error with the table than the parallelogram stimuli and participants without autism made a more severe error than those with autism; there was no interaction effect between participant group and type of stimulus.

Conclusion: Participants with autism had relatively low susceptibility to a dimensionality illusion whether the stimulus had strong or weak 3-D properties. It seems that individuals with autism perceive the world more ‘objectively’ in some cases than those without autism.
Oral Session #7
Early Diagnosis

Chair: Nurit Yirmiya

Speakers:
Elizabeth R Crais, Linda R Watson, Grace T Baranek, Brian A Boyd,
Heather L Miller, Kaitlyn P Wilson, University of North Carolina at Chapel Hill
Isabel M Smith, Susan Bryson, Lonnie Zwaigenbaum, Jessica Brian, Wendy Roberts, Peter Szatmari, Katherine Gotham, Dalhousie University
Pamela Ventola, Jamie Kleinman, Juhi Pandey, Leandra Wilson, Emma Esser, Hilary Boorstein, Saasha Sutera, Alyssa Verbalis, Michael Rosenthal, Thyde Dumont-Mathieu, Gail Marshia, Marianne Barton, Sarah Hodgson, James Green, Diana Robins, Fred Volkmar, Katarzyna Chawarska, Tammy Babitz, Deborah Fein, University of Connecticut
Grace T. Baranek, Lonnie Zwaigenbaum, J. Steven Reznick, Linda R. Watson, Elizabeth R. Crais, Susan Bryson, University of North Carolina at Chapel Hill

ABSTRACTS

DEVELOPMENTAL PATTERNS OF GESTURE USE IN INFANTS WITH AUTISM SPECTRUM DISORDERS Elizabeth R Crais, Linda R Watson, Grace T Baranek, Brian A Boyd, Heather L Miller, Kaitlyn P Wilson, University of North Carolina at Chapel Hill

Background: Studies of gesture use by infants with ASD have focused on diversity of gestures and intentions, and sampling at a single time point rather than longitudinally. This investigation examines early developmental patterns in communicative gesture use at two age points among infants with ASD, developmental disabilities (DD), and typical development (TD).

Objectives: (1) Compare quantity and function of gestures across groups, (2) Identify developmental trajectories of gesture use from 9-12 to 15-18 months, (3) Determine relationship between early gesture use and adaptive outcomes at preschool age.

Methods: Home videotapes of infants are coded for social interaction, joint attention, and behavior regulation gestures. Preschool Vineland scores are obtained on all children. To date, we have coded 27 infants with ASD, 12 with DD, and 17 with TD at 9-12 months; and 19 infants with ASD, 3 with DD and 7 with TD at 15-18 months. Additional data will be added when coded.

Results: Significant (p<.05) group differences of total gestures (time 1 & 2): greater gesture use by TD than ASD group, with DD group in between. Mean total use of gestures increases across the two time points for each group. Differences between groups were seen in which gesture categories increased over time. Multiple regression analyses to predict Vineland ABC scores at preschool age resulted in R2 of .26 (F=3.8, p=.04).

Conclusion: Infants with ASD show relative strengths in social interaction gestures at 9-12 months, with deficits in behavior regulation & joint attention gestures. The gap in gesture use between the ASD and TD groups dramatically increases over time. Gesture use is an important area for early intervention, and deficits in both behavior regulation & joint attention should be addressed.

Source: Cure Autism Now, NIH HD42168, UNC University Research Council, Medical School Faculty Grant
COMPARISON OF OLD AND NEW ADOS ALGORITHMS IN THE CLASSIFICATION OF INFANT SIBLINGS

Isabel M Smith, Susan Bryson, Lonnie Zwaigenbaum, Jessica Brian, Wendy Roberts, Peter Szatmari, Katherine Gotham, Dalhousie University

Background: Infant siblings of children with ASD present a rich opportunity to evaluate prospectively, in very young children, diagnostic measures such as the ADOS.

Objectives: To assess the sensitivity and specificity of 18- and 24-month ADOS relative to independent diagnoses at 36 months, and to compare classification under existing (“old”; Lord et al., 2000) and new (Gotham et al., submitted) ADOS algorithms.

Method: Prospective data were collected on 100 infant siblings of children with ASD. The ADOS was given at 18, 24, and 36 months; scores were calculated according to old and new algorithms. At 36 months, infants received a blinded diagnostic evaluation yielding a clinical diagnosis based on: ADOS, ADI-R + DSM IV-TR).

Results: The sensitivity of the ADOS at 18 months, and at 24 months, for a clinical diagnosis of ASD at 36 months was 92% for both algorithms. Specificity ranged from 68% to 79%, with no systematic advantage for either algorithm. Classification by old and new ADOS algorithms was compared: at 36 months, 16/100 participants were classified as autism by both algorithms; of 13 ASD (old), 6 shifted to autism (new); of 71 classified as NonASD (old), 4 shifted to ASD (new).

Summary: Old and new ADOS algorithm classifications at 18 and 24 months showed comparable sensitivity and specificity in predicting clinical ASD diagnoses at 3 years. The revised ADOS algorithm produced a shift toward more ASD classifications among infant siblings.

Sponsor: CIHR, NAAR

DIFFERENTIATING BETWEEN AUTISM SPECTRUM DISORDERS AND OTHER DEVELOPMENTAL DISABILITIES IN CHILDREN WHO FAILED A SCREENING INSTRUMENT FOR ASD

Pamela Ventola, Jamie Kleinman, Juh Pande, Leandra Wilson, Emma Esser, Hilary Boorstie, Saasha Sutera, Alyssa Verbals, Michael Rosenthal, Thylde Dumont-Mathieu, Gail Marshia, Marianne Barton, Sarah Hodgson, James Green, Diana Robins, Fred Volkmar, Katarzyna Chawarska, Tammy Babitz, Deborah Fein, University of Connecticut

Background: Toddlers with autistic spectrum disorders (ASD) and toddlers with DD/DLD (who display some characteristics of ASD) share many features, which can create challenges for differential diagnosis.

Objective: To compare the behavioral presentation of children with ASD and children with DD/DLD (who display some characteristics of ASD) to help clarify behaviors that can be used in the differential diagnosis of ASD in toddlers.

Methods: Participants were 195 children (mean age = 27 months) who failed the Modified Checklist for Autism in Toddlers (M-CHAT; Robins et al., 2001) and were diagnosed with ASD, DD or DLD.

Results: Children were compared on the diagnostic algorithm items from the Autism Diagnostic Observation Schedule (ADOS), the Childhood Autism Rating Scale (CARS), the M-CHAT, the Vineland Adaptive Behavior Scales (Vineland), and the Mullen Scales of Early Learning. For all of the analyses, the children were matched on Vineland communication level. In comparison to the children with DD/DLD, the children with ASD had prominent and consistent impairments in socialization skills, especially joint attention skills, and they were more impaired in some aspects of communication, play, and sensory processing. The children with ASD had significantly lower scores on all adaptive skills (socialization, motor, daily living, and communication) and on visual reception skills as measured by the Mullen. The groups did not differ on the other cognitive domains (expressive language, receptive language, and fine motor skills).

Conclusion: Children with ASD and children with DD/DLD share common features but certain behavioral markers can be used to differentiate the groups.

Sponsors: NIH and MCH

COMPARISON OF THE FIRST YEAR INVENTORY AND THE AUTISM OBSERVATION SCALE FOR INFANTS IN 12-MONTH OLD SIBLINGS OF CHILDREN WITH AUTISM

Grace T. Baranek, Lonnie Zwaigenbaum, J. Steven Reznick, Linda R. Watson, Elizabeth R. Crais, Susan Bryson, University of North Carolina at Chapel Hill

Background: Retrospective studies of children with autism indicate that social-communicative and sensory-motor deficits are present in infancy. Preliminary prospective data suggest that the Autism Observation Scale for Infants (AOSI; Bryson et al., in press) identifies 12-month markers that are predictive of a later diagnosis of autism. However, parent-report measures such as the First Year Inventory (FYI; Baranek et al, 2003) may have greater utility for broad-based surveillance.
Objectives: Determine agreement between the FYI and AOSI in identifying symptoms in 12-month-old siblings of children with autism.

Methods: Thus far, 31 infants have been assessed using AOSI and FYI. AOSI scores are calculated on 16 items in a play-based format. The FYI has 61 parent-report items (8 constructs of social-communicative/sensory-regulatory functions).

Results: Group differences were significant \[F(2, 1328)=32.98, p<.0001\]. The infant sib group had the highest FYI scores (sibs M=14.5; controls M=3.2, norm M=5.9). The correlation between total FYI and AOSI scores was significant \(r=.38, p<.05\). Risk cut-points (AOSI markers e 5; FYI total c12) identified 8 children positively, and 15 negatively on both measures (74% agreement; Chi-square 6.45, p=.011).

Conclusions: Parent-report and observational measures at 12 months of age are correlated, albeit modestly. Preliminary validity of the FYI using the AOSI as the criterion measure is supported. Research utilizing larger samples with well established diagnostic outcomes at age 2-3 years is needed to calculate absolute sensitivity/specificity.

Sponsors: NDRC; NIH HD42168; CIHR 62924, NAAR

Oral Session #8
Perception

Chair: Marcos Mercadante

Speakers:
Robert Michael Joseph, Brandon Keehn, Christine Connolly, Boston University School of Medicine
Shannon E. Morgan, Wendy L. Stone, Vanderbilt University
Dagmara Annaz, Anna Remington, Elizabeth Milne, Ruth Campbell, Mike Coleman, John Swettenham, University College London, UK
Laurent Mottron, Marie-Josée Caron, Department of psychiatry, Université de Montréal

ABSTRACTS

MECHANISMS UNDERLYING SUPERIOR VISUAL SEARCH IN AUTISM Robert Michael Joseph, Brandon Keehn, Christine Connolly, Boston University School of Medicine

Background: Individuals with autism excel at visual search, but the mechanisms underlying superior search skills in autism have not been determined.

Objective: To assess whether autistic search superiority in a standard static visual search is maintained in a dynamic condition in which the target and distracters change locations every 500 ms, precluding a serial search strategy.

Method: Participants were 21 high-ability adolescents with autism and 21 age- and NVIQ-matched typically developing (TD) individuals. The target was an L and distracters were Ts in four different orientations. Set size (15, 20, 25) and target presence varied randomly within six 30-trial blocks alternating between conditions. Eye-tracking was conducted for the entire procedure.

Results: The groups did not differ in rate of error. The autism group exhibited faster mean RT than the TD group in both static, \(F(1,40)=3.6, p<.06\), and dynamic, \(F(1,40)=10.5, p<.002\), conditions. The TD group showed an increase in RT in the dynamic relative to the static search, \(F(1,20)=34.3, p<.001\). RT for the autism group did not differ significantly between test conditions, \(F(1,20)=1.6, p>.20\). Whereas there were no group differences in number of fixations or amplitude of saccades, the autism group made fixations of significantly briefer duration, \(F(1,37)=7.8, p<.01\).

Conclusion: The autism group’s consistent performance across static and dynamic conditions, in conjunction with the eye-tracking findings, suggests that superior search skills in autism derive from enhanced perceptual processing of visual stimuli rather than from differences in the deployment of visual attention.

Funding: NIDCD(U19 DC03610)/CPEA.
DO CHILDREN WITH AUTISM DISPLAY THE "POP-OUT" EFFECT? Shannon E. Morgan, Wendy L. Stone, Vanderbilt University

Background: The "pop-out" effect, which occurs when certain items within a visual scene are perceived as "popping out" from distractor stimuli, has been found for nonsocial stimuli (e.g., colors, shapes) as well as social stimuli (e.g., direct-gaze eyes). This effect has not yet been assessed in children with autism.

Objectives: To determine whether children with autism exhibit the pop-out effect when viewing social versus nonsocial stimuli.

Methods: Participants were 11 children with autism (mean age=5.6 years), 12 typically developing children (mean age=4.7 years) and 5 adults. Schematic drawings of human eyes, as well as 2 control tasks (geometric patterns resembling eyes and schematics of dogs varying in color) were presented via computer monitor during a visual search task.

Results and Conclusions: As expected, the pop-out effect occurred for the direct-gaze eyes and the dog stimuli and not for the geometric stimuli. Unlike the other groups, the ASD group exhibited the pop-out effect for both the averted as well as the direct-gaze eyes. Findings suggest that children with ASD: 1) display the pop-out effect with both nonsocial and social stimuli; 2) perceive the salience of direct-gaze eyes apart from their spatial components; and 3) may display heightened sensitivity to eye stimuli, even when averted. Results are consistent with recent fMRI findings of amygdala functioning in ASD.

Sponsor: NIHCD grant #T32HD07226

DOTS BUZZING AROUND? PERCEPTION OF BIOLOGICAL MOTION IN AUTISM. Dagmara Annaz, Anna Remington, Elizabeth Milne, Ruth Campbell, Mike Coleman, John Swettenham, University College London, UK

Background: Perception of human motion such as walking or running can be easily identified even by young children (Johansson, 1972) and may be important for the development of social communication, which appears to be impaired in autism. One possibility is that this deficit is underpinned by a lower sensitivity in the perception of the movement in human action (e.g., Blake, 2003).

Objectives: The aim was to explore the development of the perception of biological motion in autism using i) a simple detection-task, ii) detection of BM embedded in distractors and iii) a developmental trajectories approach (Karmiloff-Smith et al., 2004).

Methods: 25 typically-developing children and 15 children with autism (aged 6 to 15 years) took part. Non-verbal and verbal IQ were obtained for each child. In study 1, children were presented with a 40 trial sequence of 1 second displays of point-light movement, 20 depicting human action and 20 depicting a scrambled display of moving dots. Each child was asked to identify whether he/she saw a person or not by pressing a relevant key. In study 2, thresholds for the perception of biological motion embedded in noise were obtained by presenting stimuli in the presence of point-light distractors and varying the signal-to-noise ratio.

Results & Conclusion: Preliminary results suggest that in study 1, children with autism show a similar developmental profile to the TD group, while study 2 revealed perception of biological motion to be particularly disrupted by distractors in the autism group, suggesting atypical profile in biological motion perception.

Sponsor: ESRC

COGNITIVE MECHANISMS, SPECIFICITY AND NEURAL UNDERPINNINGS OF THE BLOCK DESIGN PEAK IN AUTISM. Laurent Mottron, Marie-Josée Caron, Department of psychiatry, Université de Montréal

Background: Among the visual tasks in which autistic individuals display superior performance, the most replicated is the block design (or BD) subtest of the Wechsler intelligence scales.

Objectives: explain the cognitive and cerebral mechanisms responsible for the block design peak in autism, and document its specificity to this condition.

Methods: 8 high functional individuals with autism with a BD peak (HFA-P) performed a BD task at various levels of perceptual cohesiveness, and several tasks tapping visuo-motor, global perception, visual memory, visual search, and speed of visual encoding. Their performance was compared to that of 8 autistics without a BD peak (HFA-NP), 10 typically developing individuals (TD), and 8 gifted comparison participants with a BD peak (TD-P).

Results: The HFA-P group displayed locally oriented perception, superior processing of global visual properties, superior visual search, faster encoding time, and superior visuo-motor performance. The inferior detrimental influence of increasing perceptual coherence was the unique
pattern of performance which was both specific (it was not observed in TD-P and TD groups) and sensitive (it occurred both in HFA-P and HFA-NP group) to autism. Conclusion: overall superior low-level processing interacts with locally-oriented processing to produce outstanding BD performance in a subgroup of autistic individuals. These findings complement existing evidence of V1 overfunctioning (Bertone et al., 2005) to indicate an enhanced functioning and role of early parvocellular pathway in autism.

Sponsor: CIHR
Oral Session #9
Genetic: Family & Twin Studies

Chair: William McMahon

Speakers:
Jeremy Parr, S Wallace, M de Jonge, H Van Engeland, A Le Couteur, M Rutter, A Pickles, A Bailey, University of Oxford
Rebecca Lynn Hefter, Emily Kathryn Kees, Carrie L Arneson, Morton Ann Gernsbacher, Harold Hill Goldsmith, University of Wisconsin
Lonnie Zwaigenbaum, Jeremy Goldberg, Peter Szatmari, Ellie Deveau, McMaster University
James S. Sutcliffe, Autism Genome Project

ABSTRACTS

THE BROADER PHENOTYPE IN PARENTS AND SIBLINGS OF AFFECTED RELATIVE PAIRS WITH PDD Jeremy Parr, S Wallace, M de Jonge, H Van Engeland, A Le Couteur, M Rutter, A Pickles, A Bailey, University of Oxford

The International Molecular Genetic Study of Autism Consortium (IMGSAC)

Aims: To characterise the broader autism phenotype (BAP) in multiplex autism families and to investigate the reliability of the revised Family History Interviews (FHI-R).

Background and methods: Relatives of individuals with ASD may show the BAP, milder traits related to the core autism phenotype. Families with two or more individuals with ASD were recruited as part of the IMGSAC. First degree relatives of ASD probands were administered the subject (FHI-S) and informant (FHI-I) versions of the FHI-R and assessed using the Impression of Interviewee (FHI-IoI) schedule. Anonymised summaries were generated and consensus scores agreed at cross-site meetings.

Results: Consensus FHI-R data on at least 300 first degree relatives (age range 4-67 years) of ASD probands were derived. Analysis of FHI-R data revealed a strong clustering of social-communication impairments and rigidity, whereas language delay and reading/spelling difficulties aggregated in a separate factor. Significant agreements were found between factors in child and adulthood on the adult FHI-I and FHI-S. Comparison of test and retest data revealed significant correlations between factors in both child and adulthood, whereas agreement between test and retest data for individual FHI-R items was more variable. Low frequency FHI-R items, and items highly discriminatory for the presence of the BAP will be discussed, as will the implications for the conceptualisation of the BAP and future FHI-R revision.

Conclusions: The FHI-R is a reliable interview which identifies social-communication impairments, rigidity and specific cognitive difficulties as the core of the BAP.

DETERMINING THE HERITABILITY OF EARLY AUTISM MARKERS BY SCREENING A STATEWIDE TWIN SAMPLE Rebecca Lynn Hefter, Emily Kathryn Kees, Carrie L Arneson, Morton Ann Gernsbacher, Harold Hill Goldsmith, University of Wisconsin

Background: Twin and family studies of diagnosed autism suggest high heritability. Recently, questions about genetic influence on a hypothetical "autism trait" in the general population have arisen.

Objectives: The primary goals of the study were (1) to screen twins from a statewide population using the six critical items from the Modified Checklist for Autism in Toddlers (M-CHAT, Robins, Fein, Barton, & Green, 2001), (2) to determine the heritability of these early indicators of autism, and (3) to replicate, in a general population, the M-CHAT items' endorsement rates reported by Robins et al (2001).

Methods: Participants were part of a statewide, unselected twin population. We administered items similar to the six critical M-CHAT items to mothers of 1217 twin pairs at two years of age. We calculated endorsement rates and concordance rates for MZ and DZ twin pairs.

Results: Preliminary analyses suggest that our population-based twin sample generates endorsement rates on the six critical M-CHAT items similar to those reported by Robins et al.
Probandwise concordance rates for MZ (43%) and DZ (20%) twins suggest only moderate heritability of these early autism indicators in the general population.

Conclusions: Previously reported endorsement rates for early autism indicators appear to generalize to our sample of twins in a general population. Genetic analyses suggest that a hypothetical "autism trait" is not as strongly heritable as diagnosed autism itself. Screening and identification of clinical cases in this population to determine sensitivity and specificity of the M-CHAT items in a twin population is ongoing.

Sponsor: NIMH

FAMILIARITY OF LANGUAGE PHENOTYPES IN AUTISM SPECTRUM DISORDER.

Lonnie Zwaigenbaum, Jeremy Goldberg, Peter Szatmari, Ellie Deveau, McMaster University

Background: Language phenotypes may be useful in genetic studies of autism in extended pedigrees, but little is known about what measures are familial.

Objectives: To assess familial concordance in 1st-degree relatives of ASD probands on measures of language, literacy and phonological processing.

Methods: Participants were recruited from families participating in ongoing ASD genetic studies, and included 24 families with at least one ASD proband and unaffected sibling, and both parents. Measures included the Peabody Picture Vocabulary Test (PPVT), Oral and Written Language Scales (OWLS - siblings only), Spelling subtest of the Wide Range Achievement Test 3 (WRAT-3), Woodcock Reading Mastery Test (WRMT), and Comprehensive Test of Phonological Processing (CTOPP). Intraclass correlations (ICC) were calculated to assess concordance among probands and their unaffected siblings, probands and parents, and among siblings and parents excluding the proband.

Results: Probands and unaffected siblings showed familial correlation on the CTOPP-Rapid letter naming subscale (ICC=.42; p=.04); no significant correlations were observed between probands and either parent. Unaffected siblings were correlated on the OWLS - oral expression subscale (ICC=.70; p=.005) and CTOPP - Elison subscale (ICC=.68; p=.005), a measure of phonological processing requiring sound elimination within words. The CTOPP-Elision scores were also correlated between unaffected siblings and each parent (sib-mother ICC=.50; p=.004 and sib-father ICC=.47; p=.007, respectively)

Conclusions: Evidence for familial concordance on measures of phonological processing was found between ASD probands and siblings, and among parents and siblings. These quantitative phenotypes may be informative for genetic studies.

Sponsor: CAN

AUTISM GENOME PROJECT

James S. Sutcliffe, Autism Genome Project

Autism is widely understood to have a predominantly genetic etiology, based on twin and family studies. With a heritability among the highest for neuropsychiatric conditions, considerable effort has been made to use genome-wide linkage methods in affected sibling pair autism families to identify candidate loci. However, the clinical and locus heterogeneity in autism substantially complicates these efforts. To overcome the inherent statistical limitations present within any one sample, most of the world's autism genetics research groups have established a collective enterprise, the "Autism Genome Project" to facilitate the identification of autism genes. The AGP is a consortium of research groups representing more than 20 Universities and Research Centers in North America and Europe. The AGP reflects a joint effort on the part of existing autism genetics consortia, including the Autism Genetics Cooperative (AGC), the Autism Genetics Resource Exchange (AGRE), the Collaborative Programs of Excellence in Autism (CPEA), the International Molecular Genetic Studies of Autism Consortium (IMGSAC), and other groups developing large simplex family samples. Together, the AGP has assembled a sample of approximately 1500 multiplex families and a similar number of independent parent-child trios representing the largest collective sample of autism families available. The AGP reports the completion of a genomic linkage screen and initial analysis of the combined multiplex sample using the Affymetrix 10k SNP platform.

Funding: The AGP gratefully acknowledges funding from the National Alliance of Autism Research, Canadian Institutes of Health Research, Cure Autism Now, European Union, Fundação para Ciência e Tecnologia, Fundação Calouste Gulbenkian, Genome Canada, Health Research Board, Howard Hughes Medical Institute, INSERM, Nancy Lurie Marks Family Foundation, National Institutes of Health (NICHD, NIMH, NINDS, NIDCD), and the Swedish Medical Research Council.
NOTES
Poster Abstracts – 4
1:00 – 6:30 pm
Themes: Genetic Studies (Families), Broader Phenotype, Structural Neuroimaging, Brain Structure/Neuroanatomy, Emotions/Faces.

PS4.1
OBSESSIVE COMPULSIVE SYMPTOMS IN FAMILY MEMBERS OF INDIVIDUALS WITH AUTISM SPECTRUM DISORDER Becky Lynn Androlo, Heather Schmidt, Jonathan Gray, Linda Brzustowicz, Charles Cartwright, University of Medicine and Dentistry of New Jersey
The relationship between repetitive behaviors and obsessive-compulsive symptoms in individuals with autism spectrum disorders and obsessive-compulsive symptoms in their parents and siblings were examined. Thirty individuals with autism spectrum disorder and their families were assessed as part of a larger genetics study. Rates of repetitive behaviors were assessed in the individual using the Autism Diagnostic Interview - Revised (ADI-R). Obsessive-compulsive symptoms were determined using the Yale-Brown Obsessive-Compulsive Scale checklist (Y-BOCS) and the Children’s Yale-Brown Obsessive-Compulsive Scale checklist (CY-BOCS). Preliminary analyses show that scores on the Restricted and Repetitive domain of the ADI-R are positively correlated with maternal Y-BOCS scores. The relationship between sibling and paternal Y-BOCS scores, as well as the Y-BOCS score from the individuals with autism, is discussed.
Funding: NIMH #1R01 MH70366-02

PS4.2
FREQUENCY OF FRAGILE X IN MULTIPLEX AUTISM: TESTING AGRE FAMILIES. William Ted Brown, Sarah L Nolin, Carl S Dobkin, George S Houck, Anne Glicksman, Sarah J Spence, Dan H Geschwind NYS Institute for Basic Research in DD
Objective and Methods: Autism has high heritability. The Autism Genetic Resource Exchange (AGRE) is a publicly available resource of well-characterized multiplex families for genetic studies of autism. To better characterize this resource, we conducted fragile X DNA analysis (Brown 93) on one proband in each of 480 AGRE families, with follow-up family studies when indicated.
Results: Testing revealed 6 families to be positive for fragile X. Review of 326 available medical records showed 114 (35%) had prior negative genetic testing. Thus, the prevalence of fragile X among the approximately 312 previously untested AGRE families was ~ 1.9%. An estimate of the IQ score of the autistic subjects was 80+35 with range 34-144, based on the Raven. Thus, the AGRE sample is likely to have a higher IQ distribution than typical for fragile X subjects (mean ~40+25). Previous prevalence studies of fragile X in autistic samples range from 0 to 16%; with mean ~4%; (Feinstein 98). Our 1.9% is similar to a report of 1.6% among 123 unrelated autistic individuals (Bailey 93), but lower than the 13% we found on an earlier multicenter study of 183 individuals (Brown 86). An additional ~100 families added to AGRE subsequent to this study have also been tested as negative for fragile X.
Conclusions: A growing awareness of fragile X syndrome may increase the probability of prior fragile X screening in multiplex autism families and their exclusion from AGRE. The observed frequency of 1.9% is lower than the expected 4%, perhaps due to higher IQs in AGRE subjects than typical for fragile X. It confirms an association of fragile X and autism.
Support: AGRE/CAN.

PS4.3
ASSOCIATION OF AUTISM WITH GABRA4 and GABRB1 IN MULTIPLE ETHNIC GROUPS WITH SEIZURES AS A STRATIFYING PHENOTYPE Ann L Collins, Deqiong Ma, Patrice L Whitehead, Eden R Martin, Harry H Wright, Ruth K Abramson, John P Hussman, Jonathan L Haines, Michael L Cuocar, John R Gilbert, Margaret A Pericak-Vance, Center for Human Genetics, Duke University Medical Center
Background: Autism is a neurodevelopmental disorder of complex genetics characterized by impairment in social interaction and communication as well as repetitive behavior. Multiple lines of evidence including alterations in levels of GABA and the GABA receptors in autistic patients indicate that the GABAergic system, which is responsible for synaptic inhibition in the adult brain, may be involved in autism.
Objective: Previous studies in our lab indicated association of single nucleotide polymorphisms (SNPs) with GABRA4, and interaction between SNPs in GABRA4 and neighboring GABRB1 within Caucasian autism patients. Studies of genetic variation in African American (AA) autism families are rare despite data supporting similar involvement of autism in this racial group.
Results: Analysis of 557 Caucasian (expanded from 470) and 54 AA families and additional SNPs within GABRB1 supported the findings within GABRA4 (rs17599165, p=0.001; rs1912960, p=0.0073; and rs17599416, p=0.0040 in Caucasians and rs2280073, p=0.0287 and rs16859788, p=0.0253 in AA). The GABRA4 and GABRB1 interaction was also validated in the Caucasian dataset (p=0.004). Analysis of a subset of families with a positive family history for seizures revealed no association to GABRA4, however three SNPs within GABRB1 showed significant allelic association; rs2351299 (p=0.0163), rs4482737 (p=0.0339), and rs3832300 (p=0.0253).
Conclusions: These results validate our earlier findings
indicating GABRA4 and GABRB1 as genes contributing to autism susceptibility extending these findings to multiple ethnic groups and suggesting seizures as a stratifying phenotype.

Funding: Grant

**PS4.4**

**HIGH DENSITY ASSOCIATION ANALYSIS OF A LARGE COHORT OF GENES INVOLVED IN NEURONAL MIGRATION AND SYNAPTOGENESIS IN AGRE FAMILIES**

*Jacqueline A Duvall, Jennifer L Stone, Rita M Cantor, Stanley F Nelson, Daniel H Geschwind, UCLA*

**Background:** Recent work suggests that defects in pathways that control synaptic plasticity and brain morphogenesis may be involved in autism.

**Objectives:** Improve power to detect an association signal by testing large groups of genes within biologically plausible pathways, rather than gene-by-gene study. Here we test genes involved in neuronal migration, axonal pathfinding and synaptogenesis for autism association, as a proof of principle.

**Methods:** 1686 single nucleotide polymorphisms (SNPs) in 35 candidate genes were genotyped at an average density of 2-4kb per SNP, in 224 AGRE autism trios (parents and affected child). The Transmission Disequilibrium Test (TDT) was performed on individual SNPs as well as haplotype blocks, and each gene was tested for an over-representation of SNPs from expected distributions.

**Results:** Nine genes showed an over-representation of significantly associated SNPs at a level of p<0.01. The most significant individual SNP and haplotype TDT results include: EFNB2, GABRB3, NTN4, PLAUR, SEMA3A, SLIT1, as well as NLGN4, NRXN1, NRXN3, which were strong a priori biological candidates. While the causal variants in most cases have not been identified, a non-synonymous change was identified in the NTN4 gene, strongly supporting its role in autism.

**Conclusion:** These findings indicate that genes involved in synaptogenesis and neuronal migration may contribute to autism in some individuals. Independent replication of these disease-associated SNPs and testing of other pathway members is ongoing. This study provides the first broad-based genetic evidence for disruption of these biological pathways in autism pathogenesis.

Funding: NIMH, UCLA STAART, UCD MIND Institute, NINDS

**PS4.5**

**THE STRUCTURE OF THE AUTISM SYMPTOM PHENOTYPE: A PROPOSED MULTIDIMENSIONAL MODEL**

*Stelios Georgiades, Peter Szatmari, Lonnie Zwaigenbaum, Eric Duku, Susan Bryson, Wendy Roberts, Jeremy Goldberg, William Mahoney, McMaster University*

**Background:** The main objective of this study is to develop a comprehensive, empirical model that will allow us to reorganize the structure of PDD symptom phenotype through factor analysis into more homogeneous dimensions.

**Methods:** The sample consists of 209 children with PDD referred for genetic studies. The twelve sub-domains of the ADI-R were used in a factor analysis and the emerged factors were then correlated with independent variables (measures of cognition, adaptive function, and diagnostic subtype). Intraclass Correlation Coefficients (ICCs) were calculated to investigate any familial relationships between sibling pairs on the derived factors.

**Results:** The autism symptom phenotype is indeed made up of three factors/domains but these are somewhat different than those used in DSM-IV. Rather, domains include social-communication (SOCOM), inflexible language and behaviour (ILB) and repetitive sensory and motor behaviour (RSMB). For the three factors, only a small amount of variance was accounted for by cognitive and adaptive functioning. Only ILB showed familial correlation between siblings.

**Conclusions:** We conclude that the PDD symptom phenotype is composed of three domains or factors; social-communication, ILB, and RSMB. Each child with PDD can be characterized by these dimensions, which give an informative picture of the clinical presentation and a quantitative estimate of the severity of the disability.

Sponsor: CIHR & OMHF
.34, RCPM = .41, and VABS domains ranged from .23 to .38 (p < .001). Analyzing just those pairs who met strict criteria for AD, ICCs were: PPVT = .43, RCPM = .39, and VABS domains ranged from .26 to .59 (p < .001). Twin correlations were higher for MZ versus DZ twins on the PPVT, RCPM, and almost all VABS domains. Conclusion: Results indicated significant familiarity for AD/PDD severity. Genetic factors explained most of the variance, however, shared-environmental factors also appeared influential.

Sponsor: CAN-NIH

PS4.7 GENOMIC SCREENING FOR PERIPHERAL BIOMARKERS OF AUTISM IN LYMPHOBLASTOID CELL LINES FROM MONOZYGOTIC TWINS DISCORDANT IN SEVERITY OF AUTISTIC DISORDER Valerie W. Hu, Bryan C. Frank, Normal H. Lee, John Quackenbush, The George Washington University Medical Center

Background: To date, diagnosis of autism spectrum disorders relies predominantly upon behavioral observations often prompted by delayed speech or aberrant behavior, and there are no known genes that can serve as definitive biomarkers for the disorders.

Objectives: To identify biomarkers of autism in cell lines derived from peripheral cells of autistic individuals and to elucidate pathways contributing to the autistic phenotype.

Methods: Gene expression profiles of lymphoblastoid cell lines from 5 pairs of male monozygotic twins with ASD who are discordant with respect to diagnosis of autism or severity of language impairment were obtained using two-color spotted DNA microarrays.

Results: Lymphoblastoid cell lines from the monozygotic twins exhibit significant differential expression of genes important to the development, structure, and/or function of the nervous system. Furthermore, many of these genes map in silico to chromosomal regions containing previously reported autism candidate genes or quantitative trait loci.

Conclusions: Our present results provide compelling evidence that candidate genes for autism may be expressed in lymphoid cell lines from individuals with autism spectrum disorders. This finding suggests the possibility of developing a molecular screen for autism using peripheral tissues. Moreover, gene networks are identified that may play a role in the pathophysiology of autism.

PS4.8 THE HUNT FOR AUTISM SUSCEPTIBILITY GENES: A RESOURCE & ROADMAP FOR THE FUTURE Clara M Lajonchere, AGRE Consortium, Cure Autism Now

Since 1997, the Autism Genetic Resource Exchange (AGRE) has been supporting the research community by providing diagnostic, medical, and genetic data to researchers worldwide. As researchers gain a better understanding of the genes responsible for autism, they may be better able to distinguish between the different variants of the disorder and to develop targeted therapies and interventions to treat them. The AGRE resource consists of banked biomaterials (DNA, immortalized cell lines, serum) and a web accessible database that contains genotypic and phenotypic data available to approved researchers. Broadening the scope of phenotypic information available to researchers is a goal for 2006. Currently, AGRE has biomaterial and diagnostic information for over 700 families, genotypic information for over 500, and detailed medical information for 240 families. To date, the AGRE resource has supported 23 candidate gene studies, 19 linkage studies, 12 endophenotype studies and 3 cytogenetic studies, to name a few. The pioneering work of AGRE researchers has identified critical regions on chromosomes 2, 7, 15, and 17 that are bringing scientists closer to understanding neurobiological mechanisms and pathways implicated in autism. An overview of the resource will be presented along with a roadmap for future discovery. The AGRE program is a novel resource that successfully promotes collaborative efforts to speed the progress of autism genetic studies. Such large-scale open efforts are critical to the identification of genes for complex neurologic or psychiatric diseases.

PS4.9 A COMPARISON OF GENOMEWIDE LINKAGE RESULTS FOR AUTISM SPECTRUM DISORDERS USING DIFFERENT DIAGNOSTIC CRITERIA Michelle Xiao-Qing Liu, Christina Chrysler, Peter Szatmari, Lonnie Zwaigenbaum, Andrew D. Paterson, The Hospital for Sick Children

Background: Genetic studies for susceptibility genes for autism typically use two well-known diagnostic instruments, the Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observation Schedule (ADOS), to define affected individuals. However, a diagnostic scheme that combines the ADI, ADOS and other instruments may produce a more reliable diagnostic trait for genetic analysis of children with the broader category of autism spectrum disorders (ASD) (Szatmari et al. in press).

Objectives: To compare the effects of different ASD diagnostic definitions on linkage results.

Methods: Non-parametric linkage analyses, using multiplex families from the Autism Genetic Resource Exchange (AGRE) data, were performed on ASD defined using 3 different criteria: ADI (broad definition); ADOS (definition of ASD); and the combination of ADI, ADOS and Vineland Adaptive Behavior Scales (combined definition). There were 292, 113 and 104 informative families in each group, respectively.

Results: A locus on chromosome 5p13.3 reached suggestive linkage (LOD score = 2.34, p = 0.0005) for ASD using the ADOS definition, while the LOD scores were 0.25 (p = 0.14) and 1.23 (p = 0.009) at this locus using the ADI broad and combined definitions, respectively.

Conclusion: Linkage analysis results varied dramatically when different instruments were used to derive ASD
dissociation of autism. Finding a trait that optimizes the genetic component in ASD is important for future genetic analysis.

Sources of funding: CIHR, Genome Canada

**PS4.10**

**WHOLE GENOME SNP LINKAGE SCREEN IN EXTENDED AUTISM FAMILIES SHOWS SIGNIFICANT EVIDENCE FOR LINKAGE TO CHROMOSOME 12q14.2 IN MALE ONLY FAMILIES.** Deqiong Ma, James Jaworski, RK Abramson, HH Wright, ML Cuccaro, JR Gilbert, JL Haines, MA Pericak-Vance, Center for Human Genetics, Duke University Medical Center

Autism is a common neurodevelopment disorder with a significant genetic component and locus heterogeneity. The use of large extended pedigrees is a powerful approach in genetic linkage studies. A genome-wide linkage analysis was performed on 26 extended autistic families (total 65 affected, 184 individuals). Each family had 2 to 4 affected individuals comprised of either avuncular or cousin pairs. For analysis, we used a high-density single-nucleotide-polymorphism (SNP) genotyping assay, the Affymetrix GeneChip Human Mapping 10K array. Preliminary analysis gave a peak 2pt LOD score of 2.67 for markers on Chromosome 12q14.2. The linkage evidence on Chromosome 12q14.2 was confirmed using multipoint parametric analysis adjusted for linkage disequilibrium (heterogeneity LOD [HLOD] = 3.51 [REC]). Families with only affected males may represent a specific subgroup of autism. The identified linkage evidence on Chromosome 12 was enhanced in the 17 families with only affected males (2-point Max HLOD of 3.34 [REC]; multi-point parametric HLOD=5.32 [REC]) suggesting a significant gender-specific effect in the etiology of autism. The novel linkage peak on chromosome 12 identified in this genome-wide screen further supports the hypothesis that there is substantial locus heterogeneity in autism and that family structure, along with gender effects, may help delineate these different loci.

**PS4.11**

**MDR-PHENOMICS COMBINES CLINICAL AND GENETIC INFORMATION TO IDENTIFY GENES IN AUTISM** Eden R. Martin, Hao Mei, John R. Gilbert, Margaret A. Pericak-Vance, Michael L. Cuccaro, Duke University Medical Center

Background: Genetic heterogeneity is a primary factor limiting the identification of disease genes in studies of complex diseases such as autism. Integration of clinical information into genetic analyses can help overcome this heterogeneity. We previously presented MDR-Phenomics (MDR-P), a novel statistical approach that incorporates clinical and genetic data.

Objective: To examine the properties of MDR-P under various genetic and phenotypic models and apply this method in a large, clinically rich autism family dataset.

Methods: MDR-P extends the multifactor dimensionality reduction-pedigree disequilibrium test (MDR-PDT), a statistical approach to test for genotype associations with high-dimensional data, to incorporate proband-specific characteristics. The algorithm identifies combinations of clinical covariates that maximize the genetic associations to identify phenotypic subsets influenced by the gene under study. The advantage of MDR-P is that no a priori hypothesis is necessary regarding which combination of variables will maximize the results. Computer simulations were used to evaluate the method, and we applied this approach to autism families. We analyzed polymorphisms in several candidate genes, including the serotonin transporter gene (SLC6A4). Covariates of interest include sex, developmental regression and compulsive behaviors.

Results: Simulations demonstrate validity of the MDR-P approach and show that the method often has greater power than stratified analysis or analysis that ignores an informative clinical covariate. Analysis of candidate loci in the autism families will be presented.

Conclusions: MDR-Phenomics provides a rigorous statistical tool to decrease heterogeneity in autism and other complex genetic diseases through incorporation of clinical information.

Sponsors: The National Institute on Aging (R01 AG20135); The National Institute for Neurological Disorders and Stroke (R01 NS36768 and P01 NS26630)

**PS4.12**

**GENETIC EFFECTS FOR PREDICTORS OF ABA TREATMENT SUCCESS** Carla A Mazefsky, Robin P. Goin-Kochel, Brien Riley, Michael C. Neale, Hermine H. Maes, Autism Genetic Resource Exchange, Virginia Institute for Psychiatric and Behavioral Genetics, Virginia Commonwealth University

Background: Applied behavioral analysis (ABA) has the most support as a treatment for children with autism, but studies indicate a bimodal response pattern with a subgroup of children who make minimal progress. A recent ABA treatment outcome study found that pretreatment Autism Diagnostic Interview (ADI) social impairment scores predicted gains in IQ and pretreatment ADI nonverbal communication scores predicted improvement in both IQ and social skills.

Objective: To examine the genetic structure of predictors of ABA response.

Methods: ADI nonverbal communication and social impairment total scores were ascertained from Autism Genetic Resource Exchange participants who were under the age of 20 and had an autism spectrum diagnosis. The sample included 1311 full siblings, 106 monozygotic twins, and 62 dizygotic twins, and was 78.5% male. Twin/sibling resemblance was assessed through correlations and univariate genetic modeling in the Mx software package.

Results: Monozygotic twin correlations were more than twice the dizygotic twin and sibling correlations for both genders and both dependent variables. Consistent with this finding, the best fitting models based on -2 log likelihoods and Akaike's Information Criterion included additive genetic, dominant genetic, and unique environmental factors. Genetic factors could be
constrained to equality for males and females for both variables, with broad heritability estimates of approximately 50% for each dependent variable.

Conclusions: Variation in ADI social and nonverbal communication scores, which are predictive of ABA treatment response, is due to both genetic and unique environmental factors among children with autism spectrum disorders.

Sponsor: NIH-CAN

PS4.13
FUNCTIONAL EPIGENOMICS IN AUTISM Raju K. Pullarkat, NYS Institute for Basic Research in Developmental Disabilities

Objective: Changes in gene expression is implicated in the etiology of complex diseases. CpG methylation is an important factor in the regulation of gene expression. Genes that are silenced by DNA methylation can be reactivated by DNA methylase inhibitors, thus providing a method for the global detection of DNA methylated genes. The objective of the study is to determine the genes that are silenced in lymphoid cells from individuals with autism.

Methods: Lymphoid cells ( AGRE) from parents and affected sib were cultured with and without DNA methylase inhibitor, 5-aza-2'-deoxycytidine (5-azadC) and histone deacetylase inhibitor trichostatin A. Genes that are activated were determined by microarray analyses on Affymetrix U133-plus2 chips. Expression levels of genes in specific regions of chromosomes 2q, 7q, 16p and 17q were tabulated.

Results: Expression levels of about 600 genes including the known imprinted genes were increased when cells treated with 5-azadC. SLC6A4 (17q11) is expressed at a reduced level in the patient and mother while father showed normal activity. On treatment with 5-azadC, the expression increased about three-fold suggesting that SLC6A4 may be a CpG-methylated gene. MEST (7q32) is a known methylated gene, which is expressed at a higher level in the patient. The expression level of MEST increased about 1.6 fold in the patient on treatment with 5-azadC.

Conclusions: Reactivation of silenced genes in lymphoid cells by 5-azadC provides a method in the global analysis of genes that are silenced in autism. Aberrant expressions of SLC6A4 and MEST suggest that they are possible candidate genes for autism. Grants: NIH (NS40691) and NYS-OMRDD.

PS4.15
EXAMINATION OF LAMB1 AND EN2 AS CANDIDATE GENES David A Skaar, James M Jaworski, Jonathan L Benton, Eden R Martin, Harry H Wright, Ruth K Abramson, Michael L Cuccaro, John R Gilbert, Margaret A Pericak-Vance*, Duke University Medical Center

Background: Multiple studies have examined candidate genes for autism on chromosome 7q, and have identified significant associations for markers within LAMB1 and EN2.

Objectives: Examine previously tested markers in LAMB1 and EN2 for significant associations in the Duke dataset.

Methods: Patients were recruited through centers at Duke and the University of South Carolina. DNA extracted from blood, and DNA obtained from the AGRE repository, was genotyped for single nucleotide polymorphisms using assays from Applied Biosystems and Nanogen. The pedigree disequilibrium test (PDT) and geno-PDT were used to calculate association p-values.

Results: Significant associations were detected for markers within LAMB1, in subsets of the entire sample group. One marker was significant for the AGRE samples, and two other markers were strongly significant for the group of affected individuals with no family history of autism. For the EN2 markers, no significant associations were found for any markers in either the entire dataset, or subsets divided by family history.

Discussion: Our results implicate LAMB1 as a
susceptibility gene, particularly for cases with no previous family history. These results do not support EN2 as an autism candidate gene in our dataset, or in any subdivision.

Funding source: NIH grant

PS4.16  
HIGH DENSITY SCREEN FOR ASSOCIATION TO AUTISM COVERING REGION OF LINKAGE TO CHROMOSOME 5 Jennifer L Stone, Barry Merriman, Daniel H Geschwind, Stanley F Nelson, UCLA

Previously, our group identified a region on chromosome 5, linked to Autism Spectrum Disorder (ASD) (MLS 2.54, Yonan et al. 2003) using multiplex families collected by the Autism Genetic Resource Exchange (AGRE). We fine-mapped this region with 3680 SNPs, assayed in a total of 219 trios from the AGRE resource as part of a larger project. A total of 17.2 MB of euchromatic sequence was interrogated using SNPs placed along the interval at 5 kb average density. Of 99 genes within the interval (NCBI MapViewer, build 35), 86 were directly tested by at least 1 SNP within 10kb of the genic interval. SNPs were additionally placed throughout intergenic regions to achieve more uniform coverage throughout the entire region of linkage. SNPs were tested individually and in combination using the transmission disequilibrium test (TDT). Single SNP analysis highlights include ITGA1 (p-value 6.74E-06), RICTOR (p-value 0.0002), and PDE4D (p-value 0.0003), while haplotype analysis highlights include PDE4D (p-value 0.0002) and an intergenic region (p-value 0.0009). Significant results from this screen are currently being tested in a replication sample.

This work was funded by NIMH grant number MH64547

PS4.17  
THE BROADER PHENOTYPE IN 10-MONTH OLD INFANT SIBLINGS OF CHILDREN WITH AUTISM Leslie J Carver, Joseph P McCleery, Sarah R Reed, Karen M Burner, Lisa M Tully, Karen R Dobkins, University of California, San Diego

Background: Previous research has identified a broader phenotype of social, communicative, and cognitive difficulties in teenage and adult first-degree relatives of individuals with autism.

Objectives: Examine the broader phenotype of social-communication behaviors in infant siblings of children with autism, compared with typically developing infants.

Methods: Fourteen 10-month old infant siblings of children with autism and twenty-eight typical controls were examined via a structured behavioral assessment of social-communication skills. A variety of behaviors were scored from videotape, and several t-tests were conducted based on hypotheses generated from previous research on infants with autism.

Results: Infant siblings demonstrated significantly less eye contact used for requesting relative to controls (p<0.05), but no differences in frequency of following points, eye contact for joint attention, requesting behaviors, following verbal commands, sharing interest, social interaction, or turn-taking. Although not predicted a priori, infant siblings also showed increased rates of eye contact used for social initiations.

Conclusion: These findings indicate that the broader autism phenotype is present in early infancy, and is characterized by atypical eye contact behavior. These early differences in eye contact may be related to deficits in social interaction behaviors that are characteristic of the broader phenotype at later ages, and may also be associated with higher risk for a later diagnosis of autism.

Support: M.I.N.D. Institute, NAAR

PS4.18  
DEVELOPMENTAL TRAJECTORIES OF QUANTITATIVE COMPONENTS OF THE AUTISTIC SYNDROME John N Constantino, Anna M Abbacchi, Leah Givens, Molly Arvin, Teddi Gray, Richard D Todd, Washington University School of Medicine

Background: Although categorical diagnoses of autism spectrum disorders (ASDs) are highly stable over time, less is known about the longitudinal course of quantitative components of the autistic syndrome.

Objective: To examine the first wave of data from a longitudinal study of heritable quantitative components of the autistic phenotype in affected children, their siblings, and in twins in the general population.

Methods: Repeated measurements using the Social Responsiveness Scale (SRS) were collected prospectively for 50 autistic preschoolers, 150 school-aged ASD probands and their siblings, and 125 school-aged male-male twin pairs. Infant head circumference measurements (birth to 24 months) were available for a sub-sample of ASD probands and their sibs.

Results: We observed, on average: a one-half standard deviation (SD) yearly improvement in SRS scores in preschoolers; no significant improvement in older ASD subjects; a one-half SD improvement over 5 years in twins. Inter-individual variations in SRS scores were highly preserved over time (r=0.75). There were substantial heritable influences on time-rated change in SRS scores in twins (monozygotic twin-twin correlation 0.66; dizygotic twin-twin correlation 0.42). The course of head circumference in infancy appears highly familial (proband-sib canonical correlation 0.60) but non-predictive of autistic impairment in the sibs.

Conclusions: Children with ASDs may be particularly amenable to improvement in core symptoms during early childhood; it is possible to measure effects of intervention on such symptoms using reliable quantitative methods. In addition to their relevance in characterizing ASD, social responsiveness and infant head circumference represent potential quantitative endophenotypic markers for gene-gene interaction in autism.

Sponsor: NICHD

PS4.19  
COGNITIVE AND LANGUAGE SKILLS OF SIBLINGS OF CHILDREN WITH AUTISM AT THE AGE OF 7 YEARS. Ifat Gamliel, Nurit Yirmiya, Marian
PHYSICAL FINDINGS IN AUTISTIC DISORDER

Sponsor: NAAR

These findings will be discussed in relation to the broad
some subtle differences among the groups were revealed.
age 7 years in terms of cognition and language. However,
Conclusion: Overall, SIBS-A were well-functioning at
below average (PS < 85 IQ) than SIBS-A-BP (0 of the 6)
significantly more SIBS-A-BP (2 of the 8) scored 1 SD
However, on the Freedom of Distractibility scale,
significantly more SIBS-A-BP (2 of the 8) scored 1 SD
below average (FD < 85 IQ) than SIBS-A-nonBP (0 of
interests/stereotyped behavior.
Objectives: To compare the cognitive and language skills
of siblings of children with autism (SIBS-A) and siblings
of typically developing children (SIBS-TD), at the age of
7 years.
Methods: All siblings are participating in our longitudinal
study of siblings of children with autism, and were seen at
age 4, 14, 24, 36 and 54 months. We identified a
subgroup of “SIBS-A-BP”, i.e., siblings who at age 14, 24
and/or 36 months revealed a delay in cognition and/or
language. The groups were now evaluated with the
WISC-III (Wechsler, 1991) and the CELF-III (Semel,
Wiig & Secord, 1995).
Results: At age 7 years, non-significant differences
emerged between the three groups: SIBS-A-BP (n = 8),
SIBS-A-nonBP (n = 25, the remaining SIBS-A who did
not reveal cognitive and/or language difficulties), and
SIBS-TD (n = 31), on any of the WISC-III mean scale
scores, nor on the CELF-III mean language scores.
However, on the Freedom of Distractibility scale,
significantly more SIBS-A-BP (2 of the 8) scored 1 SD
below average (FD < 85 IQ) than SIBS-A-nonBP (0 of
the 24) and SIBS-TD (0 of the 31, Likelihood Ratio =
8.74, p = .01). Interestingly, on the Processing Speed
scale, more SIBS-A-nonBP (5 of the 23) scored 1 SD
below average (PS < 85 IQ) than SIBS-A-BP (0 of the 6)
and SIBS-TD (0 of the 30, Likelihood Ratio = 10.16, p =
.006).
Conclusion: Overall, SIBS-A were well-functioning at
age 7 years in terms of cognition and language. However,
some subtle differences among the groups were revealed.
These findings will be discussed in relation to the broad
phenotype of autism.

Sponsor: NAAR

PS4.20
PHYSICAL FINDINGS IN AUTISTIC DISORDER

Theresa A. Grebe, Sharman E. Ober-Reynolds, Susan M.
Stephens, R.Curt Bay, Janet E. Kirwan, Joshua J. Jones,
Raun D. Melmed, Theresa A. Grebe/Southwest Autism
Research and Resource Center

Background: With the exception of macrocephaly, no
consistent physical findings have been reported in autistic
disorder (AD). Dysmorphic features are seen in children
with autistic disorder and chromosome disorders or
genetic syndromes, but there is no common phenotype.
Objectives: To identify phenotypic subtypes of AD based
on physical features and dysmorphology.
Methods: A cohort of 113 boys, ages 3-10, with autistic
disorder was studied. The DSM-IV criteria for AD were
met along with confirmation by ADOS and ADIR testing.
All had normal high-resolution chromosomes and Fragile
X DNA testing. Excluded were children with extreme
prematurity, cerebral palsy, seizures, or genetic
syndromes. Each boy underwent a complete
dysmorphology evaluation, including pertinent
measurements.
Results: 60 boys (53.1%) exhibited ≥3 physical findings.
The most frequent findings were hypotonia, seen in 54
(47.8%); connective tissue findings, including joint laxity,
velvety skin, and pes planus in 47 (41.6%); macrocephaly
in 22 (19.5%); and macroorchidism in 21 (18.6%) boys.
The combination of connective tissue findings and
macroorchidism was seen in 11 boys (9.7%), while
connective tissue findings and macrocephaly were present
in 10 boys (8.8%). Hypotonia, macrocephaly, and
connective tissue findings were seen in 6 (5.3%).
Discussion: Connective tissue findings and
macroorchidism have not previously been reported in AD,
except in Fragile X syndrome. These patterns of physical
findings may represent specific phenotypes of AD that
will direct the search for additional candidate genes.
Correlation with other neurologic disorders involving
connective tissue changes, including Fragile X syndrome,
will elucidate potential pathogenic mechanisms in autistic
disorder.

PS4.21
BEHAVIOR AND SENSORY INTERESTS

INTERVIEW

Ellen Hanson, Lindsay Jackson, Elizabeth Baroni, Rachel Hundleby, Janice Ware, Children's Hospital, Harvard Medical School

Background: There has been increasing interest in better
phenotyping for children with developmental issues,
particularly those with possible autism spectrum
disorders. Better phenotyping is considered essential for
research and clinical work.
Objectives: Develop a new instrument that systematically
describes a broad range of atypical behaviors which are
frequently seen in children with developmental
disabilities, particularly in autism spectrum disorders.
Description: The BSI is designed to assist clinicians and
researchers in the assessment and analysis of a number of
behaviors which are often observed to be atypical in their
type, number and intensity in children with developmental
issues. The questionnaire includes categories of
Stereotyped Behaviors; Compulsive and Ritualistic
Behaviors; Rigidity; Aggression and Self Injurious
Behavior; Language Perseveration and Perseverative
Interests. The instrument was conceptualized to be used in
both clinical and research settings. It is also designed to
partner, when appropriate, with the Autism Diagnostic
Interview - Revised (ADI-R; Rutter et al., 1994) and the
Autism Diagnostic Observation Schedule (Lord et al.
2001). Use of this instrument involves an informant (a
parent or caregiver who is familiar with both the
developmental history and the current behaviors of the
individual). The individual being assessed does not have
to have a minimum developmental level and does not
have to be present during the interview. The BSI takes
approximately 10-15 minutes. Standardization is currently
being conducted.
SOcio-communicative deficits of children with Williams Syndrome with Autism spectrum classifications

Bonita P. Klein-Tasman, Kristin D. Phillips, University of Wisconsin-Milwaukee

Background: Williams syndrome (WS) is a genetically-based neurodevelopmental disorder with a unique pattern of cognitive and personality characteristics. Although children with WS are sociable and may ultimately show a relative strength in their linguistic abilities, some aspects of socio-communicative development are typically delayed.

Study Objectives: To examine patterns of overlap in socio-communicative deficits of young children with WS with the autism spectrum.

Methods: ADOS Module 1 was administered to 29 2½ to 5 ½ year olds with WS.

Results: Almost half of the participants with WS showed difficulties resulting in ADOS classifications of Autism Spectrum. These participants generally had significantly weaker expressive and receptive language skills. Even when language abilities were statistically taken into account, however, they continued to show more communication and reciprocal social interaction deficits.

At the item level, they differed in Frequency of Directed Vocalization, Unusual Eye Contact, Directed Facial Expressions and Quality of Social Overtures. Trends toward differences in Social Smiling, Integration of Gaze and Other Behaviors, and Initiation of Joint Attention were also noted. Difficulties with gestures and pointing were common regardless of ADOS classification, and most of the participants showed no abnormality in Shared Enjoyment.

Conclusions: Certain socio-communicative behaviors appear to be impaired for many children with Williams syndrome, including pointing and gesturing. Some young children with WS with limited language show additional abnormalities in communication and reciprocal interaction that are not accounted for by language delays. Implications will be discussed.

This research was supported by a University of Wisconsin-Milwaukee Graduate School Research Award and NIMH grant R03MH069400 to Bonita Klein-Tasman.

PS4.23

Measuring social traits of the Autism phenotype in multiplex and extended pedigree family members

Lori Krosny, Heidi Block, Judith S. Miller, Hilary Coon, Megan Farley, Michele E. Villalobos, M Ann Ashcraft, Danielle Siniscalchi, William M McMahon, Utah Autism Research Program

Background: Measuring traits of autism and the broader autism phenotype in family members may speed the discovery of autism susceptibility genes. Methods for obtaining this information are limited and often time consuming. Few studies have compared different methods.

Objectives: Compare two quantitative measures of social impairment.

Methods: Multiplex family members were recruited and assessed using two methods: 1) the Social Reciprocity Scale (SRS) questionnaire (Constantino, 1998, 2002) completed by an informant, and 2) the Broader Phenotype Autism Symptom Scale (BPASS) interview (Dawson, 2004), conducted by self report or parent informant.

BPASS and SRS data were obtained from 59 subjects: 22 children and 37 adults. Fourteen children and 5 adults met Autism Diagnostic Observation Schedule (ADOS) criteria for autism.

Results: Analysis of the current sample revealed a significant correlation between measures for the total sample (r(59) = 0.807, p < 0.01) and child sample (r(22) = 0.763, p < 0.01). A significant correlation also existed for the adult sample (r(37) = 0.652, p < 0.01).

Conclusions: The SRS and BPASS appear to be well correlated.

Sponsor: This research was conducted by one of the NICHD Collaborative Programs of Excellence in Autism (Grant # 5 U19 HD035476).

PS4.24

Relationship between the language abilities of children with autism and their first-degree relatives

Kristen A. Lindgren, Susan E. Folstein, J. Bruce Tomblin, Helen Tager-Flusberg, Boston University School of Medicine

Background: Family studies have noted impaired language abilities among first-degree relatives of children with autism. Research also suggests that language impairment (LI) in autism has a genetic basis.

Objective: To examine the language abilities of first-degree relatives of children with autism with respect to those of the proband using measures sensitive in identifying LI.

Methods: Participants were 32 autistic children with language impairment (ALI), 20 autistic children with normal linguistic abilities (ALN), and their siblings and parents. The ALN and ALI sibling, mother, and father groups did not differ on non-verbal IQ. The siblings group also did not differ on age and verbal IQ. All participants were administered the non-word repetition (NWR) subtest of the CTOPP. Siblings and probands were also administered the CELF-III. Family members were categorized as LI if either the total language ability (TLA) on the CELF-III or the NWR score was more than one standard deviation below the mean.

Results: The percentage of relatives with LI was significantly higher in relatives of ALI children (27%) than in relatives of ALN children (12%). There was a significant positive relationship between the TLA of the autistic probands and their siblings (r = 0.36, p < 0.05), and the TLA of siblings of ALN children was significantly higher than that of siblings of ALI children (t(47) = 3.18, p < 0.01). In addition, there was a significant positive relationship between the NWR scores of the autistic probands and their mothers (r = 0.31, p < 0.05), and the mothers of ALN children exhibited a trend towards higher NWR scores than mothers of ALI children (t(48) = 1.7, p < 0.10).
Conclusions: These findings support the hypothesis that there is differential heritability of some components of language and that there is a maternal influence on the genetics of language impairment in autism.

Sponsors: NINDS (R01 NS 38668), NIDCD (U19 DC 03610), and NAAR

**PS4.25**
INVESTIGATING THE NEUROPSYCHOLOGICAL BASIS OF THE BROAD AUTISM PHENOTYPE
Molly Losh, Joseph Piven, University of North Carolina, Chapel Hill

OBJECTIVE: This project investigated the neuropsychological basis of the broad autism phenotype (or, BAP) by examining links between clinically-defined personality features of the BAP (e.g., ‘aloof’ and ‘rigid/perfectionistic’ personality styles, thought to correspond to the social deficits and restricted interest/repetitive behaviors in autism, respectively), and three neuropsychological domains hypothesized to play a central role in autism (social cognition, executive function, and central coherence).

METHODS: Eighty parents of high-functioning children with autism and 31 age- and IQ-matched control parents participated in this study. Direct clinical assessment with the Modified Personality Assessment Schedule-Revised (MPAS-R) was used to identify autism parents exhibiting aloof and/or rigid/perfectionistic traits. It was hypothesized that these personality traits would co-segregate with impairments in conceptually similar neuropsychological domains: 1) ‘aloof’ personality was hypothesized to co-segregate with deficits in social-cognition; and 2) the ‘rigid/perfectionistic’ trait was expected to relate to mild impairments on executive functioning tasks and weak central coherence.

RESULTS: Contrary to expectations, deficits in all neuropsychological domains (executive function, central coherence, and social-cognition) were observed in the aloof group, whereas the group of parents displaying rigid/perfectionistic personalities performed comparably to controls across all domains. No differences were observed between controls and autism parents who demonstrated neither characteristic.

CONCLUSIONS: These findings and their implications for understanding the pathogenesis of autism will be discussed.

SPONSOR: STAART grant U54 MH66418

**PS4.26**
NEURAL CORRELATES OF FACE PROCESSING IN INFANT SIBLINGS OF CHILDREN WITH AUTISM
Joseph P McCleery, Karen M Burner, Karen R Dobkins, Leslie J Carver, University of California, San Diego

Background: Research using event-related potentials has shown that, unlike controls, individuals with autism and their family members do not show a temporal advantage for faces over non-face objects in the N170 component, and do not show right-stronger-than-left N170 activations to faces. These atypicalities in face processing may be a marker for genetic susceptibility to autism, perhaps resulting from abnormalities in social systems in the first year of life.

Objectives: Compare face and object processing in 10-month old siblings of children with autism and control infants.

Methods: Infants were presented with pictures of familiar and unfamiliar faces and objects, and event-related potentials were recorded.

Results: Typically developing controls showed a faster P400 ERP component to faces than to objects (faces=435ms, objects=454ms, p=0.004), whereas at-risk infants had equivalent P400s for faces and objects (faces=448ms, objects=445ms). Controls also showed right-stronger-than-left activations in the N290 (an infant equivalent of the N170) for faces (left=-2.59mV, right=-9.52mV, p=0.003), but not for objects (left=-7.61mV, right=-9.99mV, p=0.21). At-risk infants showed a similar pattern with a non-significant trend toward right lateralization in the N290 for faces (left=-3.64mV, right=-7.48mV, p=0.10) and not for objects (left=1.824mV, right=-2.5mV, p=0.46).

Conclusion: These preliminary data are consistent with the hypothesis that atypical face processing is present early in life in families affected by autism.

Support: M.I.N.D. Institute, NAAR

**PS4.27**
INVESTIGATING THE RELATION BETWEEN SOCIO-COMMUNICATIVE DEFICITS AND INTELLECTUAL AND LANGUAGE ABILITIES IN CHILDREN WITH WILLIAMS SYNDROME USING THE AUTISM DIAGNOSTIC OBSERVATION SCALE (ADOS) Rebecca H McNally, Bonita P Klein-Tasman, John E Angela, Susan Risi, Kristin D. Phillips, Carolyn B. Mervis, University of Louisville

Background: Williams syndrome (WS) is a neurodevelopmental disorder caused by a microdeletion of chromosome 7q11.23, resulting in mild to moderate mental retardation or learning disabilities and a unique behavioral phenotype. Although individuals with WS have a relative strength in vocabulary and structural language abilities and tend to be highly gregarious, they demonstrate weaknesses in pragmatics and social interactions.

Objectives: The aim of this study was to investigate the relation between socio-communicative deficits and intellectual and language abilities in children with WS using the Autism Diagnostic Observation Scale-Generic (ADOS-G) (Lord et al., 2001). The ADOS-G is a semi-structured assessment of social-interaction, communication, and play designed to be independent of intellectual and expressive language abilities.

Methods: Participants to date are 24 (14 male, 10 female) children (mean ĈA: 5.66 years, range: 4-9 years) with a genetically confirmed diagnosis of WS. ADOS-G (Modules 1 or 2), Differential Ability Scales (DAS), and Peabody Picture Vocabulary Test-III were administered to all participants. Children’s DAS general conceptual
ability (GCA) standard scores ranged from <25 (the lowest possible) to 91.

Results: Intellectual and language abilities were negatively correlated with both ADOS-G Module 1 Communication and Reciprocal Social Interaction total scores (r = -.74, p = .02; r = -.67, p = .05, respectively) and Module 2 Communication and Reciprocal Social Interaction scores (r = -.59, p = .02; r = -.74, p = .002, respectively).

Conclusion: Preliminary results suggest that intellectual and language abilities are associated with socio-communicative functioning in children with WS, even though the ADOS was designed to be independent of these abilities.

This research was supported by NIH grants R37 HD29957 and R01 NS35102 to Carolyn B. Mervis.

**PS4.28**

**LANGUAGE DIFFICULTIES IN ADOLESCENTS WITH AUTISM SPECTRUM DISORDERS: THE ROLE OF PHONOLOGICAL SHORT-TERM MEMORY**

*Nick G Riches, Tom Loucas, Gillian Baird, Newncomen Centre, Guy’s and St Thomas’s Hospital*

Background: Recently, it has been argued that the language profiles of children with ASD who have “specific” language difficulties (i.e. difficulties with language, but good non-verbal abilities), are similar to those of children who have specific language difficulties but no ASD, i.e. children with Specific Language Impairment (SLI). In particular, both groups are reported to have difficulties with phonological short-term memory, as assessed by tests of non-word repetition. It is therefore possible that poor phonological short-term memory (STM) plays a role in the language difficulties of both groups.

Objectives: To investigate whether poor phonological STM is a causal mechanism for specific language difficulties in both ASD and non-ASD individuals.

Method: Tests of non-word repetition and non-word discrimination were conducted on adolescents (14-15 years old) from five experimental groups - ASD plus specific language difficulties, high-functioning ASD, SLI, and age- and language-matched typically developing control group.

Results: Data collection is still in progress. We will report findings on the data collected so far.

Conclusion: The findings will allow us to investigate the possible overlap between autism and language impairment, and whether the language difficulties of children with ASD are qualitatively similar to those of children with SLI and no ASD. This possible overlap is of particular interest in the light of recent genetic and epidemiological studies which indicate that language difficulties and autistic traits tend to co-occur in both individuals and families, suggesting the existence of a broader phenotype.

**PS4.29**

**ALEXITHYMIA IN PARENTS OF CHILDREN WITH PERVERSIVE DEVELOPMENTAL DISORDERS**

*Peter Szatmari, Jeremy Goldberg, Lonnie Zwaigenbaum, Stelios Georgiades, Eric Duku, McMaster University*

Background: There is some evidence that individuals with Pervasive Developmental Disorders (PDD) are more impaired in their emotion processing than individuals without PDD. We hypothesized that parents of children with PDD will also demonstrate such difficulties when compared to a control group and that traits of impairments in emotion processing will be correlated within parents of a PDD child.

Methods: Toronto Alexithymia Scale (TAS-20) is a reliable and valid measure of emotion processing in adults which includes 3 subscales: Difficulty Identifying Feelings, Difficulty Describing Feelings, and Externally-Oriented Thinking. Data were collected on 439 parents of children with PDD and a control group of 45 parents of children with Prader Willi syndrome (PWS). Intraclass Correlation Coefficients (ICC) for parent couples were calculated using Hierarchical Linear Modeling (HLM) for the three dimensions of the TAS-20.

Results: Parents of PDD children had significantly higher scores on the TAS-20 than parents of PWS children. Analyses also indicate significant correlation on the trait Difficulty Identifying Feelings between mothers and fathers of PDD children (ICC=0.26, p < .001), but not for the control group (p > .05).

Conclusions: We conclude that the alexithymia trait is a potential endophenotype of the autism genotype. We also report some evidence for the assortative mating of alexithymia traits in parents of children with PDD.

Sponsor: CHIR & OMHF

**PS4.30**

**EARLY SOCIAL AND COMMUNICATION IMPAIRMENTS IN YOUNG SIBLINGS OF CHILDREN WITH AUTISM**

*Karen Toth, Geraldine Dawson, Andrew Meltzoff, Jessica Greenson, Deborah Fein, University of Washington*

Siblings of children with autism may be at risk not only for an autism spectrum disorder (ASD), but also for social, communication, and learning impairments similar to, but subtler than, those found in autism. Thus far, however, there have been very few prospective studies of very young siblings.

The present study examined forty 18-24 month old non-ASD siblings across a range of domains as compared to 12 typically developing (TD) toddlers. The ADOS, Vineland SEEC, CSBS-DP, and Meltzoff imitation battery assessed social abilities. The Mullen and Vineland Adaptive Behavior Scales (VABS) measured communication skills.

Siblings scored significantly lower than TD children on the Vineland SEEC Interpersonal Relationships domain, but not on Play and Leisure. No group differences were found on the VABS communication, daily living, and motor domains. On the ADOS, siblings pointed and responded to social smiling less than TD children. On the CSBS-DP, siblings demonstrated lower overall rates of communicating, lower language comprehension, and
fewer word combinations, but similar rates of joint attention, social interaction, gaze and point following, as compared to TD children. No differences were found on any of the Mullen domains, although there was a trend for siblings to score lower on receptive language than TD toddlers. Also, no significant differences were found on imitation. These results suggest that there are not cross-the-board deficits in young non-ASD siblings of children with autism, but that nonetheless certain aspects of language and social communication may be affected at an early age and should be closely monitored.

We should also consider the social and communicative deficits of ASD.

**PS4.32**

**AGENESIS OF THE CORPUS CALLOSUM AND AUTISTIC DISORDER: A CASE REPORT Sabri Herguner, Nahit Motavalli Mukaddes, Department of Child and Adolescent Psychiatry, Istanbul Faculty of Medicine**

**Background:** The role of corpus callosum in the etiopathogenesis of autism is controversial. While some studies showed reduction of total corpus callosum and anterior, middle, and posterior callosal sub-regions in individuals with autism, others did not. According to our knowledge, there is no report on complete agenesis of corpus callosum in subjects with AD.

**Objective:** To report a case with autistic disorder (AD), mental retardation (MR), treatment-resistant epilepsy, and complete agenesis of corpus callosum, and also to discuss the influence of corpus callosum agenesis in clinical outcome.

**Methods:** Case description: A 12-year-old non-verbal boy was referred to our clinic because of the lack of verbal and non-verbal communication, and repetitive behaviors. He had severe motor developmental delay and grand-mal seizures with no response to antiepileptics. He had also dysmorphic features such as midfacial hypoplasia, dysplastic ears, mandibular prognathism, and bilateral fifth finger clinodactyly.

**Results:** His extensive metabolic and genetic screenings were normal. His cranial MRI revealed the complete absence of the corpus callosum and the enlargement of the posterior and temporal horns of the lateral ventricles. Conclusion: The clinical outcome in this case could be related with complete agenesis of corpus callosum.

Although it is premature to generalize these findings, however it may be concluded that the complete agenesis of corpus callosum and the diminished inter-hemispheric connectivity might have an impact on the more severe clinical presentation such as the co-occurrence of dysmorphic features, autism, mental retardation and epilepsy.

**PS4.33**

**STRUCTURAL MRI OF THE BASAL GANGLIA IN AUTISM Mariëlle Langen, Sarah Durston, Wouter G. Staal, Saskia J. Palmen, Herman van Engeland, Department of Child and Adolescent Psychiatry, Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht**

**Background:** Autism research has often focused on the social and communicative deficits observed in autistic individuals, and less on the third defining behavioral abnormality, repetitive and stereotyped behavior. Imaging and laboratory studies in humans have implicated the basal ganglia, and in particular the striatum (comprised of the caudate nucleus and putamen), in the development of stereotypy and other repetitive behaviours in multiple neuropsychiatric disorders.

**Objectives:** To compare basal ganglia volumes between autistic and typically developing children and adolescents.
Methods: Basal ganglia volumes were assessed on anatomical MRI-scans in forty-two medication-naïve, high-functioning children and adolescents meeting DSM-IV criteria for autism or Asperger’s syndrome and in 42 typically developing individuals matched for age, gender, IQ, height, weight, handedness, and parental education. Basal ganglia structures were traced manually by a single experienced rater (ML), blind to subject identity. Results: Preliminary results in 2 x 21 matched individuals showed an overall enlargement of the basal ganglia in autistic subjects, mostly due to an enlarged caudate nucleus. Conclusion: These results suggest that there may be a role for the basal ganglia in autism, in addition to the involvement of other brain areas.

PS4.34 EXPLORING STRUCTURAL BRAIN DIFFERENCES IN ASPERGER SYNDROME Kavita Ruparelia, Stella Tsermetseli, Janine V Spencer, Justin M D O’Brien, Brunel University, Centre for Cognition and Neuroimaging

Background: Magnetic Resonance Imaging (MRI) has been useful in revealing subtle structural brain differences in Autistic Spectrum Disorder (ASD). Recent studies have begun to elucidate the underlying neuroanatomical abnormalities in autism, with the most consistent finding being increased brain volume. Objectives: Comparing structural brain differences in adults with Asperger Syndrome and typically developing adults.

Methods: Participants were recruited from colleges specialising in ASD. The sample tested consisted of 9 subjects diagnosed with Asperger Syndrome (mean age=25.65, sd=9.23) and 9 control subjects closely matched by age and gender (mean age=27.81, sd=8.57). Whole-brain T1-weighted MRI scans were acquired with a Siemens Trio 3T MRI scanner; images were segmented using SPM5 before implementation of Voxel-Based Morphometry (VBM).

Results: A significantly higher gray matter volume was found in the Asperger Syndrome group compared to the control group, while white matter volume was identical. The difference of 11.5% in gray matter volume is consistent with, although slightly larger than, that found in previous studies. VBM analysis of gray matter densities indicates increased thickness in a number of bilateral foci, including: Inferior Occipital Gyrus, Superior Temporal Gyrus, Inferior Parietal Lobule, Middle Frontal Gyrus and in the Transverse Temporal Gyrus.

Conclusion: Preliminary findings of this study support previous suggestions of increased brain volume in ASD, and in parallel with our work on ASD/non-ASD sibling pairs is helping to develop a better understanding of the neurological basis of ASD.

Sponsor: FCT

PS4.35 INCREASED RESTRICTED DIFFUSION IN YOUNG CHILDREN WITH AUTISM Dafna Ben Bashat, Vered Kronfeld, Ariela Even, Ditza Tzachor, Yonata Levy, Liat Ben Sira, Tel Aviv Sourasky Medical Center

Background: Previous work reported increased cerebral volume in young children with autism, arguing for abnormal neural growth patterns and regulation early in development. Further work detected decreased anisotropy in adolescents with autism.

Objectives: To detect differences in white matter structure between young children with Autism and control children, using advanced MR methods.

Method: Research group included ten children (2 years to 7 years) with a confirmed diagnosis of Autism (ADOS; diagnosis for the younger children re-established at age 4). Control group included 36 normal individuals (6 months to 23 years). Diffusion tensor imaging (DTI) and high b value diffusion weighted imaging (DWI) were applied to both groups. Region of interest analysis was conducted in seven regions in the cerebrum. Values of fractional anisotropy (FA), probability and displacement were measured and normal developmental curves were derived. Individual data points of the research participants were plotted against the normal curves.

Results: Comparing these individual data points to the expected normal values, no differences were detected in the centrum-semi-ovale area and in the forceps major area. However, increased restriction and anisotropy were observed in the anterior limb of the internal-capsule and in the left side of the superior longitudinal fasiculus.

Conclusion: Our results show for the first time increased restricted diffusion in young children with autism. These findings demonstrate high packing density of the white matter in some regions supporting previous claims of over myelination/connectivity in young children with autism.

Supported by: March of Dimes Birth Defects Foundation

PS4.36 NEUROINFORMATICS IN AUTISM RESEARCH: THE AUTISM TISSUE PROGRAM DATA PORTAL Michael B Brimacombe, Jane Pickett, Richard Pickett, New Jersey Medical School - UMDNJ

Background: The Autism Tissue Program (ATP) maintains a database of approximately 6,000 tissue donation registrants and manages a collection of brain tissue from autistic and control individuals. The ATP makes tissue available to researchers and the ATP Data Portal (www.atpportal.org) integrates clinical and research data resulting from these projects.

Objectives: The Portal contains clinical, diagnostic and research data for a common group of subjects and can thus be employed for investigation of hypotheses and potential multi-dimensional associations related to autism. A Neuroinformatics Advisory Committee provides guidance for selection of informatics software tools appropriate for this autism related neuroinformatics resource.

Methods: Neuroinformatic environments require the processing and integration of data: intake, processing and
standardization of data from collaborating labs, integration of information into existing relational databases. The Portal includes donor registry, medical history, genetic tests and post-mortem imagery. Basic statistical methods are used to examine patterns and hypotheses.

Results: By August of 2005, the ATP acquired 78 autism cases, and a total of 181 combined autism, autism relatives and control cases. Ages range from (autistic) 2 years 9 months-66 and (controls) 1-71. Currently 39 research projects have been supplied with ATP tissue. Data integration is ongoing. Distributions of brain weights by gender are normally distributed and show autistic brains to be significantly heavier (p-value < 0.01).

Conclusions: The ATP Data Portal incorporates clinical, diagnostic and research data and provides a neuroinformatics research environment that will allow for detailed investigation of hypotheses and associations for complex autism syndromes.

Sponsor: ATP.

PS4.37
INCREASED WHITE MATTER VOLUME IS CORRELATED WITH GREATER POSTCENTRAL SULCAL COMPLEXITY IN CHILDREN WITH AUTISM, DLD, AND CONTROLS Curtis K Deutsch, David A Ziegler, Nora Braun, Steve Hodge, Nikos Makris, Martha R Herbert, Shriner Center

Background: Increased white matter volume has been found in children with autism and developmental language disorder (DLD). There is also evidence that gyriﬁcation patterns are aberrant among individuals with these disorders.

Objectives: Determine the extent to which white matter volume correlates with postcentral sulcal branching patterns.

Methods: This study explored morphology of the postcentral sulcus, of potential relevance to autism and DLD based on previous studies, as a function of white matter volume. MRI scans from 84 children (30 autism, 24 DLD, 30 typically developing subjects) were classified by three sulcus conﬁgurations: single, double, and branched (Y-shaped). This was documented in the left hemisphere, which had greater complexity than the right (p=0.002). White matter volume differed signiﬁcantly by sulcal morphology (p=0.03), yet the diagnosis by POCS interaction was not signiﬁcant. Regardless of diagnosis, children with left hemisphere branching displayed greater white matter volume than those with a single sulcus.

Conclusions: Increased white matter volume was positively correlated with more complex postcentral sulcal branching, regardless of diagnosis. Further studies are required to determine whether this correlation generalizes to other sulci.

Sponsor: NINDS, NIMH, NICHD, Cure Autism Now

PS4.38
A CASE-CONTROL 3.0 TESLA MRI MORPHOMETRIC STUDY OF AUTISM WITH AND WITHOUT ATTENTION

DEFICIT/HYPERACTIVITY DISORDER Jed Thomas Elison, Erin Bigler, Judith S. Miller, Jeffrey Lu, E.K. Jeong, Janet E. Lainhart, Utah Autism Research Program

Background: Signs of ADHD frequently occur in children with autism. Neuroimaging studies have not yet identified brain correlates of ADHD in autism or considered the effects of ADHD-related morphometry in autism-control studies.

Objectives: This pilot study compares regional white and gray matter densities in the brains of children with autism who have co-occurring ADHD (autism+ADHD), autism without ADHD (autism-ADHD), and typically developing controls (TD).

Methods: Three groups of males, 6.5 to 13.5 years of age were matched on age, performance IQ, and handedness: 1) autism+ADHD (n = 11), 2) autism-ADHD (n = 10), and 3) TD (n = 12). Autism was diagnosed using the ADI-R and ADOS-G. Signs of ADHD were measured using the Conners ADHD/DSM-IV scale (parent version). Imaging data were collected on a 3Tesla Siemens Trio scanner and analyzed using statistical parametric mapping and voxel-based morphometry (statistical threshold p<.001).

Results: The autism+ADHD group had decreased gray matter density in the right inferior cerebellum compared to autism-ADHD and TD.

Conclusions: The authors reject the null hypothesis that there are no white or gray matter density differences between individuals with autism with versus without ADHD and identify the right inferior cerebellum as a region of interest.

Sponsor: NICHD U19 HD035476

PS4.39
DOES AMYGDALA SIZE DIFFER IN INDIVIDUALS ON THE AUTISM SPECTRUM COMPARED TO TYPICALLY DEVELOPING INDIVIDUALS?: A META-ANALYSIS Jennifer L Frymiare, Rebecca L Hefer, H.Hill Goldsmith, Morton Ann Gernsbacher, University of Wisconsin-Madison

Background: A greater understanding of hypothesized structural differences in the amygdala may help explain differences in behavior between individuals on the autism spectrum and typically developing individuals.

Objective: The present meta-analysis examined whether a difference in amygdala size exists between individuals on the autism spectrum and typically developing individuals.

Methods: A computerized search of PubMed and PsycInfo databases and a manual search of abstracts from the 2005 International Meeting for Autism Research were conducted to identify ten relevant studies. Effect sizes were calculated for each study and then subsequently corrected for biases using formulas provided by Hedges and Becker (1986).

Results: Overall, individuals on the autism spectrum and typically developing individuals did not differ in amygdala size (d = 0.07).

Conclusion: Preliminary findings of this meta-analysis suggest that mean amygdala size does not differ between
individuals on the autism spectrum and typically developing individuals. Significant heterogeneity of the effect sizes suggests the presence of one or more moderating variables.

Sponsor: NIMH

**PS4.40**

**BRAIN VOLUME IN PARENTS OF CHILDREN WITH AUTISM**

Jeremy Goldberg, Peter Szatmari, Lonnie Zwaigenbaum, Geoffrey B.C. Hall, Department Psychiatry and Behavioural Neurosciences, McMaster University

**BACKGROUND:** Altered total brain volume (TBV), and altered volumes of amygdala, hippocampus and corpus callosum have been suggested as potential endophenotypes of the ASD’s.

**OBJECTIVE:** To determine if TBV and amygdala, hippocampal and corpus callosum volumes are altered in ASD parents and therefore represent true endophenotypes.

**SAMPLE** The sample consisted of 14 parents (6 males and 8 females; average age 44.8, sd =6.1) from 7 families with two or more affected children and 13 control subjects (8 males and 5 females; average age 40.7, sd = 10.6). Inclusion criteria were age 18-60, no history of substance abuse, neurological or medical illness.

**METHODS Measurement:** Magnetic Resonance Images (MRI) were obtained using a 1.5 T GE Genesis-based Echo-Speed scanner. Images (1.2mm) were acquired in the sagittal plane with a 3D FSPGR/20 sequence; TE 3.9 msec; TR 21.2 msec; 512x256 matrix, saved in DICOM, loaded into ANALYZE and converted to isometric cubic voxels. Segmentation was performed using Analyze V software (Robb 1989) and a method similar to that of Mills-Schumann (2004).

**RESULTS** After controlling for age and sex, there was no difference in TBV between parents and controls. Adding TBV as an additional co-variante, there was no difference in volumes of left (p=.15) and right hippocampus (p=.14), and in left (p=.32) and right amygdala (p=.75). Corpus Callosum measures are pending.

**CONCLUSIONS** Based on the data available to date, there are no differences in TBV or in hippocampus and amygdala volumes between parents of ASD children and controls. These data do not support the suggestion that these are potential endophenotypes of autism.

Funding: NAAR, OMHF, HHSF.

**PS4.41**

**THE ANATOMY OF PERISylvIAN LANGUAGE CORTEX IN AUTISM**

Tracey A. Knaus, Kristen A. Lindgren, Andrew M. Silver, Helen Tager-Flusberg, Boston University School of Medicine

**Background:** Language deficits are one of the core symptoms of autism and different subgroups based on language abilities have been suggested. Leftward asymmetry of critical language areas including Heschl’s gyrus (HG), the planum temporale (PT), the pars triangularis (PTR), and the pars opercularis (POP) has been found in healthy individuals. These anatomical asymmetries may be related to left hemispheric language dominance. Few studies have examined the anatomy of language cortex in autism; however, a few studies have suggested reduced asymmetries.

**Objective:** The purpose of this study was to examine the anatomy of language cortex in autistic children with and without language impairment and typically developing children and to relate these to language measures.

**Methods:** Gray matter volume of HG, PT, PTR, and POP was measured on volumetric MRI in 15 autistic children with language impairment, 15 autistic children without language impairment, and 15 typically developing children. Volume, proportional to total brain volume, and asymmetry quotients (AQs) were examined and correlations with language tests were performed.

**Results:** As expected, HG and PT volume were larger in the left than right hemisphere (p<.01). There were no group or group-by-hemisphere differences. No differences between groups in degree or direction of AQs were found. In the autistic groups, there were significant correlations of PT, PTR, and POP measures with a non-word repetition test.

**Conclusion:** These findings suggest that differences in the anatomy of these language regions may be less related to differences between groups in language abilities in general and may be more specific to differences in phonological processing.

This research was funded by the NIDCD (U19 DC 03610)

**PS4.42**

**INCREASED VOLUME IN THE CORPUS CALLOSUM: AN MRI CASE STUDY OF ASPERGER’S DISORDER IN A FEMALE ADULT**

Kelly Marie McVeary, Maxine Janes, Andrew Worth, Georgetown University

**Background:** MRI studies of adults on the autism spectrum report decreased corpus callosum volumes compared to healthy controls. Although white matter abnormalities are widely reported in the autism literature, neuromorphometric data are not readily available that distinguish white matter volumes in adults with Asperger’s Disorder from other adults on the autism spectrum.

**Methods:** We perform region of interest analysis of the corpus callosum in native space using mid-sagittal T1-weighted images of an adult female with Asperger’s Disorder, and a typically developing female matched for age, gender, and socioeconomic status. We trace the corpus callosum using semi-automated software NVM and then we subdivide the corpus callosum into 7 regions (genu, rostrum, rostral body, anterior midbody, posterior midbody, isthmus, and splenium) by drawing five lines perpendicular to the anterior-posterior axis using the Palmer method. We calculate the volume (mm3) for each sub-region and for the whole region in order to compare volumes (a) between subjects, and (b) to previous morphological studies of the corpus callosum in healthy adults.

**Results:** The corpus callosum is 69% larger in the Asperger’s female compared to the control. Additionally,
except for the rostrum, all sub-regions are larger in the Asperger’s brain than in the control brain, with the greatest differences present, in descending order, in the genu, anterior midbody, and splenium. Finally, this Asperger’s corpus callosum volume exceeds normal neuroanatomic variation reported in healthy adults. Conclusions: Preliminary findings of this pilot study do not support morphometric evidence that the corpus callosum is reduced in adults on the autism spectrum, across subtypes.

**PS4.43**

**AGE-RELATED MICROSTRUCTURAL DIFFERENCES IN LIMBIC WHITE MATTER IN INDIVIDUALS WITH AUTISM**

Brendon M Nacewicz, Emelia M McAuliff, Kim M Dalton, Mariana A Lazar, Andrew L Alexander, Richard J Davidson, Waisman Laboratory for Brain Imaging & Behavior

Reports of abnormal white matter volumes and functional connectivity in individuals with autism suggest that physical connectivity is potentially abnormal. The limbic system is important for both social and emotional processing, but the small diameter connections and proximity to larger white matter tracts make limbic circuits difficult to measure by coregistration/voxelwise and probabilistic tract-tracing techniques. We therefore employed a region of interest analysis of the cingulum, the largest limbic fiber bundle, to evaluate the integrity of this circuit.

Objective: To investigate potential microstructural differences in limbic white matter on diffusion tensor images (DTI) from individuals with autism.

Design/Method: Participants included 12 individuals with ASD (mean 14.3 y), including some with mental retardation, and 15 age-matched, typically developing controls (mean 14.6 y). Diffusion weighted images were acquired on a GE 3T scanner, and eyetracking was acquired during a facial recognition task.

Results: We found no group differences in cingulum volume or DTI measures, nor was there an interaction of these measures with anterior-posterior position. While both groups showed increased volume with age, only the ASD group showed an increase in density (inverse of apparent diffusion coefficient, ADC; p = 0.01) and coherence (linear anisotropy, LA; p = 0.04) with age. These microstructural changes were strongly related to eye-fixation even after correction for age.

Conclusions: Individuals with ASD show an abnormal relationship between cingulum integrity and age, which is further associated with laboratory measures of gaze avoidance.

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**PS4.44**

**OXIDATIVE STRESS-INDUCED, ISOBER-SPECIFIC GFAP MODIFICATION IN THE AUTISTIC CEREBELLUM**

Elizabeth Maria Sajdel-Sulkowska, Boguslaw Lipinski, Dept. Psychiatry, Harvard Medical School and BWH

Oxidative stress - specifically, reactive oxygen species (ROS) - affect gene and protein expression during brain development and may contribute to changes in brain structure and function. The objective of these studies was to examine the relationship between oxidative stress and oxidative protein modification in the autistic cerebellum. Specifically, we have previously reported increased expression of GFAP in autistic cerebella. Increased expression of GFAP has also been observed during brain inflammatory responses and in a number of neurodegenerative disorders such as Alzheimer’s disease. Western blot analysis revealed an altered pattern of GFAP isoforms. While the patterns of both control and autistic cerebellar samples showed multiple GFAP forms, the autistic cerebellar samples showed an increase in the slower moving forms. Different mobility of the GFAP isoforms is most likely related to different degree of protein phosphorylation. Thus, our results suggest a higher degree of phosphorylation of GFAP in the autistic cerebellum. Hyper-phosphorylation of tau protein is one of the hallmarks of Alzheimer’s disease. We are now examining cerebellar oxidative stress in terms of 3-nitrotyrosine (3-NT) and relating GFAP phosphorylation to the extent of oxidative stress. While the function of modified GFAP isoforms remains to be clarified, these studies contribute to our understanding of oxidative stress-induced brain injury in autism. Furthermore, understanding the role of oxidative stress may support prevention and treatment strategies such as dietary recommendations and nutritional interventions.

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**PS4.45**

**INFOLDING OF PREFRONTAL CORTEX IN AUTISM: AN EXPLORATORY STUDY**

Katherine Helen Taber, Michael E Brandt, Deborah A Pearson, Katherine A Loveland, Baylor College of Medicine

The purpose of this exploratory study was to quantitatively compare the three dimensional conformations of the cortex in subjects with and without autism. The surface of each hemisphere was computer-reconstructed by segmenting magnetic resonance images of 14-18 year old normal IQ subjects (3 with, 6 without autism). These surfaces were converted to flat maps and regions-of-interest (ROIs) were drawn that separated prefrontal cortex (PFC) into dorsolateral, ventrolateral, anterior, lateral orbital, medial orbital and medial areas. Measures obtained from or calculated for each ROI included surface area, gyrification index (ratio between the total cortical surface and the exposed cortical surface), absolute average of depth, absolute average of folding and absolute average of intrinsic (Gaussian) curvature. One subject with autism had a smaller than average brain size, two were within the normal range. All three differed from the normal group on many measures. In dorsolateral PFC, for instance, the subject with a smaller brain had a gyrification index and average depth below the normal range, whereas both folding and intrinsic curvature were
above the normal range. In contrast, the two subjects with normal brain size had gyrification indices and average depth above the normal range, whereas both folding and intrinsic curvature were within or below the normal range. These patterns suggest that the subject with autism and a smaller than average brain size had more gyri and shallower sulci in this area of PFC, whereas the two subjects with normal brain size had fewer gyri and deeper sulci, supporting the concept of multiple developmental trajectories in autism.

**PS4.46**

**STRUCTURAL INTEGRITY OF WHITE MATTER FIBER TRACTS IN VENTRAL CORTEX IN AUTISM**

Cibu Paul Thomas, Kate Humphreys, Kwan-jin Jung, Nancy Minshew, Marlene Behrmann, Psychology Department, Carnegie Mellon University

Introduction: Individuals with autism have been known to possess atypical visuo-perceptual skills. It is possible that abnormalities in white matter connectivity (under connectivity/over connectivity) could give rise to their abnormal visual processing abilities. However, direct evidence of alterations in structural connectivity has only begun to emerge.

Objective: To quantify the structural integrity of the white matter tracts in the ventral cortex in individuals with autism using diffusion tensor imaging (DTI) and fiber tracking.

Method: DTI data were acquired from 10 adults with autism and 10 normal control subjects. Fiber tracking was performed using DTI studio (Mori, et al., 2002), with FA threshold of 0.20 and critical angle of 40. The fasciculi of interest (FOI) included the inferior fronto-occipital fasciculus, the inferior longitudinal fasciculus, and the forceps major. The dependent measures included mean FA values within a FOI, the number of voxels that indicate the presence of a fiber, and a connectivity score derived by documenting whether the fibers in a particular FOI terminate at a predefined cortical region.

Results: Preliminary analyses indicate that, in contrast with the control group, some individuals in the autism group show a disruption in structural connectivity in the inferior fronto-occipital fasciculus.

Conclusions: The discrepancy in structural connectivity in the fiber tract between the frontal cortex and the occipital cortex may help elucidate the mechanisms underlying the autistic individuals’ difficulty in aspects of visual cognition such as face processing.

Funding: This research was funded by a grant to Marlene Behrmann (PI: Nancy Minshew), from the NICHD/NICD HD39459-04 and grants from Cure Autism Now, the Institute for Brain Potential and the Hussman Foundation.

**PS4.47**

**FUNCTIONAL STATUS OF THE CEREBELLAR INTERNEURONS AND PURKINJE CELLS IN AUTISTIC BRAIN**

Jane R Yip, Jean-Jacques Soghomonian, Margaret L Bauman, Thomas L Kemper, Gene J Blatt, Boston University

Background: Although a decrease in number of GABAergic Purkinje cells (PCs) in the autistic brain is widely reported, little is known about the functional status of the remaining PCs, their attendant GABAergic basket (BC) and stellate cells (SC), or of their glutamatergic climbing fiber (CF) input.

Objectives: Quantify GABA synthesis in PCs, BCs, and SCs using in situ hybridization of glutamate decarboxylase 67 (GAD67; GABA-synthesizing enzyme) and visualize glutamatergic olivocerebellar CFs.

Methods: Fresh frozen blocks were taken through the lateral part of the posterior cerebellar hemispheres of 8 autistics, and 8 controls matched for age, PMI, gender and pH. Sections were processed with a 35S-GAD67 probe, and PC counts and mRNA levels in BC/SC were measured by computerized analysis of silver grains on sections processed by emulsion radioautography. The class III neurofilament antibody to peripherin labeled CFs and the cross-sectional width of CFs was estimated using NIH image.

Results: In autistic brain, GAD67 mRNA level was reduced in the PCs by 40% (p<0.0001) and in BCs increased by 28% (p<0.0001). Stellate cells showed a trend toward a small increase but did not reach significance. PC number was not significantly different between autistic and controls. Increased width of CFs was observed in 4/9 autism cases and hyperinnervation of PCs by CFs was sometimes observed.

Conclusions: The functional state of the remaining PCs as measured by a decreased GAD67 mRNA level, is altered. This is associated with upregulation of GAD67 mRNA level in basket cells and downregulation of GAD67 mRNA levels in PCs. The increased width of the CFs suggests the possibility of enhanced glutamatergic input to PCs.

Tissue was provided by the Harvard Brain Tissue Resource Center and The Autism Tissue Program. Supported by NICHD HD39459-04 and grants from Cure Autism Now, the Institute for Brain Potential and the Hussman Foundation.

**PS4.48**

**BRAIN ABNORMALITIES DETECTED IN PATIENTS WITH NON-SYNDROMIC AUTISM: REPORT FROM 152 MRIS**

Nathalie Boddaert, Nadia Chabane, Isabelle Meresse, Anne Philippe, Laurence Robel, Marie Bourgeois, Marie-Christine Mouren, Catherine Barthelemy, Laurence Laurier, Arnold Munnich, Francis Brunelle, Yves Samson, Monica Zilbovicius, URM 0205 « Brain imaging in psychiatry », INSERM-CEA, Service Hospitalier Frédéric Joliot, CEA, Orsay, France ; 2 Hôpital Necker Enfants Malades, AP-HP, Paris V, Paris France

Background: There is still no consensus about the need to systematically perform MRI in autism.

Objectives: In order to search for brain abnormalities in person with non-syndromic autism, we have performed a visual retrospective examination of MRI.

Methods: 152 patients with autism (2.3 to 22.1 years; mean: 7.6 years; sd: 3.9; 30 females) were examined. All...
met the DSM-IV criteria for autism. We excluded patients
with infectious, metabolic, genetic diseases; seizures or
neurological symptoms. MRI was performed on 1.5-T
Signa GE (3-D T1-FSPGR, T2, FLAIR coronal and axial
sequences). Two neuroradiologists inspected cortical and
sub-cortical regions: cerebellum, brainstem,
hippocampus, corpus callosum, white matter, ventricles
and cortex. Only major abnormalities were retained.
Results: 54% of the MRI were found to be abnormal (82);
34% were normal (52) and 12% were not fully
interpretable (18). Abnormalities were: ventricle
enlargement: 9% (14), posterior fossa cysts: 2% (3),
vermian atrophy: 6% (9), abnormal hypersignal of dentate
nucleus: 0.7% (1), arachnoids cyst: 2% (3); heterotopia:
0.7% (1), abnormal hippocampus shape: 14% (21),
temporal lobe white matter anomalies (> 4 years old):
34% (52); major extra-temporal white matter
abnormalities: 25% (38) and major dilated Virchow-robin
spaces: 7% (10).
Conclusions: The present results show an unexpected
high prevalence of MRI abnormalities in a large group of
autistic patients considered a priori to have a non-
syndromic autism. These results indicate the need to
perform MRI examination in patients with autism.
Sponsor: France Telecom Foundation and France
Foundation.

PS4.49
THE AMYGDALA-HIPPOCAMPAL REGION IN
AUTISTIC SPECTRUM DISORDER: A sMRI
STUDY. Eileen Daly, Brian Hallahan, Fiona Toal,
Sarah Curran, Dene Robertson, Clodagh Murphy, Eva
Loth, Francesca Happe, Patrick Bolton, Quinton Deelye,
Kieran Murphy, Declan M. Murphy, Section of Brain
Maturation, King’s College London Institute of Psychiatry
Background: It has been proposed that people
with autistic spectrum disorder (ASD) have abnormalities in
the development of limbic areas; and particularly of the
amygdala-hippocampal region. However prior studies
have reported differing results. Perhaps because they
studied different age groups, and clinical phenotypes.
Objectives: Measure volume of amygdala-hippocampal
region in people diagnosed along the autistic spectrum
and compare to controls.
Methods: As part of the MRC UK A.I.M.S.program we
used volumetric magnetic resonance imaging and hand
tracing (MEASURE) to investigate the volume of the
amygdala-hippocampal region in 82 adults with ASD (54
people with Asperger syndrome, 18 people with HFA and
10 people with autism) and 50 age-matched controls.
Results: When all people with ASD were combined as
one group, compared to controls, they were no volume
differences. However, we found significant differences
within people with ASD compared to controls according
to clinical phenotype. In the Asperger group there were
increases of right amygdala (p<.05) volume for the
Asperger group and left hippocampus (p<.06) for the
autism group. There were also decreases in
hippocampus (p<.05) and left amygdala (p<.02) for the
HFA group.
Conclusion: People with ASD did not have significant
differences from controls in the bulk volume of the
amygdala-hippocampal region. Further, variation in the
behavioural phenotype of ASD is associated with
difference volumes of these brain regions. Our findings
may also partially explain the variable results from prior
studies of ASD: because many studied people from
different parts of the autistic spectrum.

PS4.50
BRAIN VOLUMES IN PATIENTS WITH AUTISTIC
SPECTRUM DISORDERS COMPARED TO
CONTROLS. Brian Hallahan, Eileen Daly, Finian
O’Brien, Fiona Toal, Grainne McAlonen, Vals Raj,
Clodagh Murphy, Susie Hales, Eva Loth, Kieran Murphy,
Declan Murphy, Beaumont Hospital
Introduction: Since 1943, when Kanner first reported
large heads in children with autism, there have been
many reports of macrocephaly in individuals with autism
spectrum disorders (ASD) MRI findings have noted
increased grey and white matter in children aged 2-4
years (Sparks et al., 2002) but in older children and adults
there has been no consistent picture (McAlonen et al,
2002).
Aim: We wanted to quantify brain volume in both
children and adults with ASD compared to a control
population using structural MRI.
Method: Subjects included 158 individuals with ASD, 142
adults and 16 children. The adults comprised 100
individuals with Asperger Syndrome, 25 with HFA, 17
with typical or atypical autism. All ASD children had
Asperger Syndrome. All participants were diagnosed both
with ICD-10 diagnostic criteria and the ADI-R. There
were 92 control subjects, (74 adults). Exclusion criteria
included individuals with physical or psychiatric disorders
affecting brain function, genetic disorders associated with
ASD and clinically abnormal MRI’s. All 250 individuals underwent MRI brains using a 1.5
Tesla, GE Sigma system. Using measure software, total
cranial volume, whole brain volume (cerebral
hemispheres, individual brain lobes, amygdala and
hippocampus), ventricles, brainstem, and cerebellum were
traced. Inter-rater reliability was attained, r > 0.95, and
raters were blinded to diagnosis.
Results: There was no difference noted in either age or IQ
for the children’s sample. IQ was controlled for in the
adult group as it was lower (but normal) in the ASD
group. In the adults sample, raw cerebellar volume (p =
0.0016), was reduced compared to controls, and lateral
ventricles (p = 0.012) and peripheral CSF was increased
(p = 0.00008). These findings were noted both for patients
with Asperger syndrome, HFA and typical autism. In the
children’s sample there was no difference noted in brain
volumes between those with Asperger syndrome and
controls.

PS4.51
AUDITORY PERCEPTION OF SPOKEN
EMOTION IN CHILDREN WITH ASPERGER'S
AND HIGHER FUNCTIONING AUTISM. Ruth
RESULTS. There were no significant task differences by group, by ear or ear interaction, or between group membership (AD, HFA, TDC) and emotion. The DTMS (F(3,96) = 6.70, p = 0.0047) and DTNS (F(1,32) = 6.51, p = 0.006) had significant effects for emotion. Tukey’s HSD post-hoc analysis of pairs of means for emotions collapsed across groups revealed happiness was significantly higher than other emotions for DTMS and DTNS and both ears were equivalent. Sadness and anger were significantly better in the left ear for DTMS and DTNS.

CONCLUSIONS: HFA, AD and TDC children had similar performances, suggesting no difference processing verbally expressed emotions. Left ear preference for perception of negative emotion is consistent with right hemisphere superiority.

PS4.52
HERE’S LOOKING AT YOU: AN EYE-TRACKING STUDY OF GAZE IN AUTISM SPECTRUM CONDITIONS
Chris Ashwin, Bruno Wicker, Simon Baron-Cohen, Autism Research Centre
Background: Autism Spectrum Conditions (ASC) are characterised by social and communication difficulties. One of the more striking social-communication features is atypical gaze behavior, though few experimental studies of gaze have been reported in ASC. Here we test the claim that autism involves an absence of the typical preference for attending to gaze. Objectives: To investigate gaze by adults with and without ASC whilst watching videos of faces with gaze directed towards different objects and locations. Methods: We tested 18 males with ASC, and 18 typical male controls matched for age, handedness, and IQ. We used a gaze-tracking paradigm to measure (1) the initial focus of interest on each trial, and (2) total looking times to eyes and objects. Results: Controls looked first at eyes, while people with ASC looked first at objects. In addition, controls spent more time looking at eyes compared to objects, with a preference for the left compared to right eye. People with ASC looked more at objects than eyes, and showed no preference for left compared to right eye. Conclusion: These results confirm and quantify the extent to which typical controls show a preference for the eyes, and rely on the left eye most when judging gaze direction, while people with ASC show a preference for looking at objects rather than gaze.

Sponsor: NAAR*

PS4.53
TYPICAL EMOTION PROCESSING FOR CARTOON BUT NOT FOR REAL FACES IN CHILDREN WITH AUTISM
Delphine Bastard Rosset, Cécile Rondan, Brigitte Assouline, Myriam Clément, David Da Fonseca, Christine Deruelle, INCM, CNRS, Marseille, FRANCE
Background: Deficits in emotion processing form a core diagnostic feature of autistic disorder. However, the visual strategies used by children with autism in facial emotion processing remain poorly understood.

Objectives: The main aim of the current study is to better delineate these strategies and in particular, the implication of local and configural processing in emotion face processing in the autistic population by way of face inversion paradigm.

Methods: 36 children participated in the current experiment with 12 children in the autistic group (ASD), 12 children matched on chronological age basis and 12 other children matched on mental age. Local and configural emotional face processing was assessed by comparing children’s ability to recognize happy, angry or sad faces displayed upright or upside-down in the context of either pictures of real faces, faces of ‘human’ cartoons or faces of ‘non human’ cartoons.

Results: The overall level of performance was similar in the three groups of children. Analysis of correct responses showed a significant inversion effect for real faces, faces of human cartoon and faces of non human cartoons in both control groups. In contrast, a significant effect of inversion is found for human and non human cartoon faces in the ASD group, but not for real faces.

Conclusion: Configural emotion processing is evidenced in typical population for both cartoon and real faces. In ASD however, a lack of configural emotion processing is showed for real faces only, suggesting a lack of expertise with this particular type of stimuli.

PS4.54
HOW WELL DO INDIVIDUALS WITH AUTISM IDENTIFY GENDER WHEN SHOWN EYE AND MOUTH REGIONS?
Catherine A. Best, Mark S. Strauss, Nancy J. Minshew, University of Pittsburgh
Background: Research suggests individuals with autism do not attend to or abstract social information from eyes but instead rely on mouth regions. Objective: To compare abilities of individuals with autism and controls in
identifying gender from eye or mouth regions when in isolation from whole faces.
Method: Patients were recruited from the Autism Center at the University of Pittsburgh’s School of Medicine and were confirmed with diagnoses of Autism/PDD from the ADI and ADOS. All were high-functioning (FSIQ >80). Controls were matched on age, gender, and FSIQ. Participants pressed keys labeled male or female while viewing eyes or mouths on a computer. Results: Data are collected on 12 individuals with autism (mean age = 23 yrs, age range = 14 to 50 yrs) and 12 controls (mean age = 23 yrs, age range 14 to 51 yrs). Preliminary analyses of gender identification showed while the autism group (77%) was significantly worse than controls (82%) with eyes, they were still relatively good at using eye regions. Like controls (60%), the autism group (59%), was worse with mouths than eyes. Conclusion: Preliminary findings of this study do not support the idea that individuals with autism focus only on the mouth region of faces. Although worse than controls, individuals with autism are better at recognizing gender from eyes alone than from mouths alone.
Sponsors: NICHD, NAAR

PS4.55
EMOTIONAL COGNITION IN CHILDREN WITH AUTISM SPECTRUM DISORDERS (ASD): IS MUSIC A DOMAIN OF SPARED ABILITY? Anjali Kiran Bhatara, Eve Marie Quintin, Eric Fombonne, Daniel J Levitin, McGill University, Department of Psychology
Background: Many studies have shown that autistic individuals are impaired in emotional understanding, both that of others’ emotional states (Gross, 2004) and of their own (Hill, Berthoz, & Frith, 2004). This presents an interesting paradox: many autistic individuals show great interest in music (Heaton, 2003), yet music is generally regarded as representing emotion.
Objective: This experiment aims to quantify the extent to which autistic adults are impaired in their understanding of emotion, using music as a medium of communication.
Methods: Our participants will listen to piano pieces which have been shown for normals to range from ‘mechanical-sounding’ to maximally expressive. We will ask the participants to rate these excerpts in three tasks on the amount of emotional expression present in the piece. We will compare the ratings from people with autism with those from unimpaired, IQ and age-matched controls.
Results: We have two alternate hypotheses. H1: Individuals with autism will be able to extract the emotional content from music, indicating that music represents a domain of relatively preserved emotional processing. H2: Individuals with autism will be unable to extract the emotional content from music, suggested that their attraction toward music is based primarily on its surface features or complexity, rather than any emotion content conveyed. By the time of the conference, we expect to have tested n=15 participants with ASD and an equal number of IQ and age-matched controls, which we expect will provide sufficient power to choose among the alternative hypotheses.
Sponsor: NAAR

PS4.56
INCREASING COMFORT VIEWING HUMAN FACES WITH STRUCTURED COMPUTER PRESENTATION Caroline Bliss Browne, Mark W. Baldwin, Service d'Adaptation et d'Integration de Montreal
Background: Individuals with Pervasive Developmental Disorders show gaze avoidance and deficits in holistic face processing. The brain region activated during holistic face processing is an expert system that is thought to be trained through repeated exposure to human faces. Although autistic individuals tend to avoid exposure to faces, whether live or in photos, it is known that they are drawn to both computers and repetitive activities.
Objectives: Improve comfort level of autistic individuals viewing human faces through exposure to a repetitive, computerized presentation of smiling faces.
Methods: Pilot study involved one 4-year-old boy with PDD, shown a slideshow of 30 smiling faces twice per day. Time viewing slideshow was assessed, as well as ability to discriminate facial expressions in a matching task.
Results: Across 15 slideshows across the week, viewing time increased from 30% of the slideshow during the first viewing to 60% for the next 2 and averaged 85% for the final 12 viewings. Parental report indicated highly positive participant response to viewing slideshow (e.g. smiling and running over to computer). On an emotion matching task involving pictures of faces, although pilot data showed no significant gains in performance, increased attentiveness to the faces was observed.
Conclusion: Computer-based slideshows offer a promising means of exposing autistic individuals to human faces. Additional data will be presented as available.
Sponsor: Social Sciences and Humanities Research Council of Canada (SSHRC) *

PS4.57
IMPAIRMENTS IN PRIMATE AND HUMAN FACE RECOGNITION IN 2-YEAR-OLD TODDLERS WITH AUTISM SPECTRUM DISORDER AND DEVELOPMENTAL DELAY Katarzyna Chawarska, Joslin Latz, Jennifer Buchanan, Paula Ogston, Fred Volkmar, Yale University School of Medicine
Background: Face recognition impairments are well documented in older children with Autism Spectrum Disorders (ASD), however the developmental course of this deficit is not clear.
Objectives: Examine face recognition in 2- and 4-year-old children with ASD, developmental delays (DD) and typically developing controls (TD)
Methods: Participants were recruited from the Yale Developmental Disabilities Clinic and their human and monkey face recognition skills were assessed using the Visual Paired Comparison (VPC) paradigm.
Results: Experiment 1 examined human and monkey face recognition in 2-year-old children with Autism Spectrum Disorder, and matched for nonverbal mental age (NVMA) developmentally delayed (DD) and typically developing children (TD). Results indicated that consistent with the other-species effect, TD controls showed enhanced recognition of human but not monkey faces; however neither ASD nor DD group showed evidence of face recognition regardless of the species. Experiment 2 examined the same question in a group of 3 to 4 year old developmentally disabled (ASD and DD) as well as typical controls and indicated that both human and monkey faces were recognized by all three groups.

Conclusion: Results of the Experiments 1 and 2 suggest that certain impairments in face processing in toddlers with ASD might not be syndrome-specific. However, it is not clear whether the deficits observed in Experiment 1 extend only to stimuli that conform to a face prototype. While in the DD group, deficits in processing and recognition might be generalized to objects as well as faces; in ASD these deficits might be face-specific. Future studies will have to examine the role of the stimulus characteristics as well as scanning strategies in both groups to help elucidate these issues.

PS4.58  
FACE PROCESSING IN 6-MONTH-OLD INFANT SIBLINGS OF CHILDREN WITH AUTISM Angeline Dijamco, Marian Sigman, University of California, Los Angeles

Research on children and adults with autism has found that these individuals display abnormal visual scanning patterns while viewing faces. Although little is known about face processing in autism in infancy, retrospective video studies have shown that inattention to faces distinguishes infants later diagnosed with autism from typically developing infants. Using non-invasive eye-tracking technology, this study examines visual scanning patterns of 6-month-olds as they habituate to happy faces, comparing a group of at-risk infant siblings of children with autism (ISCAs) with typically developing controls (TDs). Subjects were part of a larger study known as Infants at Risk of Autism: A Longitudinal Study.

For the eye-tracking task, infants were shown images of happy faces from the NimStim MacBrain face stimulus set on a Tobii 1750 eye-tracking monitor. Using an infant-controlled habituation procedure, the length and number of stimulus presentations was determined by each infant’s visual attention. Preliminary analyses on 10 ISCAs and 10 TDs revealed between-group differences. ISCAs spent significantly less time looking at the eyes (t = 2.54, p < .05; mean for ISCAs=47.4%, mean for TDs=71.0%). These differences were not related to receptive or expressive language scores on the Mullen Scales of Early Learning. Preliminary findings support the hypothesis that ISCAs process faces differently than TDs, particularly in the portion of time spent attending to the eye region.

Sponsor: STAART Grant MH068172*

PS4.60  
DO TODDLERS WITH AUTISM UNDERSTAND THE REFERENTIAL NATURE OF EMOTIONS? Richard Griffin, Simon Baron-Cohen, Autism Research Centre, Cambridge University

By at least 14 months of age, and possibly earlier, typically developing children understand that emotional expressions (facial and vocal) refer to specific targets. This is implicit because they will modify their behavior toward those targets as a function of another individual’s emotional expression (social/emotional referencing). Children with autism spectrum conditions (ASC) are delayed or deviant in developing joint attention and gaze monitoring, though basic emotional referencing without gaze monitoring demands has yet to be tested. In Experiment 1, we tested emotional referencing abilities in a group of toddlers with autism (n=18), and compared them to typically developing and language-delayed controls. Results suggest that toddlers with autism do not systematically modify their search behaviour as a function of another’s emotional (happy, or disgust) facial expression. Experiment 2 employed a preferential-looking, still-face procedure to test whether toddlers with autism (n = 20) can categorise emotional expressions along a continuum from happy to fearful. Results indicate that toddlers with ASC can distinguish between happy and fearful expressions. However, they spent proportionately less time looking at fearful faces, and their within-category discrimination abilities were less acute compared to language-delayed and typically developing controls. These findings are discussed in terms of dyadic (two-way) and triadic (three-way) theories of autistic dysfunction, as well as the development of configural/expert processing of faces and its relation to cortical development and amygdala function.

PS4.61  
EMOTION PROCESSING AND SPATIAL FREQUENCY IN ADULTS WITH AUTISTIC SYNDROME DISORDERS Benedicte Hubert, Laurent Mottron, Patrik Vuilleumier, Fabienne Samson, Christine Deruelle, INCM, Marseille, France, 13008

Pervasive developmental disorders specialized clinic, Rivières-des-Prairies hospital, & Unité de neuroimagerie fonctionnelle, Geriatric Institute of the University of Montreal, Montreal, Quebec, Canada.

Background: Deficits in emotion processing are documented in persons with autism spectrum disorders (ASD), but their neural basis remain largely unknown. Objectives: Our study aimed to identify the cerebral networks involved in implicit emotion processing in the ASD population. Implicit processing of facial emotions was assessed by means of low-spatial frequency filtered faces, previously shown to implicate partly subcortical pathways.

Methods: 13 adults with ASD and 15 typically developing adults were included. Hybrid face stimuli were generated, with one face of one gender low-pass filtered combined with a high-pass filtered face of the opposite gender. In the LSF condition, the LSF face was emotional (fearful)
and the HSF face was neutral, whereas in the HSF condition, the HSF face was emotional but LSF neutral. In the control condition, both faces were neutral. Subjects had to make a gender judgement on these hybrid faces.

Results: Behavioural performance showed no spatial frequency bias in both groups. fMRI showed that, in contrast to control population, patients with ASD recruited similar regions in the LSF and HSF conditions. Direct comparisons between groups revealed in the ASD group: 1- reduced activation in superior temporal and superior parietal regions, but higher activation in inferior parietal and anterior cingular regions in the LSF condition; 2- reduced activation in the occipital, superior parietal and insular regions, but higher activation in the inferior parietal and anterior cingular regions in the HSF condition.

Conclusion: These findings suggest that high and low spatial frequencies are processed in a less specialized way in population with ASD.

**PS4.62**

**IMPLICIT FACE PERCEPTION IN AUTISM.**
Brandon M Keehn, Christine Connolly, Robert Joseph, Boston University School of Medicine

Background: It is frequently assumed that autistic deficits in face processing derive from a primary impairment of holistic perception.

Objective: To use a perceptual priming paradigm to investigate holistic perceptual processes independently of attention in adolescents with autism.

Method: Participants included 18 high-ability adolescents with autism and 18 age- and NVIQ-matched typically developing (TD) individuals. Each trial included a forward mask of the experimenter's face (1500 ms) with eyes and mouth closed, a prime of the experimenter's face (33 ms) with either eyes, mouth, or both opened, and a backward mask of an unfamiliar target face (2000 ms max.) with either eyes or mouth opened. Primes were either wholly or partly congruent with the target face. Participants made a speeded button-box judgment whether the target's eyes or mouth were opened in upright and inverted test conditions.

Results: The TD group showed a reaction time advantage of whole over part primes in the upright (t=4.1, p<.002) but not the inverted (t=.5, p>.6) condition. The autism group evidenced a similar whole prime advantage for upright faces (t=5.6, p<.001), but they also showed a whole advantage for inverted faces (t=2.5, p>.05)

Conclusion: The robust reaction time advantage for whole relative to part face primes indicates intact holistic perception in the autism group, but their relatively diminished inversion effect suggests that faces are not accorded a special status in their visual world.

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increased activation of muscles congruent with the stimulus expression combined with no simultaneous increase in activation of muscles incongruent with the stimulus expression. Mean activation levels of stimulus-congruent vs. stimulus-incongruent muscles across participants and stimuli were also compared.

Results: For each stimulus emotion, 2-4 participants showed some evidence of mimicry. However, none demonstrated mimicry across emotional stimulus expressions. Overall, there was no difference in activation levels between stimulus-congruent and stimulus-incongruent muscles, t(8)=.06, p=.95.

Conclusion: Like adults with ASD, children with ASD do not appear to rapidly mimic emotional facial expressions.

Sponsor: NIMH Developmental Training Grant (MH15780-22); University of Denver; NICHD (U19HD35468-07) CPEA (PI = Rogers).

PS4.65 DETECTING FACIAL MOVEMENT IN AUTISM

Mandy Suzanne Plumb, Andrew D Wilson, Justin Williams, Ben C Jones, Lisa M de Bruine, Mark Mon-Williams, University of Aberdeen

Background: Children with autism have problems interpreting facial expression. These problems may stem from an inability to detect subtle and separate facial movements.

Objectives: To test whether children with autism could integrate two subtle facial cues.

Methods: 40 control children (5-11 years) and 11 children with ASD (6-15 years) were asked to press a key on their left when a central arrow pointed left and vice versa. In Experiment 1, arrow direction was precued using a highly realistic computer generated face where the eyes could look left or right. These trials were embedded with trials where the eyes were stationary (no precue information). In experiment 2, the eyes looked to the left or the right and the corners of the mouth would turn either upwards or downwards by a small amount. Upwards indicated that arrow direction was concurrent with eye direction whilst downwards indicated incongruency between arrow and eye direction.

Results: In experiment 1, the children with ASD were able to obtain the same precue advantage from eye direction as the controls. In experiment 2, the ASD population were able to integrate eye direction with mouth movement and showed the same precue advantage as controls.

Conclusion: The data suggest that children with ASD can detect and integrate two separate and subtle facial cues to prepare an action. Thus problems with interpreting facial expression in ASD can not be explained simply by deficits in detecting subtle facial movements.

Objective: Research suggests that individuals with autism exhibit a deficit in emotion recognition abilities. Although numerous studies have examined this deficit, few have attempted to elucidate the developmental trajectory of these emotion recognition difficulties. The present study utilized a cross-sectional design to explore this issue.

Methods: High functioning adults and children with autism (N = 43) and age and IQ matched controls (N = 42) were tested on an emotion recognition task. Six basic emotional expressions were presented dynamically, with each expression edited into four 2000 millisecond videos exhibiting graded increases in the movement of appropriate facial muscles necessary to model each emotion. Participants were shown each video to determine the level at which they could accurately identify the expression.

Results: As a group, individuals with autism performed significantly worse than controls. Also, results demonstrated that for controls, performance on the task improved in the higher age group. However, this was not true for individuals with autism. The performance of the adults with autism was in fact poorer than that of the younger individuals with autism.

Conclusion: Contrary to expectation and in contrast to control participants, adults with autism were worse at identifying facial expression than were younger individuals with autism. One possible explanation for this cohort effect is that many of the younger individuals with autism in our sample may have been exposed to interventions incorporating emotion recognition components. This and other possibilities will be discussed.

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PS4.67 VISUAL SCANNING AND EMOTION RECOGNITION OF SOCIAL SCENES IN AUTISM

Noah James Sasson, Joseph Piven, Robert Hurley, Nao Tsuchiya, University of North Carolina at Chapel Hill

Background: Amygdala dysfunction may contribute to impairments in emotion recognition in autism.

Objectives: Compare visual scanning patterns and emotion judgments in HFA and controls on an established task that implicates amygdala functioning.

Methods: Eye movements of 10 HFA participants and 10 controls were recorded as they judged the emotions displayed in a series of statically presented complex social scenes in which faces were either included or digitally erased.

Results: In contrast to previous reports of amygdala lesion patients whose emotion recognition performance did not benefit from the presence of facial expressions, both HFA and control participants were more accurate in recognizing emotions when facial expressions were included. However, scanpath analysis revealed a significant group X condition (face present vs. absent) interaction indicating that controls increased their viewing
time on the face region when faces were present to a significantly greater degree than HFA participants.

Conclusions: Individuals with HFA may not utilize facial information to the same degree as typicals when assessing the emotional content of a social scene. This finding is consistent with recent research suggesting a role of the amygdala in orienting attention to socially relevant information and suggests that individuals with HFA may have achieved comparable behavioral performance through compensatory strategies that rely less on facial affect and more on contextual information.

Sponsor: STAART grant U54 MH66418

PS4.68
HOW DO CHILDREN WITH AUTISTIC SPECTRUM DISORDERS LEARN NEW FACES?
Rebecca Wilson, Mark Blades, Olivier Pascalis, University of Sheffield

Face recognition is essential for effective socialisation and communication, however children with autistic spectrum disorders (ASD) have been shown to display deficits in face recognition. Most studies have focussed on unfamiliar face recognition with little research considering how a face becomes familiar.

Objective: To investigate the process by which a face becomes familiar in children with ASD, with reference to the part of face used for recognition.

Design/Methods: Video exposure to 6 novel faces over three consecutive days. Forced choice recognition of familiarised faces by their internal and external face parts. Data were collected on 15 children with ASD (CA: 9.5 years) compared to three age groups of typically developing children (5-6yrs, 7-8yrs &10-11yrs).

Results: Typical Development: The oldest two groups showed the same pattern of face learning with increased accuracy on internal and external face parts over the three days. The youngest group (5-6yrs) however showed learning on the external face part condition but no evidence of learning on the internal face part condition.

ASD: The ASD group only showed evidence of learning on the external face part condition, with no evidence of learning on the internal face part condition.

Conclusions: The ASD group appeared to show learning consistent with younger TD children, with no evidence of learning on the internal face parts. The use of internal face parts for recognition is a more advanced strategy in face recognition, therefore suggesting the ASD group may have an impaired process of face learning.

Sponsor: ESRC

PS4.69
A COMPUTER-BASED BATTERY TO ASSESS FACE PROCESSING SKILLS IN INDIVIDUALS WITH AUTISM SPECTRUM DISORDERS
Julie M. Wolf, Cheryl Klaiman, Kathy Koenig, Carla Brown, Jim W. Tanaka, Robert T. Schultz, Yale University, Child Study Center

Background and Objectives: A large literature suggests that individuals with autism spectrum disorders (ASD) have deficits in face processing ability. Yet no comprehensive battery exists to test these skills. We have thus developed a computer-based face processing battery.

The present study investigates whether individuals with ASD demonstrate face processing deficits on this battery.

Methods: Forty-seven participants with ASD and 68 age and IQ-matched typically developing controls were administered the battery, which includes a measure of immediate memory for faces; three face matching tasks (emotion matching, identity matching, and identity matching with parts of the face concealed); an emotion labeling task; two parts-whole identification tasks (identity and emotion); two same-different tasks (faces and houses); and a visual scanning task (animals and faces).

Results: A multivariate analysis of covariance was conducted comparing the ASD and control groups, with age and IQ as covariates and percentage of correct responses on each task as dependent variables. Individuals with ASD were significantly impaired relative to controls on the immediate memory task, all three face matching tasks, and the parts-whole face identity task. Individuals with ASD performed significantly better than controls on the same-different house perception task.

Conclusion: Deficits in face identity and emotion perception are confirmed, in the presence of preserved non-social object perception. These results suggest that the computer-based battery has the potential to be a useful tool for assessing face processing deficits in individuals with ASD.

Sponsor: NIMH STAART
**Oral Session #10**  
**Early Detection**

Chair: Kasia Chawarska

Speakers:
Jessica Ann Brian, Lonnie Zwaigenbaum, Susan E Bryson, Wendy Roberts, Peter Szatmari, Isabel Smith, Autism Research Unit, Hosp. Sick Children
Amy M Wetherby, Lindee Morgan, Nola Watt, Stacy Shumway, Rebecca Niehus, Rachel Petrak, Susan Risi, Catherine Lord, Florida State University
University of Michigan Autism and Communication Disorders Center
Lindee Morgan, Amy M. Wetherby, Angie Barber, Rachel Petrak, Shanping Qiu, Susan Risi, Catherine Lord, Florida State University FIRST WORDS Project, University of Michigan Autism and Communication Disorders Center
Devin M Casenhiser, Stuart Shanker, Stanley Greenspan, Lisa Bayrami, York University

**ABSTRACTS**

**PREDICTIVE VALIDITY OF THE AUTISM OBSERVATION SCALE FOR INFANTS**  
Jessica Ann Brian, Lonnie Zwaigenbaum, Susan E Bryson, Wendy Roberts, Peter Szatmari, Isabel Smith, Autism Research Unit, Hosp. Sick Children

Background: The Autism Observation Scale for Infants (AOSI; Bryson et al., under rev.) is a semi-structured play-based assessment developed to aid systematic data collection on early signs of autism in high-risk infants.

Objectives: To assess predictive validity of the AOSI at 12 months for a diagnosis of ASD at 3 years.

Method: Prospective data were collected on 92 infant siblings of children with ASD and 42 low-risk controls. The 16-item AOSI was given at 12 and 18 months. Independent diagnostic evaluation blind to prior study data was completed at 3 years; a clinical diagnosis of ASD was based on ADOS, ADI-R + DSM IV-TR. Mean AOSI scores at 12mo in sibs diagnosed with ASD at 3yr, undiagnosed sibs, and controls were compared using 1-way ANOVA; chi-squared analyses were used to compare groups on AOSI items (critical p<.003 for multiple tests).

Results: Of 92 siblings, 12 were diagnosed with ASD at 3yr (13%). AOSI scores at 12mo were higher in siblings with ASD (mean=10.0, SD=6.0) than undiagnosed siblings (mean=3.4, SD=3.0) and controls (mean=1.7, SD=1.6) (F2,131=33.2; p<.001). An AOSI cut-off score of 9 at 12mo correctly identified 7 of 12 siblings with ASD (sensitivity=58% within sibling sample) and 74 of 80 undiagnosed sibs (specificity=93%); all low-risk controls scored below this cut-off. Specific markers that distinguished children with ASD from both comparison groups at 12mo include atypical visual tracking, orienting to name, imitation, eye contact, social smile, behavioural reactivity, and social interest and affect.

Conclusions: The AOSI distinguishes siblings with ASD from undiagnosed siblings and controls at 12 months.

Sponsors: CIHR, NAAR

**SOCIAL COMMUNICATION PROFILES OF CHILDREN WITH AUTISM SPECTRUM DISORDERS IN THE SECOND AND THIRD YEARS OF LIFE**  
Amy M Wetherby, Lindee Morgan, Nola Watt, Stacy Shumway, Rebecca Niehus, Rachel Petrak, Susan Risi, Catherine Lord, Florida State University FIRST WORDS Project; University of Michigan Autism and Communication Disorders Center

Objective: The purpose of this longitudinal study of the FIRST WORDS Project was to examine social communication profiles of children with autism spectrum disorders (ASD), developmental delay (DD), and typical development (TD) from 12 to 36 months.
MEASURES OF REPETITIVE BEHAVIORS USING THE CSBS DP IN CHILDREN WITH AUTISM SPECTRUM DISORDERS IN THE SECOND AND THIRD YEARS OF LIFE

Lindee Morgan, Amy M. Wetherby, Angie Barber, Rachel Petrak, Shanping Qiu, Susan Risi, Catherine Lord, Florida State University FIRST WORDS Project; University of Michigan Autism and Communication Disorders Center

Objective: The purpose of this longitudinal study of the FIRST WORDS Project was to measure repetitive and stereotyped behaviors of children with autism spectrum disorders ( ASD), developmental delay (DD), and typical development (TD) from 12 to 36 months of age. 

Method: CSBS DP Behavior Samples were videotaped for 100 children later diagnosed with ASD, with 1/3 of the children videotaped more than once; 88 samples were collected between 12 and 23 months of age and 80 samples between 24 and 36 months. Samples were also collected from 37 children with DD and 93 children with TD in the second year. Scores were computed for the rate and inventory of repetitive movement or posturing of the body (RMB) and repetitive or stereotyped movement with objects (RMO). Measures of developmental level using the Mullen and autism symptoms using the ADOS were obtained at an average age of 36 months.

Results: Preliminary analyses of 67 samples indicate that the ASD group displayed RMB and RMO early in the second year and that the rate and inventory size did not change significantly from the second to the third year, although the behaviors varied. In the second year of life, the ASD group showed significantly higher measures of RMB and RMO than the TD group and significantly higher measures of only RMO than the DD group. Moderate correlations were observed between RMB and RMO and the Restricted and Repetitive Behaviors domain score on the ADOS. Moderate correlations were also observed between RMO and the Social Affect domain on the ADOS. RMB and RMO did not show significant correlations with developmental level.

Conclusions: Repetitive and stereotyped behaviors are evident in children with ASD down to 12 months of age using the CSBS DP. These findings have important implications for understanding the unfolding of core features of ASD in the second and third years and for improving early identification.

Sponsors: USDOE, OSERS; Simons Foundation
9:1-12.0, and 12:1-15:0 time intervals. We discuss as supporting the theories presented in Greenspan and Shanker's The First Idea (2004), and outline a diagnostic tool based on the findings.

**Oral Session #11**

**Instruments**

**Chair:** Jonathan Green

**Speakers:**
- EJ Honey, K McClintock, HR McConachie, SR Leekam, University of Durham
- Crystal J Gray, G.L. Burns, Psychology Department, Washington State University
- Carrie Allison, Simon Baron-Cohen, Sally Wheelwright, Tony Charman, Carol Brayne, Autism Research Centre
- Katherine Oberle Gotham, Susan Risi, Catherine Lord, University of Michigan

**ABSTRACTS**

**A NEW MEASURE FOR IMAGINATION WITHIN THE ADOS. EJ Honey, K McClintock, HR McConachie, SR Leekam, University of Durham**

Background: Imaginative play is known to be impaired in children with ASD. Within DSM-IV it is categorised within the domain of impairments in communication. However, the triad of impairments proposed by Wing & Gould associates poor imaginative play with repetitive behaviours. The Autism Diagnostic Observation Schedule (ADOS) is a semi-structured standardised tool used in clinical and research fields of ASD. The ADOS includes a number of opportunities to assess a child’s imagination and does not categorise imagination with either communication impairments or repetitiveness. However, only a summary rating is made.

Objectives: To develop a coding scheme for use alongside ADOS ratings to obtain detailed information about imaginative play in ASD.

Methods: The Pretend Play Scale (PPS) (Honey & McClintock, 2005) was developed to measure play actions performed by children in the ADOS across three dimensions: decontextualisation, decentration and integration, for both spontaneous and prompted play. Summary scores of the overall level of complexity and elaborateness of play observed are then calculated.

Results: The coding scheme was applied to video taped ADOS's of 163 children aged 2-8 years with ASD, specific language impairments and of normative development. Preliminary analysis of the PPS indicates very good inter-rater reliability. Data on relationships between the PPS, the ADOS and parent-reported repetitive behaviours and play will be reported for several samples of pre-school children.

Conclusion: The PPS will allow clinicians and researchers to gain additional detailed information about play abilities from an already validated and widely used measure.

Sponsor: Economic and Social Research Council *

**THE PSYCHOMETRIC PROPERTIES OF THE PERVERSIVE DEVELOPMENTAL DISORDER BEHAVIOR INVENTORY WITH CHILDREN ON THE AUTISM SPECTRUM** Crystal J Gray, G.L. Burns, Psychology Department, Washington State University

Background: The PDDBI (Cohen et al., 2003) is a parent and teacher rating scale used to assess the adaptive and maladaptive skills of children with Pervasive Developmental Disorders (PDD). The original study provided positive support for the psychometric properties of this measure.

Objective: The purpose of the current study was to further assess the psychometric properties of the PDDBI with a separate sample of children with PDD from another part of the country.

Methods: Parents and teachers of children ages 3 through 13 years with a PDD in Washington...
State were recruited to participate. The sample population consisted of 237 children, 156 diagnosed with autism, 51 with aspergers, and 30 with PDD-NOS. Two parents and two teachers of each child completed the PDDBI.

Results: Our analyses on the PDDBI indicated that the 11 scales have excellent internal consistency, moderate to good inter-rater reliability for the within situation ratings for the seven maladaptive scales, and excellent inter-rater reliability for the within and across situation ratings for the four adaptive scales. In addition, the structural validity of the measure was excellent with there being clear maladaptive and adaptive factors. These results were nearly identical to the findings reported by Cohen et al. (2003) for his sample of children with PDD from New York.

Conclusion: The PDDBI appears to be both reliable and valid, demonstrating sound psychometric properties for the measurement of maladaptive and adaptive skills in children with PDD.

Sponsor: The Arc of Washington Trust Fund*

DEVELOPMENT OF THE Q-CHAT, A REVISED SCREENING INSTRUMENT FOR AUTISM SPECTRUM CONDITIONS IN TODDLERS BETWEEN 18 - 24 MONTHS

Carrie Allison, Simon Baron-Cohen, Sally Wheelwright, Tony Charman, Carol Brayne, Autism Research Centre

Background: There is a need for early identification of autism spectrum conditions in order to appropriately target interventions and to help parents recognise their child’s needs. Objectives: Psychometrically evaluate the test re-test reliability of a revised version of the Checklist for Autism in Toddlers (the Quantitative - Checklist for Autism in Toddlers [Q-CHAT]). Methods: The Q-CHAT was sent to parents of 18 - 24 months olds from a general population in Cambridgeshire. The distribution of scores on the Q-CHAT was assessed and sex differences were examined. The Q-CHAT has a minimum score of 0 and a maximum of 100. Pilot data from already diagnosed children with ASC suggests a cut-point of >44. Test re-test reliability was analysed as a whole scale and in three score categories. Results: n=751 Q-CHAT questionnaires were available from the total population of 2360. The median score was 26 (range 7 - 57). Provisional score bands of d 40, 41 - 43 and > 44 were chosen. 1.9% of the sample scored above the cut-point of 44. The median score for boys was 27 and 25 for girls. The score distributions were significantly different (Mann-Whitney, p=0.03). Test re-test data were available for 330 pairs of Q-CHAT questionnaires. Overall agreement across three score groups was P0= 95% (95% CI: 92, 97) and weighted kappa was 0.52. The correlation between the two test scores was 0.78 (Spearman’s rho). Conclusion: Preliminary findings show moderate test-retest reliability of the Q-CHAT. Examination of its clinical validity and test properties is underway.

MEASURING ASD SEVERITY WITH CALIBRATED AUTISM DIAGNOSTIC OBSERVATION SCHEDULE (ADOS) SCORES

Katherine Oberle Gotham, Susan Risi, Catherine Lord, University of Michigan

Background: In genetic and neuroscience research, severity of autism has been estimated using ADOS scores. These scores were not normalized for such a purpose and are affected by verbal level, chronological age, and IQ.

Objective: Standardized scores from revised ADOS totals will be generated from a large dataset to approximate a severity metric for the construct of Autism as it is measured on this instrument. Methods: Analyses were conducted using a dataset of ADOS and psychometric scores for 960 children aged 12 to 192 months, some with repeated assessments for a total of 1368 cases. Individuals with autism comprised 948 cases; 438 had PDD-NOS. The sample was divided into cells determined by chronological age and language level. Calibrated scores based on ADOS scores were then generated within each cell.

Results: Preliminary findings indicate that 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) 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. This study was funded by the National Institute of Mental Health (Validity of Diagnostic Measures for Autism Spectrum Disorders: NIMH RO1 MH066469).
Oral Session #12
Genetic Studies: Cytogenetic & Molecular

Chair: Matthew State

Speakers:
Raman P Nagarajan, Michelle R Martin, Amber R Hogart, Janine M LaSalle, University of California, Davis
Marwan Shinawi, Ellen Montz, Yong-Hui Jiang, Roger Stevenson, Arthur L Beaudet, Dept Molec & Human Genetics, Baylor Col Medicine
Patrick Malenfant, Xudong Liu, Christine L Hall, Maryam Koochek, Ying Qiao, Chansonette Harvard, Albert E Chudley, Evica Rajcan-Separovic, Suzanne ME Lewis, Jeanette JA Holden, ASD-CARC, Queen's University

ABSTRACTS

IDENTIFICATION OF AUTOSOMAL RECESSIVE GENES FOR FAMILIAL AUTISM AND MENTAL RETARDATION. Eric M Morrow, Seung-Yun Yoo, Russell J Ferland, Robert Sean Hill, Adria Bodell, Kira A Apse, Samira Al-Saad, Asif Hashmi, Soher Balkhy, Generoso Gascon, S Herguner, NM Mukaddes, Robert M Joseph, Elaine LeClair, Leonard A Rappaport, Janice Ware, Christopher A Walsh, Harvard Medical School

Background: Identification of disease-causing mutations in autism promises to enhance our understanding of this disorder. Chromosomal anomalies are common; however, few definitive autism genes have been identified. The genes thus far identified explain a small percentage of cases, or a limited degree of the variance of the phenotype.

Objectives: To identify autosomal recessive genes for familial autism by conducting homozygosity linkage mapping in large, multiplex families who share common ancestors (ie have cousin-marriages). Previous studies from our laboratory have shown that homozygosity mapping in pedigrees with cousin-marriages is a viable approach to identify autosomal recessive genes that cause neurodevelopmental disease.

Methods: Families with cousin-marriages and children affected by autism, with or without mental retardation, were ascertained in multiple international centers. Special efforts were made to identify families with multiple affected children. Patients with autism initially underwent Fragile X testing and array-CGH. Homozygosity mapping was conducted on multiplex families.

Results: Chromosomal abnormalities were common (nearly 20%) in autistic children in families wherein only one child was affected, but were not detected in multiplex families. Homozygosity mapping has generated support for linkage in several families. Implicated loci are thus far heterogeneous across families. One family implicates a known autism locus on 7q, while other families support novel autism loci. One family implicates a single locus on 6q and generates a LOD score of 2.78.

Conclusions: Chromosomal abnormalities likely represent de novo mutations. The identification of diverse loci across families supports the notion of profound genetic heterogeneity in autism. Support: HHMI, Nancy Lurie Marks Family Foundation, Marilyn and Jim Simons Foundation, CAN, NAAR, Daland Award, Pfizer Scholars Grant for Clinical Psychiatry.

REDUCED MECP2 EXPRESSION IS FREQUENT IN AUTISM FRONTAL CORTEX AND CORRELATES WITH ABBERRANT MECP2 PROMOTER METHYLATION Raman P Nagarajan, Michelle R Martin, Amber R Hogart, Janine M LaSalle, University of California, Davis
Mutations in MECP2, encoding methyl CpG binding protein 2 (MeCP2), cause most cases of Rett syndrome (RTT), an X-linked neurodevelopmental disorder. Both RTT and autism share a loss of social, cognitive and language skills and a gain in repetitive stereotyped behavior, following apparently normal perinatal development. Although MECP2 coding mutations are a rare cause of autism, MeCP2 expression defects were previously found in autism brain.

Objective: Determine the frequency of MeCP2 expression defects in autism brain and test the hypothesis that MECP2 promoter methylation correlates with reduced expression.

Methods: MeCP2 protein expression in autism and other neurodevelopmental disorders was compared with control post-mortem cerebral cortex samples on a large tissue microarray. MeCP2 immunofluorescence was detected with laser scanning cytometry and normalized to control histone H1 staining. Bisulfite sequencing was performed on genomic DNA from these same samples to determine DNA methylation patterns in the MECP2 promoter.

Results: Significantly reduced expression of total MeCP2 was found in 11/14 autism brain samples (79%) compared to multiple age-matched controls. Bisulfite sequencing revealed significantly increased MECP2 promoter methylation in autism males compared to controls. Furthermore, percent methylation of MECP2 inversely correlated with MeCP2 protein expression.

Conclusions: These results suggest that aberrant DNA methylation of the MECP2 promoter could be important in the etiology of autism.

ANALYSIS OF EPIGENETIC CONTROL OF MECP2 IN AUTISM. Marwan Shinawi, Ellen Montz, Yong-Hui Jiang, Roger Stevenson, Arthur L Beaudet, Dept Molec & Human Genetics, Baylor Col Medicine

BACKGROUND: Genetic predisposition to autism is evident from family and twin studies. So far, genome-wide linkage studies have failed to provide a strong evidence for major autism-related loci. Male sex is the strongest and most consistent risk factor in autism. MECP2 is an X-linked gene encoding a methyl-CpG binding protein that has been implicated recently in regulating genes involved in social behavior. Despite the resemblance between the phenotypes of autism and Rett syndrome, MECP2 mutations are an infrequent cause of essential autism. AIMS: We are testing the hypothesis that epigenetic abnormalities (epimutations) rather than mutations of MECP2 might be a more common cause of autism. METHODS: We analyzed the methylation of the CpG island at the promoter of MECP2 in lymphoblast cell lines of 44 autistic males and 14 autistic females from the AGRE, NIMH, and South Carolina Autism Project collections, and compared these to 28 controls (13 females and 15 males). In addition, brain samples from 8 autistic individuals were examined and compared to 5 normal brains. The methylation status was tested by Southern blot analysis after digestion with methylation sensitive enzyme and by bisulfite sequencing.

RESULTS: In all lymphoblast and brain samples from males, the DNA was completely unmethylated. For all brain samples and lymphoblast lines from control females and for most lymphoblast lines from females with autism, the data were consistent with the interpretation that the inactive X chromosome was methylated and the active X unmethylated. However, three lymphoblast cell lines from unrelated females with autism demonstrated hypomethylation. Additional studies are underway to test more brain and fresh blood samples to avoid the possible artifacts of methylation arising in cell culture.

CONCLUSIONS: We propose that epigenetic dysregulation of MECP2 could be a causative factor in some fraction of autistic patients.

MICRODELETIONS AND MICRODUPLOCATIONS IN SUBJECTS WITH AUTISM SPECTRUM DISORDERS Patrick Malenfant, Xudong Liu, Christine L Hall, Maryam Koochek, Ying Qiao, Chansonette Harvard, Albert E Chudley, Evica Rajcan-Separovic, Suzanne ME Lewis, Jeanette JA Holden, ASD-CARC, Queen’s University

BACKGROUND: Extensive searches for candidate genes and whole genome scans have led to the identification of regions that appear to be associated with susceptibility to autism, but the identification of major genes has not been achieved to date. However, there are several reports of deletions and duplications in individuals with ASDs, some of which have been found in more than one person. In most cases, the mechanisms involved in generating these abnormalities and their frequencies are unknown as they are identified serendipitously in one or a few individuals.

OBJECTIVES: To a) detect and characterize microdeletions and microduplications found in persons with ASDs; b) determine their frequencies; and c) identify the culprit genes.

METHODS: Individuals with autism are tested using CGH microarrays. Following the identification of micro-deletions and duplications, a large number of individuals with autism is screened using an ABI Prism 7900 light cycler thus combining the sensitivity of genomic microarrays to the high throughput and relatively low cost capacity of real time PCR. The use of
quantitative PCR allows us to rapidly refine the breakpoints of each abnormality. A minimum of 150 controls and 500 individuals with ASD are then tested to determine whether there are additional cases with the same or similar abnormalities and to determine whether the changes are normal polymorphisms or may be involved in the ASD phenotype.

RESULTS AND CONCLUSIONS: A total of 29 rearrangements were identified in 21 of the 43 individuals tested with microarrays: deletions on chromosomes 2p, 3p, 4q, 7q, 9p, 13q, 14q, 15q, 20p and Xp and duplications on chromosomes 2p, 3q, 7q, 6q, 10q, 11p, 12q, 14q, 15q, 16q, 16p and Yp. These are confirmed using molecular markers and the size of the abnormalities are determined. The results of the breakpoint analysis studies and screening of controls and individuals with ASDs will be presented.

Funded by CIHR, CIHR/NAAR Training Grant, and OMHF.
Keynote Address #3

Genomic and Bioinformatic Approaches to Mapping Autism Spectrum Disorder Susceptibility Loci

Conrad Gilliam, The University of Chicago

One of the major challenges to biomedical research in the 21st century is to devise strategies to identify the multigenic transmission patterns that correlate with common heritable disorders. Modern gene mapping studies are remarkably efficient for tracking the single-gene mutations responsible for most rare, Mendelian disorders, but largely inept for tracking the multigene inheritance patterns that predispose individuals to the type common heritable disorders that constitute the bulk of today’s public health burden. To date, the vast majority genetic linkage and association studies have detected relatively weak genotype: phenotype correlations when the phenotype is a disease classification and the underlying genetic etiology is believed to be multifactorial. We are exploring experimental and computational genomic strategies to predict biologically meaningful interactions between key autism candidate genes with the hope that a systematic survey of allelic variation across predicted ‘candidate gene networks’ will lead to improved genotype: phenotype correlation, and insight into the genetic basis of ASD.
Invited Educational Symposium #5
Latest Trends In Research On Psychosocial Interventions

Speakers:
Tristram Smith, University of Rochester Medical Center
Peter Mundy, The Center for Autism & Related Disabilities, University of Miami
Connie Kasari, Psychological Studies in Education
Paul Yoder, Vanderbilt University

ABSTRACTS

EVALUATING THE EVIDENCE BASE FOR CURRENT PSYCHOSOCIAL INTERVENTIONS Tristram Smith, University of Rochester Medical Center
Although autism is a neurobiological disorder, psychosocial interventions are currently the primary form of treatment. Influential psychosocial intervention models include applied behavior analytic, developmental, and eclectic approaches. Applied behavior analysis (ABA) has generated the most research and has evolved over time based on empirical findings. However, the research consists largely of small-N, initial efficacy studies. An NIMH work group recently formulated a model for going beyond initial efficacy studies to validate and disseminate psychosocial interventions in autism. The model emphasizes the formulation of treatment manuals, followed by randomized clinical trials in research settings and evaluations of effectiveness in community settings. Methodological considerations at each stage of research are outlined, and priorities for future research are identified.

BEYOND PRESCHOOL: INTERVENTIONS FOR OLDER HIGH FUNCTIONING CHILDREN Peter Mundy, The Center for Autism & Related Disabilities, University of Miami
This talk will consider the intervention needs and related research literature on older higher functioning children with autism (HFA). One outcome of national efforts to improve early identification and intervention for autism may be an increase of children with autism who achieve typical levels of intellectual function (IQ range 80 to 130). Ironically, though, there is currently inadequate information to develop empirically based interventions that meet the specific needs of these HFA children (Bauminger, 2002; Kielenen et al., 2000; Rutter, 1996). Therefore, there is a problem of continuity of care for these children, and their long-term outcomes remain poor (Engstrom et al., 2002). This discussion will focus on some of the current research that is relevant to assessing the needs of HFA children and providing effective interventions for this group. In particular, three studies from Dr. Mundy’s current program of research on individual differences in social impairments and comorbidity among HFA children will be described. These studies suggest that several dimensions of neuropsychological and family process may be important to consider in developing effective intervention for HFA children. These include: 1) anterior EEG asymmetry measures related to motivation and appetitive drives, 2) self-monitoring and EEG error related negativity measures of anterior cingulate functions, and 3) family factors such as family cohesion and parent expressed emotion.

WHAT ARE THE ACTIVE INGREDIENTS OF INTERVENTIONS? Connie Kasari, Psychological Studies in Education
This talk will consider the extent to which we understand the necessary and sufficient elements ‘the active ingredients’ of a treatment program. Many interventions share common elements but also diverge in unique ways. A new emphasis in research is addressing the active ingredients of intervention—those components of intervention that are most important for optimal outcome for specific children. The evidence base for the following active ingredients will be examined: intensity/dose, timing, and content. To what extent do we have evidence that more intensive interventions result in significantly better outcomes than those achieved by less intensive outcomes? To what extent do we have empirical evidence that ‘earlier is better’ in terms of developmental outcomes and family adaptation? Finally, does it matter what is taught as much as how something is taught or who does the teaching? Studies will be highlighted that examine the effect of specific content aimed at improving core deficits in children with autism.
WHY PREDICTING OUTCOME AND GROWTH IS NOT THE SAME AS PREDICTING
Paul Yoder, Vanderbilt University

This talk will discuss issues related to measuring treatment response. It is widely accepted that not all children benefit from an intervention, and an important goal of treatment research is to better understand for whom a specific intervention works and for which outcomes. This talk will examine important predictors of treatment response, and appropriate methods for measuring treatment response. In particular, the talk will highlight two commonly used, but inadequate ways to identify predictors of treatment response and two adequate ways to do so. Also discussed will be ways to differentiate growth while in treatment from growth due to treatment. Finally, commonly overlooked threats to internal validity in treatment studies of children with autism will be examined.

SPECIAL SYMPOSIUM #1
Autism Epidemiology: Who Counts & How Do We Count Them?

Speakers:
 Marshalyn Yeargin-Allsopp, CDC
 Tony Charman, Institute of Child Health, University College London
 Craig J Newschaffer, Center for Autism & Developmental Disabilities Epidemiology, Johns Hopkins University Bloomberg School of Public Health
 Christopher Gilberg, University of Göteborg, Sweden, and University of Strathclyde, Glasgow, UK

ABSTRACTS

THE EVOLVING PREVALENCE OF AUTISM Marshalyn Yeargin-Allsopp, CDC

Background: The reported prevalence of autism has increased considerably over time - from 4-5 per 10,000 children with autism spectrum disorders (ASD) from non-US epidemiologic studies reported before 1985 to 2 to 6 per 1,000 children with ASD from US and non-US studies reported since 2000. Similar increases have also been seen using administrative data over time from US service providers where large increases in numbers of individuals receiving services have also been reported.

Objective: This presentation will focus on the impact of the use of differing case definitions and methods of ascertainment over time on the reported prevalence of ASD.

Methods: Using data from various population-based studies including data from the CDC study in metropolitan Atlanta, the prevalence of ASD over time will be presented.

Results: The prevalence of ASD has increased more than ten-fold over time.

Conclusions: Examination of rates from different populations using different methods makes comparing rates across sites and over time difficult. The question of whether the ‘true prevalence’ or incidence of ASD has increased over time is hotly debated yet largely irresolvable given changing diagnostic criteria, increased awareness and recent increased availability of services.

Sponsor: Centers for Disease Control and Prevention, Atlanta GA

The findings and conclusions in this presentation are those of the presenter and do not necessarily represent the views of the Centers for Disease Control and Prevention.

THE INFLUENCE OF CASE ASCERTAINMENT AND CASE DEFINITIONS ON PREVALENCE: HOW YOU COUNT, WHEN YOU COUNT AND WHAT YOU COUNT AS AUTISM COUNTS! Tony Charman, Institute of Child Health, University College London

Background: Recent reports have suggested that the prevalence of autism and related pervasive developmental disorders (PDDs) is considerably higher than previously recognised.

Objectives: Taking a recent single study as an example, this presentation will explore how methodological factors are critical to the prevalence figures that are found in any particular study.

Methods: Within a total population of children age 9 to 10 years all those with a current clinical diagnosis of PDD or considered ‘at risk’ for being an undetected case were screened. A stratified subsample received a comprehensive diagnostic assessment. ICD-10 clinical consensus diagnoses
of childhood autism and ‘other PDDs’ were derived as was case positive/negative status on the ADI and ADOS. A sample weighting procedure was used to estimate prevalence.

Results: Prevalence rates varied by a factor of 4 times depending on which metrics of diagnosis were applied. Associated factors (sex, IQ, family characteristics, likelihood of previous identification) also differed according to which metric of ‘autism’ or ‘PDD’ was used.

Conclusions: The issues raised by use of different ascertainment methods, studying populations of different ages and use of different definitions of autism are important not just to answer questions about the prevalence of PDDs, as well as for service planning. They go to the heart of the definition and boundaries of the autism phenotype and have implications for studies investigating aetiology, brain pathology, cognition function and the effectiveness of interventions.

Sponsor: Wellcome Trust, Department of Health.

THE CHALLENGES OF CONDUCTING EPIDEMIOLOGIC STUDIES IN DEVELOPING COUNTRY SETTINGS - THE CHINA EXAMPLE Craig J Newschaffer, Center for Autism & Developmental Disabilities Epidemiology, Johns Hopkins University Bloomberg School of Public Health

Background: Population-based epidemiologic research on autism, be it prevalence surveys or risk factor studies, has been conducted, almost exclusively, in developed countries. Building capacity for population-based research in developing countries will enhance our understanding of the descriptive epidemiology of this complex disorder and could prove valuable in detecting genetic and/or environmental risk factors.

Objective: Report on our experience preparing for, and implementing, a pilot study for a population-based ASD prevalence study in Weichang district, Shandong province, China.

Methods: The first stage of the project involved translation and cultural adaptation of the Social Communication Questionnaire (SCQ) and the Autism Diagnostic Interview-Revised (ADI-R) as well training of expert clinicians in the research use of these tools. The next stage involves fielding a two-stage prevalence survey of approximately 3,800 3-5 year old children using a range of parent self-report questions. All children with positive SCQs will receive an ADI-R.

Results/Discussion: The translation/adaptation process revealed numerous language and cultural issues to be surmounted in creating parent-report tools for use in China. Pre-pilot results suggested high false positive rates on SCQs. Because of this we incorporated a re-screening step for children with SCQ scores in the 13-17 range. I will discuss issues in translation/adaptation and report on the performance of the SCQ and of shorter tools that could potentially be used as a Stage I screener for epidemiologic research on autism in China.

(Supported by NIH FIC 1 R21 TW06697)

AUTISM SPECTRUM CONDITIONS: WHAT ARE THE ASSOCIATED PROBLEMS AND WHAT CAN THEY TELL US? Christopher Gilberg, University of Göteborg, Sweden, and University of Strathclyde, Glasgow, UK

Autism Spectrum Conditions (ASCs) are relatively common neurodevelopmental syndromes, affecting 0.5-1.0% of the general population of children, and causing severe to moderate functional disability for those affected, sometimes throughout the life span. ASCs rarely, if ever, are ‘pure’ syndromes. There are virtually always some associated physical, cognitive, or psychopathological problems. The physical problems range from well-defined genetic syndromes (such as tuberous sclerosis, fragile X, and 22q11 deletion) and specific teratological syndromes (thalidomide, alcohol, valproic, and some instances of Moebius syndrome) on the one hand to epilepsy, motor, visual, hearing, and gastrointestinal problems on the other. Major cognitive associated problems range from various degrees of mental retardation/learning disability to non-verbal learning disability, and dyslexia/hyperlexia. In addition, a whole range of psychiatric disorders/conditions is clearly much overrepresented in ASCs. These include attention-deficit/hyperactivity disorder, tic disorders, emotional disorders, self-injurious and violent behaviours, and disruption of circadian rhythm (including severe sleep disorders). The range of problems, and their implications for understanding autism pathogenesis and improving ASC interventions, will be reviewed.
Invited Educational Symposium #6
Mouse Models Of Autism

Speakers:
Jacqueline Crawley, STAART Center
James Bodfish, University of North Carolina at Chapel Hill
Emanuel DiCicco-Bloom, NAAR

ABSTRACTS

STRATEGIES FOR DESIGNING MOUSE BEHAVIORAL TASKS RELEVANT TO THE SYMPTOMS OF AUTISM
Jacqueline Crawley, STAART Center

This lecture will focus on mouse behavioral tasks with conceptual analogies to the fundamental and associated symptoms of autism. A simple, automated social interaction task and more in-depth scoring of juvenile play behaviors are designed to model the first diagnostic symptom, deficits in reciprocal social interaction. Ultrasonic vocalizations and olfactory responses are designed to model the second diagnostic criterion, deficits in social communication. Reversal tasks and exploration of novel objects are designed to model the third diagnostic domain of stereotypies, repetitive ritualistic behaviors, insistence on sameness, and narrow restricted interests. Standard mouse tasks measuring learning and memory, anxiety-like traits, sensory reactivity, motor clumsiness, and other analogies of associated symptoms of autism will be described. Photographs and videoclips of mouse behavioral tasks will be included. Promising discoveries of inbred strains of mice with autism-like phenotypes on one or more of these behavioral tasks suggest that robust mouse models are emerging.

MODELING STEREOTYPED MOVEMENTS, RESTRICTED INTERESTS, AND BEHAVIORAL RIGIDITY
James Bodfish, University of North Carolina at Chapel Hill

This presentation will focus on a set of parallel clinical and mouse model studies of the repetitive behavior domain in autism. We have used human studies to disaggregate the clinical phenotype and guide the design of conceptually valid mouse behavioral testing procedures. In our clinical studies we have found that a variety of forms of repetitive behavior characterize persons with autism. This includes the co-occurrence of ‘lower-order’ stereotyped movements (e.g. body / object stereotypes, compulsive / ritualistic actions) and ‘higher-order’ stereotyped patterns of cognition (e.g. insistence on sameness, restricted interests) along with an overall restricted or ‘rigid’ repertoire of activity. To model this complex phenotype in mice we are combining (a) observational coding of stereotyped movements in home cage environments, (b) cognitive performance tasks that measure habit learning and novel object interest / exploration, and (c) dynamical measures of the complexity and flexibility of behavioral repertoires during an exploration task. These testing procedures will be described and results from strains with co-occurring deficits in these areas will be presented. Strains that demonstrate this complex phenotype appear to be reasonable candidates for studies modeling the pathogenesis and treatment of repetitive behavior in autism.

MANIPULATING EXPRESSION OF ENGRAILED 2 (EN2), AN AUTISM ASSOCIATED GENE, TO DISCOVER MECHANISMS OF DEVELOPMENTAL DYSFUNCTION
Emanuel DiCicco-Bloom, NAAR

Recently, the association of EN2 with autism has been replicated in three separate human populations, and data suggest it contributes to ASD in ~40% of cases. In past studies, both gene deletion and over-expression models indicate that cerebellar size and cell composition in mice are altered in ways that phenocopy the human autism neuropathology. However, underlying cellular mechanisms by which En2 acts remain undefined. To define functions, we are using En2 knock out mice, isolated cerebellar granule neurons, gene over-expression (transfection) strategies and gene profiling to characterize its roles in brain development. We find that mis-regulation of En2 expression levels alters 1) the neuroanatomy of the cerebellum, 2) the transition from proliferation to differentiation, 3) selected growth factor and gene signaling pathways, and 4) the behavioral phenotype. The richness of the animal data is providing new insights into autism causation and demonstrates the utility of this approach that can be applied to future autism genes as they are
identified.

NOTES
PS5.1 INVESTIGATING INTERNAL MODELS THROUGH A MOTOR IMAGERY PARADIGM IN ADOLESCENTS WITH AUTISM SPECTRUM DISORDER Suparna Choudhury, Tony Charman, Sarah-Jayne Blakemore, Behavioural and Brain Sciences Unit, Institute of Child Health, University College London Background: Autism is characterised by deficits in social communication skills and often by problems in motor coordination. The mirror neuron system is thought to be necessary not only for the execution of one’s own and the representation of another’s actions, but also for the understanding of other minds.

Objective: Here we investigated internal models, neural representations of intentions and their interaction with the external world, in autistic adolescents compared with typically developing adolescents.

Method: Three motor imagery tasks, including a visually guided pointing task, a hand posture task and a drawing task designed to tap internal models, were administered to 20 adolescents with and 20 adolescents without autism spectrum disorder (ASD), matched for IQ. The tasks relied on the chronometry of executed (E) and imagined (I) actions. The association between timing of E and I were analysed for each group. Previous studies have shown that in typical individuals E and I are highly correlated but in individuals with parietal damage or DCD, the association breaks down for imagined actions. Our prediction is that this will also be true for the individuals with ASD.

Results: Data collection is still in progress. We will report findings on the data collected so far, comparing the association between E and I for the ASD and non-ASD groups.

Conclusion: Our findings will shed new light on motor theories of social cognition and theories of mirror neuron dysfunction about autism.

Sponsors: Medical Research Council, Child Health Research Appeal Trust, Royal Society UK*

PS5.2 IMPACT OF SENSORY PROCESSING AND MOTOR SKILLS ON DAILY LIVING SKILLS IN CHILDREN WITH AUTISM SPECTRUM DISORDERS Melanie Couture, Emmanuelle Jasmin, Erika Gisel, Eric Fombonne, Gregory Reid, Montreal Children’s Hospital Research Institute Background: The nature and extent of motor and sensory processing difficulties in children with autism spectrum disorders (ASD) remain controversial and have not been linked to self-care skills. No studies exist to describe the development of these skills across childhood.

Objective: To describe the gross and fine motor skills, sensory processing and their association with self-care skills of children with ASD.

Methods: This is a cross-sectional study of children with ASD, 3 to 10 years of age. There will be 4 groups of 30 children with ASD: 3-4, 5-6, 7-8, and 9-10 years old. A control group of 30 children for each age segment will be divided into 3 groups of 10 children: 1) mental retardation, 2) developmental language delay, or 3) typical development.

Results: Presently 20 children, aged 3 to 4 years, with ASD have been recruited and assessed. All children with ASD except 3 (84%), presented sensory symptoms. Their total motor quotient on the Peabody Developmental Motor Scale was 71. They had a mean functional independence quotient of 67 and 56 on self-care skills, both scores 2 SD below the normative mean. Self-care skills were significantly related to fine motor skills only (r=.526, p=.025).

Conclusion: A high percentage of young children with ASD have sensory symptoms, poor motor and self-care skills. This study will provide necessary preliminary, developmentally oriented empirical data that will guide the planning, implementation and evaluation of targeted interventions for children with ASD relevant to their self-care skills.

PS5.3 MOTOR DEFICITS CONTRIBUTE TO, BUT DO NOT ENTIRELY ACCOUNT FOR, DYSPRAXIA IN AUTISM Melissa Ann Dziuk, Jennifer C Gidley Larson, Andreea Apostu, E. Mark Mahone, Martha B Denckla, Stewart H Mostofsky, Kennedy Krieger Institute, Johns Hopkins University School of Medicine Background: Impaired performance of skilled gestures, referred to as dyspraxia, is consistently reported in children with autism. The neurological basis of dyspraxia in autism is not well understood. Basic motor skill deficits are also observed in children with autism, and may contribute to dyspraxia.

Objectives: Determine the association of basic motor skill deficits with praxis performance in children with autism.

Methods: Forty-three high-functioning children with autism (HFA) and forty typically-developing controls, ages 8-12 years, completed: (1) the PANESS, a normed motor examination for children and (2) a praxis examination that includes gestures to command, to imitation, and with tool-use. Hierarchical regression was used to examine the association of appendicular motor skill performance (summed times to complete repetitive limb movements on PANESS) with praxis performance (total percent of correct gestures).

Results: After accounting for age and IQ, there was a
significant effect of motor skill performance on praxis (R2 change=0.09, p=0.004). There remained a significant effect of diagnosis on praxis after accounting for motor skill performance, along with age and IQ (R2 change=0.12, p<0.001), with the HFA group showing worse performance on praxis compared with controls. Conclusion: The findings suggest that basic motor skill impairments do contribute to dyspraxia in autism. However, impaired praxis in the HFA group could not be entirely accounted for by basic motor skill deficits, suggesting that additional factors (e.g. impaired formation of spatial representations of movement) are contributing to dyspraxia in autism. Further exploration of the basis of dyspraxia could provide greater insight into the neurological basis of autism.

Sponsors: National Alliance for Autism Research and NIH K02NS44850, R01NS048527, and M01RR00052.

**PS5.4**

**POSTURAL CONTROL IN AUTISM** Kimberly A Fournier, Krestin J Radonovich, Mark D Tillman, John W Chow, University of Florida

Background: ‘Clumsiness’ has been described as a characteristic of ASD and motor disturbances can be considered the earliest indicators of autism.

Objectives: To compare postural stability of children with autism with that of typically developing children.

Methods: Subjects were recruited from the Child & Adolescent Psychiatry Clinic at the University of Florida. Static balance trials were collected for 5 autistic subjects (5.6 ± 1.8 years) and 5 control subjects (4.6 ± 1.2 years). Using a forceplate, ground reaction forces (sampling rate of 100Hz) were recorded and the location of the center of pressure (COP) was computed for each trial. Using COP data, typical static balance measures were calculated (Anterior/Posterior and Medial/Lateral Ranges, Sway Area, Path Length and Path Length Average Speed). The maximal trial length attained by all subjects (5 seconds) was used for subsequent analyses.

Results: The data were rank ordered and one-tailed Mann-Whitney U-tests were used to compare the autistic children and the control children for the 5 COP balance measures. The results indicated a significantly larger Anterior/Posterior Range for autistic children (U = 4, p d 0.05). No significant differences were detected for the Medial/Lateral Range, Sway Area, Path Length and Path Length Average Speed (U e 5, p > 0.05).

Conclusions: Preliminary findings suggest that ‘clumsiness’ observed in autistic children may be due, in part, to deficits in postural control, particularly in the anterior/posterior direction.

Sponsor: NIH Grant # MH073402

**PS5.5**

**NORMAL ADAPTATION IN CHILDREN WITH AUTISM IN TASKS REQUIRING THE CEREBELLUM** Jennifer C Gidley, Amy J Larson, Opher Donchin, Reza Shadmehr, Stewart H Mostofsky, Kennedy Krieger Institute

Background: Cerebellar pathology is a consistently reported post-mortem examination finding in individuals with autism. Previous research in adults has found that individuals with cerebellar damage are significantly impaired in their ability to adapt to visual and force perturbations.

Objectives: We examined both visual and somatosensory dependant motor adaptation in children with high-functioning autism (HFA), hypothesizing it would be impaired compared to controls.

Methods: Children with HFA and typically developing controls, ages 8-12 years, participated in three tasks of motor adaptation: 1) Prism Adaptation (HFA n=10, control n=11), subjects were instructed to throw a ball at a target while wearing prism goggles causing a 10Ú horizontal optical shift. 2) Reaching Adaptation: Force Perturbation and 3) Reaching Adaptation: Visual Perturbation (HFA n=11, control n=8), for both tasks subjects used a planar two joint manipulandum, and were instructed to make rapid reaching movements to targets presented on screen in front of them, in the Force Perturbation condition, movements were perturbed by forces applied by the manipulandum; in the Visual Perturbation condition, movements were perturbed using distortion of the visual feedback. All tasks consisted of baseline, adaptation, and post-adaptation phases; adaptation rates, learning indices, and post-adaptation after-effect were dependant measures.

Results: For all three adaptation tasks, there were no significant differences in motor adaptation, learning indices, or post-adaptation after-effect between children with HFA or typically developing children.

Conclusions: The findings from three separate adaptation tasks indicate that children with autism show normal motor adaptation, suggesting this aspect of cerebellar function is normal or is compensated in autism.

Sponsors: National Alliance for Autism Research and NIH K02NS44850, R01NS048527, P30HD-24061, M01RR00052.

**PS5.6**

**IMITATION AND THE MIRROR NEURON SYSTEM IN AUTISTIC CHILDREN** Emily Kathryn Kees, Nicole Ann Krause, Rachel Jane Hopticker, Harold Hill Goldsmith, Morton Ann Gernsbacher, University of Wisconsin, Department of Psychology

Background: Recent research has linked the imitation difficulties exhibited by many autistic individuals with an impairment in the mirror neuron system, citing deficits in the perception of others’ actions rather than in the production of their own actions.

Objective: The current study aims to determine 1) whether imitation deficits in autistic children vary as a function of early (birth to 3) motor skills and 2) whether autistic children’s action perception is as impaired as their action imitation and production.

Methods: Two groups of autistic children, one with severe early oral- and manual-motor impairments (n=21) and one without (n=21), were tested on their ability to produce on command, imitate, and discriminate 20 different gestures and pantomimes (including conventional gestures: wave
goodbye, shake head, nod head, beckon; natural gestures: indicate too hot, too cold, too noisy, too smelly; buccofacial pantomimes: cough, sniff, blow, suck; object pantomimes: use pencil, hammer, key, pitcher; object pantomimes on self: use toothbrush, comb, hat, binoculars). The discrimination task required distinguishing a target pantomime or gesture from a lure pantomime or gesture. Results: Preliminary analyses reveal greater imitation deficits in the group with early motor impairment, F(1,41) = 59.21, p < .0001. Additional analyses currently in progress will examine whether this imitation difficulty lies within the perception of others' actions or within the production of their own actions. Conclusion: These data will have the potential to distinguish action perception from action execution.

Sponsor: NAAR and NIMH

**PS5.7**

DEVELOPMENTAL DYSPRAXIA IS NOT LIMITED TO IMITATION IN CHILDREN WITH AUTISM SPECTRUM DISORDERS **Stewart Mostofsky, Prachi Dubey, Vandana K Jerath, Melissa C Goldberg, Martha Bridge Denckla, Kennedy Krieger Institute, Johns Hopkins University School of Medicine**

Background: Impaired imitation of skilled gestures is commonly reported in autism. Questions, however, remain as to whether impaired imitation is associated with a more generalized deficit in performance of gestures consistent with a dyspraxia and whether the pattern of errors differs from that observed in typically developing children. Objectives: To examine the profile of errors associated with impaired gestural performance in children with autism and to determine whether impaired performance is specific to imitation or whether it is associated with a more generalized deficit consistent with a dyspraxia. Methods: Praxis was examined in 21 high-functioning children with autism spectrum disorders (ASD) and 24 typically developing controls using a traditional approach in which performance during Gesture to Command, Gesture to Imitation and Gesture with Tool Use was evaluated through detailed examination of error types. Results: Children with ASD produced significantly fewer correct responses not only during Gesture to Imitation (p=0.005), but also during Gesture to Command (p=0.001) and with Tool Use (p<0.001). The pattern of errors in ASD was similar to that of controls with spatial errors being most common in both groups; however, body-part-for-tool errors were more common in children with ASD, suggesting dyspraxia is not entirely attributable to motor deficits. Conclusion: The findings suggest that autism is associated with a generalized praxis deficit, rather than a deficit specific to imitation. In a developmental disorder such as autism, the findings may reflect abnormalities in frontal/parietal-subcortical circuits important for acquisition/learning of sensory representations of movement and/or the motor sequence programs necessary to execute them.

Sponsors: National Alliance for Autism Research and NIH K02NS44850, R01NS048527, and M01RR00052

**PS5.8**

IMPAIRED MOTOR LEARNING IN CHILDREN WITH HIGH-FUNCTIONING AUTISM **Megan B Roeder, Jennifer C Gidley Larson, Melissa Dzuik, Andreea Apostu, Stewart H Mostofsky, Kennedy Krieger Institute**

Background: Few published studies have examined motor sequence learning in children with autism. Given that autism is developmental disability impairments in motor skill learning may contribute to the social and communicative deficits characteristic to autism. Objectives: We examined visuomotor sequence learning in children with high functioning autism (HFA) and hypothesized that children with HFA will not only have problems with motor execution, but will also demonstrate impaired ability acquire new motor patterns (i.e., sequence learning). Methods: Participants included 33 males with HFA and 34 typically developing male controls, ages 8-13 years Motor sequence learning was assessed using a Rotary Pursuit task. The paradigm consisted of four successive blocks of four 20 second trials, during which subjects tracked a moving light in a continuous pattern at a speed of 20 rpm. A circular pattern was presented during blocks 1, 2, and 4; in block 3 a square pattern was presented. Learning was assessed by examining change in time-on-target across successive blocks of trials. Results: Repeated measure ANOVA indicated a significant difference between groups on overall performance across the blocks, with the autism group showing overall less time-on-target than did controls (p < .001). Across the two groups, there was a significant change in performance over blocks of trials (p < .001). There was a significant group-by-block interaction (p < .001), with children with HFA showing less change across successive blocks of trials than did controls. Conclusion: Our findings indicate that children with HFA show decreased Rotary Pursuit learning compared to control children. The difference in time on target across blocks suggests that motor execution, as well as visuomotor sequence learning, is impaired in children with autism.

Sponsor: National Alliance for Autism Research and NIH K02NS44850, R01NS048527, P30HD-24061, M01RR00052.

**PS5.9**

DEVELOPMENT OF A GROSS MOTOR TASK TO ASSESS MOTOR PLANNING OF CHILDREN WITH AUTISM SPECTRUM DISORDERS **Kerri Staples, Greg Reid, McGill University**

Background: Children with ASD do not perform movement skills consistent with their chronological age. An exploration of component processes such as motor planning may assist to better understand these movement differences. Objectives: To develop and evaluate a functional gross
motor task for motor planning.
Methods: Ten male students with ASD (based on DSM-IV criteria) performed the Test of Gross Motor Development and an obstacle course of 8 horizontal barriers. Motor planning was inferred from acts of hesitation and hesitation time. Homeroom teachers completed the Behavior Rating Inventory of Executive Functions (BRIEF) for each participant.
Results: The correlations between acts of hesitation and scores from the BRIEF and planning component of the BRIEF were \( r = .775 \) and \( r = .733 \), respectively. The correlations between hesitation time and scores from the BRIEF and planning component of the BRIEF were \( r = .667 \) and \( r = .648 \), respectively. These correlations supported the validity of the motor planning inferences based on the number and duration of hesitations during the obstacle course performance. Internal consistency (Chronbach’s alpha) of the motor planning measures were sufficiently high (\( .491 \) - .856) to support the reliability of this obstacle course task.
Conclusion: The initial use and development of this obstacle course task provides both valid inferences and reliable measures of motor planning.

PS5.10
A DESCRIPTIVE ANALYSIS OF MOTOR DELAYS AND DEFICITS IN AUTISTIC INDIVIDUALS FROM A LARGE FAMILIAL IDIOPATHIC AUTISM SAMPLE FROM THE AUTISM GENETIC RESOURCE EXCHANGE ( AGRE).
Margaret M Swaine, David O Black, Sarah J Spence, UCLA
OBJECTIVE: Motor impairments in ASD are understudied, limiting our understanding of their impact on the clinical course of the disorder. We investigated the prevalence of delays and deficits within a familial sample of ASD individuals from AGRE.
METHODS: Prevalence of motor milestone delays and current motor deficits was obtained from parent report measures (ADI-R, VABS, Medical Histories) and investigator observation for ~400 ASD subjects (mean age 9.6 yrs; 77% male).
RESULTS: Overall, the means for age of attainment of milestones were within the normal range but showed great variability (roll 4.3 months; sit 6.6 months; walk 13.3 months). However, ~10% of the sample showed clinically significant delay (>25% beyond the norm for the milestone) for both sitting and walking. 28% of subjects had reported gait abnormalities. 39% had reported coordination abnormalities. 38% had observed tone abnormalities. VABS scores were available for only a small subset (n=28) but a striking 68% showed standard scores for motor domain of >1 SD below the norm, with a mean score of 74.
CONCLUSIONS: Findings suggest that motor deficits (gait, coordination and tone) are present in approximately 1/3 of the ASD sample, whether or not there were reported motor milestone delays. Although milestone delays were not as prevalent as motor deficits, there was still a subset (~10%) of the sample with clinically significant delays. Although only available in a small subset, the VABS appeared most sensitive in detecting motor abnormalities (68%). This may be due to this scale providing a more comprehensive index of motor deficits and their impact on functional skills. The presence of abnormalities in all variables examined indicates the importance of further study of motor abnormalities in ASD. The relationship between motor and cognitive variables will also be examined.
SPONSOR: NIH R01MH64547

PS5.11
USE OF ICE PACKS TO REDUCE SELF-INJURY IN A YOUNG CHILD WITH AUTISM
Tasha Nicole Aper, Helena C. G. Huckabee, Emerge, P.C
Background: Children with autism are frequently at risk for self-injury as a result of abnormal sensory processing and language impairment.
Objectives: Evaluate if ice could be a safer stimulant of the spinothalamic tract.
Methods: A single subject was exposed to nonverbal redirection and praise compared with holding an ice pack in an alternating treatment design. Participant was a 7-year-old, nonfluent male with a 6-month history of biting and slapping his hands resulting in significant calluses and swelling. Participant has significant word retrieval difficulties and uses pictures combined with words to communicate. To facilitate subsequent spontaneous requesting, introduction of the ice pack was paired with the word ‘ice’ and presentation of a small picture.
Results: Baseline data indicated rates of biting and slapping averaged 6 times and 40 times in a 5 minute interval, respectively. Rates of biting and slapping during intervals of nonverbal redirection and praise decreased by 67% and 94%, respectively. Incidents of biting and slapping were completely eliminated during intervals with an ice pack. Incidents of screeching and high pitched screaming were also eliminated during presentation of an ice pack (baseline rate=2.1 during 5 minute interval). Rates of self-injury when ice is available continue to remain low or non-existent 3 months following initial treatment. Participant occasionally requests ice spontaneously.
Conclusion: Ice packs could be used to reduce or eliminate self-injury in other persons.

PS5.12
ANALYSIS OF THE PUTATIVE NEUROPSYCHOLOGICAL AND DEVELOPMENTAL DISTINCTION BETWEEN ASPERGER SYNDROME AND HIGH FUNCTIONING AUTISM
Jacqueline Beckett, Kathy DeOrnellas, Texas Woman’s University
Background: The current system of distinguishing between autism subtypes lacks empirical support and may obscure actual intra-group differences within the autism spectrum.
Methods: Children with high functioning autism (HFA), Asperger syndrome (AS), and pervasive developmental disorder (PDD) were assessed by a research team from Texas Woman’s University. Cluster analysis was
employed to determine how such children group by nonverbal IQ, language functioning (including verbal IQ), visual motor ability, and executive function. Analysis of variance and discriminant function analysis were conducted on neuropsychological and developmental variables by diagnostic and cluster designations. Neuropsychological and developmental data were collected via individually administered batteries of standardized tests and a structured developmental history questionnaire.

Results: Preliminary results include data from 45 child volunteers (39 boys and 6 girls) ranging in age from 8 years, 0 months to 17 years, 9 months, with a mean age of 11 years, 6 months. All children met study inclusion criteria of having a full scale IQ of 85 or above and a previous diagnosis of AS, HFA, or PDD. In addition, all participants met screening criteria provided by a questionnaire modeled after the DSM-IV-TR (APA, 2000). No significant group differences were found between AS and HFA on measures of neuropsychological functioning or developmental language acquisition. Cluster analysis revealed distinct neuropsychological profiles within the sample population, which arose independent of participant diagnosis.

Conclusion: The preliminary results of this study do not support the current system of distinguishing autism subtypes. However, these data suggest the presence of distinct neuropsychological profile patterns within the autism spectrum, which may provide a more nosologically sound and treatment-directed approach to diagnosis.

PS5.13
REPETITIVE BEHAVIORS AND EXECUTIVE FUNCTIONS IN AUTISM SPECTRUM DISORDERS
Anne Della Rosa, David Black, Lisa Gilotty, Greg Wallace, Amy Schropp, Philip Lee, Lauren Kenworthy, Center for Autism Spectrum Disorders, Children’s National Medical Center, Washington, DC

Background: Diagnosis of an autism spectrum disorder (ASD) requires presence of repetitive/rigid behavior, or circumscribed interests. Executive dysfunction is a common finding in ASD. Components of executive dysfunction, like inflexibility, disinhibition, poor divided attention and weak generativity could all drive repetitive behaviors in autism.

Objective: To identify a relationship between specific executive dysfunctions and the repetitive behaviors in ASD.

Methods: 25 high functioning children with ASD, consecutively seen in an autism clinic, were administered a comprehensive neuropsychological battery as well as diagnostic measures (Autism Diagnostic Observation Schedule-General (ADOS-G); Autism Diagnostic Interview (ADI-R)). We looked for correlations between scores on tests of divided attention, inhibition, flexibility and generativity and the Repetitive/Stereotypic behaviors domains of the ADI and ADOS.

Results: We found: 1-No significant correlations between the global ADI and ADOS Repetitive/Stereotypic behaviors domains and the executive measures, 2-Negative correlations between the following: sensory interests (from the ADOS and ADI) and divided attention; and repetitive use of objects (ADI) and flexibility, 3-A positive correlation between attention to visual detail and circumscribed interests/repetitive use of objects (ADOS). Conclusions: Specific repetitive behaviors diagnostic of autism are related to specific strengths and weaknesses in executive functions.

PS5.14
SLEEP AND PERFORMANCE IN AUTISM Élyse Limoges, Christianne Bolduc, Laurent Mottron, Roger Godbout, Centre de recherche Fernand-Seguin & Neurodevelopmental Disorders Program, Hôpital Rivière-des-Prairies, and Dept. Psychiatry, Université de Montréal

Introduction: Studies relating sleep quality to attention and memory abound. We verified if sleep disorders known to exist in Autism Spectrum Disorders (ASD) can be associated to daytime cognitive performance using non-verbal tasks.

Methods: 17 young adults with ASD and normal intelligence (16M, 1F, 21.7±3.5 years), and 14 typically developed matched controls (13M, 1F, 21.8±4.1 years) were recorded in a sleep laboratory and tested in the morning of the second night. Results are reported for sustained (visual choice reaction time) and selective (visual search) attention, and four types of memory: working (Corsi block tapping), declarative (figure learning), sensory-motor procedural (Pursuit rotor) and cognitive procedural (Tower of London).

Results: Compared to controls, participants with ASD had a longer sleep latency, more light sleep, less deep slow-wave sleep (SWS), less EEG sleep spindles ans less eye movements during REM sleep. In the morning, participants with ASD differed from controls on response speed (longer reaction time and execution time) but not on accuracy (number of errors). Signs of poor sleep in ASD were significantly correlated with either normal performance (selective attention and declarative memory) or performance inferior to that of controls (sensory-motor and cognitive procedural memories).

Conclusions: Poor sleep in adults with ASD is correlated with slower performance on non verbal tasks. Since a significant statistical correlation cannot be translated into a causal relationship, it still needs to be determined whether the atypical performance is associated with autism itself, or with poor sleep, or both. Supported by CIHR

PS5.15
TOP-DOWN MODULATION IN AUTISM SPECTRUM DISORDERS: THE INFLUENCE OF PRIOR KNOWLEDGE ON ATTENTION AND MEMORY
Eva Loth, Francesca G.E. Happé, MRC SGDP Centre, Institute of Psychiatry, King’s College London

Background: The notion of top-down modulation refers to the influence of prior knowledge and expectation on
attention, perception, and memory. Abnormalities in top-down modulation in ASD have recently been suggested at the cognitive and neuro-functional levels.

Objective: To investigate the role of prior knowledge on attention and memory of scenes and stories.

Method: 28 norm-IQ adolescents with a clinical diagnosis of Asperger Syndrome (8-15 years) and 25 typically developing (TD) boys participated in this study. Experiment 1 tested the role of perspective on scene recall. Participants read short stories manipulating perspective and were then asked to inspect pictures containing items that were relevant or irrelevant to the context. Experiment 2 tested the role of script knowledge on story recall. Stories contained canonical activities related to the event, specific details, disruptions, and irrelevancies. Severity of autistic symptoms was assessed using the CAST.

Results: In Experiment 1, the TD boys recalled significantly more context relevant than irrelevant items, while there was no difference between item-types in the AS group. In the AS group, difference scores were negatively related to level of autistic symptoms. We will also present preliminary eye-tracking data to delineate whether differences relate to attention or memory. In Experiment 2, the boys with AS retained significantly more details than the controls and relative to recall of canonical activities.

Conclusions: These findings suggest that cognitive processes appear to be less influenced by prior knowledge in ASD. Implications for abnormalities in social understanding and neuro-functional research will be discussed.

Funding: ESRC

PS5.16

PREFRONTAL-LIMBIC DYSFUNCTION AND SOCIAL-EMOTIONAL PERFORMANCE IN CHILDREN AND ADOLESCENTS WITH AUTISM.

Katherine Anne Loveland, Jocelyne Bachevalier, Deborah A Pearson, David M Lane, Stacy Reddoch, University of Texas Medical School, Houston

Performance of children and adolescents VIQ > 45 (Autism n=76; Controls n=58) on four neuropsychological tasks: Spatial Delayed Alternation (SDA); Spatial Span; Facial Emotion and Facial Identity Recognition - Delayed Non-match to Sample (FE, FI-DNMS); and Object Discrimination Reversal (ODR) was compared with their performance on laboratory tasks of social-emotional skills including Joint Attention (JA); Intermodal Perception of Affect (IPA); and Social Cognition (ToM). Previous findings showed that subjects differed significantly by group on the neuropsychological tasks. Verbal IQ was controlled in all comparisons. JA tasks were significantly predicted by DNMS facial expression and facial identity, Spatial Span, and SDA but not ODR. IPA percent looking to the matching side was significantly predicted by FI- and FE-DNMS and approached significance with Spatial Span. ToM was significantly predicted by FI-DNMS and by SDA. Results suggest that for both groups joint attention and ToM were related to both frontal and medial temporal tasks, while intermodal emotion matching was related primarily to medial temporal tasks.

Sponsor: NICHD

PS5.17

NEUROPSYCHOLOGICAL DIFFERENTIATION BETWEEN CHILDREN DIAGNOSED PERVERSIVE DEVELOPMENTAL DISORDER- NOT OTHERWISE SPECIFIED AND HIGH FUNCTIONING AUTISM Sara M McCracken, Greg L Wallace, Anne Della Rosa, Amy Schropp, Ilana Levy, Lisa Gilotty, Lauren Kenworthy, Center for Autism Spectrum Disorders, Children’s National Medical Center, Washington DC

Background: Autism spectrum disorders present along a wide spectrum cognitively and behaviorally. Neuropsychological profiles may be used to examine subgroups within this spectrum.

Objective: Compare neuropsychological profiles and diagnostic variables between children diagnosed Pervasive Developmental Disorder, Not Otherwise Specified (PDD-NOS) and children diagnosed High Functioning Autism (HFA).

Methods: 27 children with PDD-NOS and 23 children with HFA, consecutively seen in an autism clinic, were administered a comprehensive neuropsychological battery as well as diagnostic measures (Autism Diagnostic Observation Schedule-General (ADOS-G); Autism Diagnostic Interview (ADI-R)). Diagnosis was assigned based on ADI-R, ADOS-G and DSM-IV-TR diagnostic criteria. Scores were compared between groups matched on age, gender and IQ. Children diagnosed with Asperger’s were excluded from this study.

Results: No statistical difference was found between groups on a broad range of neuropsychological measures tapping into the following domains: general intelligence, executive functioning, learning and memory, motor functioning and visual motor integration. There were significant differences in the language domain, with the PDD-NOS group scoring significantly better on the Vineland communication scale and a sentence repetition task. No statistical difference was found between groups on ADI-R scores, but children with HFA showed greater symptomatic expression as measured by the ADOS-G (Communication, Qualitative Impairments in Reciprocal Social Interaction, and Stereotyped Behaviors and Restricted Interests).

Conclusion: Among striking cognitive similarities, language abilities appear to be an area of difference between children with HFA and PDD-NOS. It is also interesting that historical diagnostic data collected by ADI-R did not differentiate these diagnostic groups, however, current observations collected by ADOS-G did.

PS5.18

COMPARING AND CONTRASTING EXECUTIVE FUNCTIONING IN CHILDREN WITH ADHD AND AUTISM Sara Rice Powers, Wynn Walker, Blythe A. Corbett, U.C. Davis, The M.I.N.D. Institute
Attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) have both been associated with deficits in executive functioning. Nevertheless, some distinctions have been observed between these diagnostic groups.

Objective: The objective of this study was to identify patterns of similarities and differences in executive function among ADHD and ASD groups.

Design/Methods: This investigation included three groups of 46 children; a control group (N=17), an ADHD group (N=16), and an ASD (N=13) group. Subjects were between six and 12 years of age and balanced for both age and gender. Children in the ASD group met DSM-IV (APA 1994) and Autism Diagnostic Observation Schedule - Generic (ADOS-G) criteria. ADHD subjects met DSM-IV criteria. Executive function was assessed using various neuropsychological measures including the Delis Kaplan Executive Function System (DKEFS).

Results: Patterns of executive function were examined between ASD, ADHD, and control groups. In general, the ASD group demonstrated greater deficits in speeded naming, inhibition, and switching than control and ADHD groups (f = 8.48, p < .005; f = 6.75, p < .005; f = 5.94, p < .005). ADHD and control groups did not differ. Measures of word and category fluency revealed no significant differences between groups.

Conclusions: Although there is report of significant overlap of executive impairment in ADHD and ASD, these findings indicate that executive functioning is more globally affected in ASD than ADHD populations, revealing patterns of functioning that can distinguish these groups. Specific profiles across executive measures will be presented.

Funded by the Debber Family Foundation.*

**PS5.19**

**AUTISM SPECTRUM DISORDERS AND NON-VERBAL LEARNING DISABILITY: SIMILAR, OVERLAPPING OR COMORBID CONDITIONS?**

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Background: Non-verbal learning disabilities (NLD) and autism spectrum disorders (ASD) (especially high-functioning autism (HFA) and Asperger's syndrome (AS)) are not mutually exclusive diagnoses since they belong to different nosologies. However, dual diagnoses are rare.

Objectives: To compare neuropsychological and behavioral profiles of children with a clinical diagnosis of NLD, HFA or AS.

Methods: A series of 3 studies were conducted in which more than 100 children with NLD, AS or HFA participated, as well as a normal control group (NC). Children were compared on a battery of neuropsychological tests that measure specific skills and deficits of the NLD-profile, on CBCL and on ASD symptomatology.

Results: The neuropsychological profile of the three clinical groups was comparable. Differences between HFA and AS were only found for a few variables. CBCL-profiles of the clinical groups were also similar. About one third of the children with NLD could be classified as having ASD.

Conclusions: A neuropsychological NLD profile is characteristic for most children with ASD. The results provide no arguments for a distinction between AS and HFA. On the other hand, a large subgroup of children with NLD appears to have ASD. A double diagnosis of ASD and NLD (we prefer the term visuo-spatial learning disability) is often indicated.

Sponsor: Ghent University Research Fund

**PS5.20**

**EXECUTIVE DYSFUNCTION IN CHILDREN WITH ASPERGER SYNDROME**

Valorie N Salimpoor, Mary E Desrocher, James Bebko, York University

Background: Executive function is an umbrella term for a group of high-order interrelated cognitive processes that are mediated by the prefrontal cortex, in the frontal lobes of the brain. These functions are responsible for planning ahead and carrying through organized goal-directed behavior, while continuously monitoring performance. While previous studies have demonstrated executive dysfunction in individuals with autism, to various extents; little research has been conducted with executive function in individuals with Asperger Syndrome (AS).

Objectives: The aim of this study was to assess executive function abilities in children with AS, though a battery of neuropsychological tests and questionnaires.

Methods: Participants included 14 children with AS and 14 age and gender matched control participants, between the ages of 7-18. An estimate of verbal and non-verbal intelligence was used as a covariate to ensure that differences in test performance were not due to IQ differences.

Results and Conclusion: Although there were no differences in IQ scores between the two groups, children with AS demonstrated significantly lower scores on several tasks of planning, initiation, inhibition, shifting, and working memory. Furthermore, children with AS displayed significant executive dysfunction on parent questionnaires that assessed executive function in everyday behavior. However, as compared with the control group children with AS did not show deficits on tasks that measured inhibition and nonverbal working memory. These results have important implications for the development of remediation programs.

This research was funded by a student grant from the Autism Society of Ontario.

**PS5.21**

**AN EXAMINATION OF THE RELATIONSHIP BETWEEN ATTENTIONAL LOAD AND SOCIAL FUNCTIONING IN CHILDREN AND ADOLESCENTS WITH AUTISM**

Amy B. Schropp, Joette James, Philip Lee, Lisa Gilotty, Greg Wallace, David Black, Lauren Kenworthy, Anne Della Rosa, Children's National Medical Center

OBJECTIVE: Children with Autism display attentional deficits, which may contribute to the impairments in social
functioning characteristic of the disorder. We hypothesized a relationship between attention weaknesses in the auditory modality and social functioning as measured by child behavior and parent report, and that this relationship would be stronger when attentional load was greater.

PARTICIPANTS AND METHODS: Participants were 20 children and adolescents with a diagnosis of Autism Spectrum Disorder age 6 to 15 years. The Score and Score DT (Dual Task) subtests from the Test of Everyday Attention in Children (TEA-Ch) were used as measures of sustained auditory attention and divided auditory attention, respectively. The Reciprocal Social Interaction summary scores of the Autism Diagnostic Observation Schedule (ADOS-G) and the Autism Diagnostic Inventory-Revised (ADI-R) were used as measures of social functioning.

RESULTS: The two attentional measures were not significantly correlated with one another (r = .181, p = .445). No significant correlations were obtained between performance on the Score task and either measure of social functioning (ADOS-G, r = -.048, p = .844; ADI-R, r = -.169). However, consistent with expectations, when the attentional load was greater (Score DT) a significant correlation was obtained between the Reciprocal Social Interaction score of the ADOS-G (r = -.516, p = .024), but not the ADI-R (r = -.026, p = .914).

CONCLUSION: These results suggest that these two attentional tasks are measuring two separate abilities with this sample. Furthermore, the ability to divide one’s attention within the auditory modality impacts social functioning.

**PS5.22**

**FIXATION BEHAVIOR IN CHILDREN AND ADOLESCENTS WITH AUTISM: PASSIVE VS. ACTIVE VIEWING OF FACIAL STIMULI**

Leigh Sepeta, Mirella Dapretto, Mari Davies, Marian Sigman, University of California, Los Angeles

This study aims to show that children and adolescents with Autism Spectrum Disorders (ASD), aged 8 to 19, show more typical processing patterns for faces when they need to use the facial information for a purpose and are actively involved in viewing facial stimuli, while their natural inclination when passively viewing faces may be to display a less typical processing pattern. In order to investigate this hypothesis, a group of high-functioning individuals with ASD (n=19) was compared to a typically developing group (n=14) using photographs of faces in two different conditions. In the passive, Observation condition the participants were instructed simply to observe the faces, while in the active, Imitation, condition the participants saw the same faces and were instructed to imitate the emotional expression displayed. Using an infrared eye-tracking device, fixation times for six areas of interest on each face, including the eye, mouth, and nose regions, were compared between the two groups. The results have indicated that overall individuals with ASD show mostly typical facial processing behavior, with the exception that they focus more on the mouth region, F(1, 31) = 6.68, p < .05. However, within the ASD group, the trend shows that they tend to focus more on the eye region as they move from passively viewing the face to a more active viewing condition. These results are preliminary, but lend support for the original hypothesis that individuals with autism may use more typical facial processing strategies under certain conditions.

This research was supported by Program Project Grant HD-DCD3547.

**PS5.23**

**WORKING MEMORY PROBLEMS IN CHILDREN WITH HIGH-FUNCTIONING AUTISM AND CHILDREN WITH ADHD**

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Background: Most studies of children with autism or attention deficit hyperactivity disorder (ADHD) investigated working memory as a unitary construct. A comprehensive investigation measuring all working memory domain-specific subcomponents is needed.

Objectives: Investigate whether: (a) maintenance of auditory-verbal information; (b) manipulation of auditory-verbal information; (c) maintenance of visual-spatial information; and (d) manipulation of visual-spatial information, are impaired in children with high-functioning autism (HFA) and ADHD, compared to normal control children.

Methods: A three-stage selection procedure was used. The Working Memory Test Battery for Children (Pickering & Gathercole, 2001) and two subtests of the Amsterdam Neuropsychological Tasks (De Sonneville, 2001) were used to measure the four working memory subcomponents.

Results: Data were collected for 48 children with HFA, 45 children with ADHD and 40 normal control children between 8 and 16 years with an IQ > 80. The groups were matched on intelligence, chronological age, and gender. Significant differences between the groups were only found for a few variables. The expected double dissociation between HFA and ADHD (i.e., HFA more impaired for auditory-verbal tasks, while ADHD more impaired for visual-spatial tasks) was not clearly found. Especially, the HFA group showed many inter-individual differences.

Conclusions: Results provide some arguments for a distinction between HFA and ADHD, but less than expected.

Sponsor: Ghent University Research Fund

**PS5.24**

**ASPECTS OF EXECUTIVE FUNCTION IN HIGH FUNCTIONING AUTISM**

Hans Bogte, Bert Flamma, Jaapvan Der Mere, Adhesie, Deventer, The Netherlands

Aim of the study

Some researchers take the view, that a deficit in executive functioning (EF) may underlie the social deficit in autistic individuals. We investigated aspects of the broad concept of EF.
Task
Traditional neuropsychological tasks only provide crude comparisons of functional deficits. Also, social interaction may confound performance. In the current study a computerised variant of the Sternberg reaction time paradigm was used.

Subjects
Thirty six adults with High Functioning Autism (HFA) participated in this study: individuals dependent of residential care (inpatients; n=24), and individuals living independently (outpatients; n=12). Twelve of the inpatients were on psychoactive medication. On average the inpatients scored much higher than the outpatients on the ADOS subscale Qualitative impairments in Reciprocal Social Interaction. The control group consisted of twenty five individuals.

Results
Divided attention
Only inpatients on medication showed a divided attention deficit. Consequently, the current study failed to provide a relationship between divided attention and autism.

Cognitive Flexibility
Contrary to the results of many earlier studies, no evidence was found that HFA is associated with problems concerning pre-setting, set-shifting, planning or response-inhibition.

Error Detection
After making an error, normal adults slow down their responding on the next trial, a compensatory mechanism geared toward improving performance. Error detection and correction appears to be affected in HFA.

Conclusion
The current study concerning several aspects of EF in HFA only showed limited error detection and correction in participants with HFA.

PS5.25
USE OF A COMPARATIVE NEUROPSYCHOLOGICAL STRATEGY TO ASSESS COGNITIVE ABILITIES OF AUTISTIC SPECTRUM DISORDER SUBJECTS: ASSOCIATIVE LEARNING AND REVERSAL
Christina de Rivera, Sherri Thiele, Danielle Pigon, Joseph A. Araujo, Isabelle Boutet, Sohail Khattak, Norton William Milgram, University of Toronto at Scarborough and CanCog Technologies Inc.

Background: Comparative neuropsychological tests are tests originally developed to assess cognitive function in animals, but adapted for use with humans. Because the tasks are non-verbal and often non-instructional, they should be useful in language-impaired populations.

Objectives: To develop a test protocol that could be used in both classification and intervention assessment of ASD subjects. The results described are specifically aimed at evaluating comparative neuropsychological tests of discrimination and reversal learning, which involve associative learning and executive function.

Methods: Autistic and age-matched controls, between 5 and 13 years old, participated in 1) an object discrimination (ODL) and reversal (ODR) task, and 2) a feature discrimination (FDL) and reversal learning (FDR) task. The discrimination tasks required that subjects learn to associate one object, or a facial expression, with a reward. The reward contingencies were switched in the reversal tasks. Timing and randomization were standardized between subjects with the use of dedicated software, which also allowed for the tracking of response latencies.

Results: ASD subjects performed better than controls on the ODL task, and more poorly on the FDL task, but these were not statistically significant. There were no significant differences between low and high functioning ASD children. Control subjects, however, responded significantly faster than ASD subjects on the ODL (p = 0.02), ODR (p = 0.009), FDL (p = 0.01), and FDR (p = 0.0001). Also, verbal ASD subjects performed significantly faster in FDL compared with non-verbal subjects (p = 0.03).

Conclusions: Comparative neuropsychological assessment protocols can be used for cognitive assessment of low functioning ASD subjects. Associative learning and simple executive function capabilities are not impaired in ASD, but ASD subjects show significantly slower response latencies, possibly reflecting attentional deficits.

Sponsor: CAN

PS5.26
PLAY BEHAVIORS PREDICT LANGUAGE OUTCOMES IN YOUNG CHILDREN WITH AUTISM SPECTRUM DISORDER
Stephany Cox, Marian Sigman, UCLA

Background: Previous studies have shown a relationship between play and language in children with autism, but these findings have not been consistent.

Objectives: Further specify the relationship between functional and symbolic play behaviors and receptive and expressive language levels in children with autism.

Methods: Twenty-five children with autism spectrum disorders (mean CA = 45.9 months) participated in a larger longitudinal study examining several areas of development; clinical diagnoses were confirmed using the ADOS and the ADI-R. A structured play assessment was administered at the initial visit, and coded for the total number of different spontaneous functional and symbolic play acts produced by the child. Using the Mullen Early Scales of Learning, expressive and receptive language levels were obtained at the first visit and again at a one-year follow-up visit.

Results: Functional play acts (r = .36, p < .05) and symbolic play acts (r = .42, p < .05) predicted receptive language levels at the follow-up visit, after controlling for initial receptive language level. However, significant correlations were not found between play acts and expressive language level.

Conclusion: Findings suggest that early symbolic and functional play acts predict later receptive language, but not expressive language, in children with autism.

Sponsor: NIMH
PS5.27
COMPREHENSION AND PRODUCTION OF LINGUISTIC AND AFFECTIVE PROSODY IN CHILDREN WITH AUTISM Danielle E Delosh, Ruth B Grossman, Rhynnion H Bemis, Christine Connolly, Karen Condouris, Daniela Plesa-Skwerer, Helen Tager-Flusberg, Boston University School of Medicine
Objective: To investigate the comprehension of affective prosody, and comprehension and production of linguistic prosody in autistic and TD children.
Methods: We gave 19 autistic and 18 age and NVIQ matched TD children (7.5-18 years): Receptive and Production Lexical Ambiguity (LAr & LAP) and Filtered Speech (FS). LAr involved auditory presentation of two syllable constructs with stress placed on the first (T1=compound word), on second syllable (T2=two-word phrase) (“HOTdog,” “hot DOG”) in a match-to-picture task. LAP asked children to produce the appropriate stress pattern for the same constructs in the context of a sentence. The FS task used pre-recorded sentences (happy, neutral, sad) that were acoustically filtered to remove lexical content while maintaining affective prosody. Children were asked to label the speakers emotion for the filtered and then the unfiltered sentences.
Results: We found no group differences in the LAr and FS tasks. The AUT group was significantly worse at linguistic stress production than the TD group (U= 98.5, p=0.026).
Conclusions: Children with autism successfully used linguistic and affective prosody to disambiguate words and to determine the emotional state of a speaker, while showing a clear deficit in linguistic prosody production.
Funding: This research was funded by NIDCD (U19 DC03610; H. Tager-Flusberg, PI) and conducted as part of the NICHD/NIDCD Collaborative Programs of Excellence in Autism, and by grant M01-RR00533 from the General Clinical Research Ctr. program of the National Center for Research Resources, National Institutes of Health.

PS5.28
ATYPICAL LEXICAL PROCESSING IN HIGH-FUNCTIONING AUTISM SPECTRUM DISORDER WITHOUT SPEECH DELAY Yoko Kamio, Diana Robins, Naoko Inada, Elizabeth Kelly, Brook Swainson, Deborah Fein, Kyushu University
Background: Although individuals with high-functioning autism spectrum disorder (HFASD) have been reported to be different in how they process language, the dependence of lexical processing on perceptual components has not been clarified.
Objectives: The present study examined automatic semantic and phonological processing in different ASD groups in comparison with typically developing (TD) individuals.
Methods: In Experiment 1, U.S. participants (AS (Asperger’s disorder and PDDNOS) n=11; TD n=11) performed a semantic decision task using an indirect priming paradigm. In Experiment 2, Japanese children and adolescents (AS n=11; HFA n=11; TD n=11) performed a similar task.
Results: Experiment 1: The TD group demonstrated only semantic priming effects, whereas there were neither semantic or phonological priming effects in the ASD participants without speech delay. Experiment 2: There were no significant differences in semantic priming effects among groups, whereas phonological priming effects differed by group, that is, greater in the HFA group than in the TD group (with no significant differences between the AS and HFA groups).
Conclusions: The findings of this study support atypical features of lexical processing, that is, enhanced phonological processing over semantic processing in ASD, which may be present regardless of the presence of speech delay.
Sponsor: RISTEX (Research Institute of Science and Technology for Society)

PS5.30
LANGUAGE ASSESSMENT AND DEVELOPMENT IN TODDLERS WITH AUTISM SPECTRUM DISORDERS Rhiannon J Layster, Mary Beth Kadlec, Anneliese Bass, Amy Gower, Christine Connolly, Alice Carter, Helen Tager-Flusberg, University of Michigan Autism and Communication Disorders Center
Background: Questions remain about the validity of language assessment and the predictors of concurrent language in young children with ASD.
Objectives: Compare three measures of early language and explore possible predictors of receptive and expressive language.
Methods: Participants are from an ongoing study on early development in children with ASD. Data include assessments of a number of the potential predictors of concurrent language (e.g., joint attention, imitation, gesture use, and play), as well as three measures of language that are appropriate for early language learners.
Results: Data were collected on 98 children with ASD (mean age=27.86 months). Analyses indicated good agreement between receptive and expressive language scores on the Mullen, MacArthur CDI and Vineland. Receptive and expressive language composites were created from the three language measures and hierarchical regressions were conducted to explore predictors of receptive and expressive language. Predictors of receptive language included gestures and response to joint attention. Predictors of expressive language included gestures and play.
Conclusion: Findings of this study indicate good agreement across parent report and direct observation of early language and suggest that both receptive and expressive language are primarily predicted by early gesture use.
PS5.31
THE ROLE OF POINTING AND VOCABULARY DEVELOPMENT IN YOUNG CHILDREN WITH AUTISM, DEVELOPMENTAL DELAY AND TYPICAL DEVELOPMENT
Ann M. Mastergeorge, Gregory S. Young, Sally J. Ozonoff, Sally J. Rogers, UC Davis/MIND Institute

Study Objectives: This study examines group differences in the use of pointing as a predictor of expressive language skills in children with autism, developmental delay (DD), and typical development.

Methods: Seventy children with autism, DD, and typically developing children were matched on nonverbal and verbal mental age as measured by the Mullen Scales of Early Learning. Children were administered the Early Social Communication Scales (ESCS) and the MacArthur Communicative Development Inventory. Based on a factor analysis for 9 nonverbal gesture behaviors in the ESCS, a pointing factor score was calculated consisting of 4 types of pointing behaviors: pointing with no eye contact (initiates behavior regulation), pointing with eye contact (initiates behavior regulation), pointing with no eye contact (initiates joint attention) and pointing with eye contact (initiates joint attention).

Results: Using vocabulary production as a dependent variable, a multiple regression analysis revealed a main effect for group, a main effect for pointing, and a group by gesture interaction effect. Further analyses indicated a significant negative correlation between pointing and vocabulary production only for typically developing children, and a significant positive correlation for children with autism.

Conclusions: Pointing appears to play a significant role in expressive language skill development in typical development. In the typical group, as vocabulary increases, pointing decreases. The opposite is true for children with autism; they do not point to augment nonverbal or verbal communicative interactions. Findings suggest important implications for development and intervention.

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PS5.32
ATYPICAL EXPRESSIVE PROSODY IN CHILDREN WITH HIGH-FUNCTIONING AUTISM AND ASPERGER’S SYNDROME: LISTENER PERCEPTIONS AND COMMUNICATIVE EFFECTIVENESS
Sue Peppe, Lianne Carroll, Robin Lickley, Pastora Martinez Castilla, Joanne McCann, Ineke Mennen, Anne O‘Hare, Marion Rutherford, Queen Margaret University College

Background: Verbal children with autism spectrum disorders frequently display atypical expressive prosody, and the question arises as to whether this affects communicative functionality.

Objectives: Discover if, in children with and without high-functioning autism (HFA)/Asperger’s syndrome (AS), judgments of atypicality of expressive prosody correlate with the ability to use prosody to make communicative distinctions.

Method: Participants were children aged 5-14: 25 with typical development (TD), 29 with HFA and 29 with AS, diagnosed using DSM-IV and ICD-10. They completed four tasks that elicited utterances in which prosody alone conveyed the meaning, and two imitation tasks. Samples of conversation from each child were rated for atypicality by two groups of judges, one phonetically aware and the other naïve, both blind to diagnosis, using magnitude estimation.

Results: In the tasks, there were significant differences (p<.01): HFA<.001 for one group, r=.612, p=.015 for the other. ANOVAs showed between-group differences similar to those found in the task results. The ratings correlated significantly (p<.01) with the task scores.

Conclusion: Correlations suggest that communicative effectiveness is reduced in children with atypical expressive prosody. Furthermore, both task results and perceptions of atypicality suggest that prosodic ability is reduced in HFA but not in AS, making it possible that prosodic deficit could be a marker to distinguish between these two types of autism spectrum disorder. Findings also support the ecological validity of the tasks for use as a clinical assessment tool.

PS5.33
PRAGMATIC LANGUAGE FUNCTIONING IN AUTISM AND WILLIAMS SYNDROME
Amy D Philofsky, Susan L Hepburn, Deborah J Fidler, Sally J Rogers, University of Colorado health Sciences Center Department of Psychiatry, University of Colorado health Sciences Center, Denver, CO, 80262

Background: While pragmatic language impairments have been documented separately in autism and Williams syndrome, the two syndromes have not been directly compared previously on this dimension (Bishop, 1998; Laws & Bishop, 2004; Young, Diehl, Morris, Hyman, & Bennetto, 2005). Comparison of autism and Williams syndrome is important for understanding how atypical social profiles impact upon pragmatic language development.

Objectives: Thus, the purpose of this study is to compare and describe the pragmatic language profiles of children with an autism spectrum disorder and Williams syndrome. Methods: 20 school-aged children with Williams syndrome will be compared with 20 school-aged children with an autism spectrum disorder on a standardized parent-report measure for pragmatic language, the Children’s Communication Checklist-2 (Bishop, 2003).

Results: Preliminary data analysis including 15 children with Williams syndrome (mean CA=9 years, 6 months) and 17 children with an autism spectrum disorder (mean CA=9 years, 8 months) suggest that both groups of children demonstrate pragmatic language impairment and that there are no group differences on this variable t (2, 30) = .858, ns. Further analysis will be conducted to elucidate a specific profile of strengths and weaknesses.
representative of each syndrome. Additionally, pragmatic language impairment was moderately associated with the Socialization domain of the Vineland Adaptive Behavior Scales r (30) = .368, p < .05. Relationships within each group will also be explored.

Conclusions: Atypical social development results in pragmatics language impairment in two disorders of social development. Implications for assessment and treatment of pragmatic language in these populations will be discussed.

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**PS5.34**

**THE EFFECTS OF THERAPIST LANGUAGE USE ON CHILD PERFORMANCE DURING BEHAVIORAL LANGUAGE TRAINING**

*Debra Rausch, Jessica Suhrheinrich, Rebecca Gutierrez, Laura Schreibman, University of California, San Diego*

Background: The effectiveness of applied behavior analysis in the treatment of autism has been well supported by research. However, there is a need for research examining specific strategies within existing behavioral interventions. This study investigates the effects of therapist verbalizations on language production of young children with autism.

Objective: To investigate how the quantity and type of therapist verbalizations affects child language production during behavioral intervention sessions.

Method: Participants were recruited from local San Diego Regional Centers and communities. Participants had an independent diagnosis of autism and were between the age of 2 and 3 at intake. Comprehensive assessments (diagnostic, language, joint attention, cognitive, imitation, motor skills) were conducted pre-, post-, and 3 month follow-up.

Results: Six children with a diagnosis of autism, ranging in ages from 2 to 3, received 185 hours of a naturalistic behavioral intervention (Pivotal Response Training). Random 10-minute samples were videotaped and coded for type and complexity of therapist and child language. Scoring definitions for therapist verbalizations included reinforcement, commenting, gaining attention, and prompting. Child verbalizations were coded for length of requests, comments, and verbal self-stimulation.

Conclusions: Preliminary analysis indicates that children perform differentially based on type and complexity of therapist language. Results will be presented and implications for more effective language training procedures will be discussed.

**PS5.35**

**PREDICTORS OF SCHOOL-AGE LANGUAGE OUTCOME IN ASD**

*Michael Aaron Rosenthal, Michael C Stevens, Elizabeth A Kelley, Michelle Dunn, Isabelle Rapin, Deborah A Fein, University of Connecticut*

Little is known about the early predictors of language development in children with autism. The aim of this study is to examine the impact that autism symptoms, nonverbal cognitive ability (nonverbal IQ), and language skills at preschool have on the language development of school-age children with autism. The sample consists of 43 children with High-Functioning Autism (HFA) and 78 children with Developmental Language Disorder (DLD), matched for preschool age, non- verbal IQ (NVIQ), age at follow-up, and time between assessments. Groups were examined at pre-school and at school-age with a battery of diagnostic, nonverbal, and language measures. A factor analysis of preschool measures yielded two factors for the DLD group: a cognitive factor, composed of language ability and NVIQ, and a socialization/autism symptoms factor. The HFA group had three factors: a language factor, a socialization/autism symptoms factor, and a NVIQ factor. Linear regressions showed that for the DLD group, preschool verbal and nonverbal cognition, but not socialization, predicted functional language, verbal IQ, receptive language, and expressive language. For the HFA group, verbal and nonverbal cognition, but not socialization/autism symptoms, predicted functional language. Language and socialization/autism symptoms predicted VIQ, but different factors predicted subscales of VIQ; in particular, understanding of absurdities was predicted by socialization/autism symptoms alone. Receptive and expressive vocabulary were predicted only by preschool language scores. Results suggest that for the DLD children, language development is constrained primarily by cognitive rather than social factors. For the HFA children, results confirm previous findings that most language factors were constrained primarily by preschool language, while functional use of language was also affected by nonverbal IQ, and language tests with social judgment were primarily constrained by preschool social development.

**PS5.36**

**THE UNDERSTANDING OF METONYMY AND METAPHOR IN CHILDREN WITH AUTISM**

*Gabriella Rundblad, Dagmara Annaz, Anna Ferdenzi, Department of Education and Professional Studies, King's College London*

Background: Problems with figurative language (especially metaphors) are well-documented for children with autism; nevertheless studies have investigated a select few types of figurative language. Though often confused with metaphor which relies on understanding of similarity as well as contiguity, metonymy (e.g. hand = cards) only requires contiguity; thus we need to explore whether the level of understanding of metonymy is correlated to metaphor problems.

Objectives: Compare the understanding and development of metonymy and metaphor in children diagnosed with autism and typically developing children (TD).

Methods: 16 typically-developing children and 8 children with autism (aged 5 to 11 years) took part in the study. Non-verbal and verbal IQ were obtained for each child. Each child was tested on comprehension of metonyms (10 stories) and metaphors (10 stories) incorporated into short, simple picture-stories.

Results: Preliminary analyses suggest that children in the TD group and autism group performed better on
with autism. This investigation can potentially show which aspects of input predict language gains, possibly shedding light on children’s differential progress with language.

Methods: Two groups of children participated in a longitudinal study: 10 boys with Autism Spectrum Disorder (ASD) and 10 typically developing children (TYP) (four boys). At Visits 1-4 (ASD: 33-45 months old; TYP: 17-29 months old) the mother-child dyads participated in 15 minute free play sessions, which were transcribed and analyzed.

Results: A significant correlation was found between maternal use of Y/N-questions at Visit 2 and the number of auxiliaries in child spontaneous speech eight months later (r=.68, p<.05) for TYP children. Maternal Y/N-questions at Visit 3 predicted the children’s auxiliaries four months later (r=.69, p<.05) for ASD children. Therefore, the TYP and the ASD groups demonstrate this well-documented input-output relationship. Conclusions: These preliminary findings indicate that significant correlations can be obtained with this small sample, and that previous findings with typically developing children can be replicated with this group of children with autism. Additionally this suggests that children with autism are ‘paying attention’ to the input of their mothers.

PS5.39
DEFICIT IN THE DEICTIC USAGE IN CHILDREN AND ADOLESCENTS WITH HIGH-FUNCTIONING AUTISM SPECTRUM DISORDER (HFADS) Yuko Tanaka, Kyushu University

Background: Although, syntactics has been considered to be relatively intact in HFASD, subtle deficits in the interface between syntactics and pragmatics has been pointed out. Objectives: The present study examined the deictic usage in children and adolescents with highly verbal ASD. Methods: 10 individuals with HFASD (mean age=11.5 years; VIQ>90) and 6 typically developing controls (TD) (mean age=14 years; VIQ>90) were presented with three different colored objects and required to answer the color which the experimenter indicated by demonstratives ("What color is [that (A-re) / this (Ko-re) / it (So-re)]? "). The physical distance between objects is crucial to distinguish between KO and A and between SO and A. In KO/SO situation, the subjects have to understand who is the speaker, whose neighborhood is the KO region, and who is the hearer, whose neighborhood is the SO region. Results: There were significant differences in the accuracy between the HFASD group and the TD group (p<.0001), indicated that the HFASD children and adolescents had a remarkable difficulty in the deictic usage of KO-SO-A. In particular, the distinction between Ko and So, which required the concept about the self and the other, was most difficult for individuals with HFASD. Conclusion: These results suggest that the individuals with ASD have difficulty in choosing appropriate demonstratives based on conversational roles.
CHARACTERISTICS OF TODDLERS WITH ASD THAT PREDICT DIFFERENCES IN THE CONTENT OF THEIR RECEP TIVE VOCABULARY. Cornelia Taylor, Paul Yoder, Wendy Stone, M Saylor, Susan Hepburn, Tony Charman, Vanderbilt University

Background: The MCDI-I is a frequently used measure of receptive vocabulary in children with ASD developed for TD infants and some of the items may not be appropriate for toddlers with ASD.

Objectives: Compare toddlers with ASD and TD infants on the probability that parents report that a child understands a word on the MCDI-I controlling for the total words understood.

Methods: The MCDI-I is a 396-item parent report vocabulary checklist used to determine the total number of words a child understands. Archival data on 272 TD infants and 242 toddlers with ASD were used to determine words on the MCDI-I that members of one group usually know that members of the other group rarely know, despite equal total scores, this is called differential item functioning (DIF; Swaminathan & Rogers, 1990). We hypothesized that the content of the vocabulary of toddlers with ASD would be different because of the following characteristics: orienting deficits, social communication deficits, and restricted object use.

Results: Words on which extreme between-group differences occurred because of hypothesized differences in orienting include ‘see,’ ‘watch,’ and ‘child’s own name;’ differences in social communication: ‘daddy,’ ‘mommy;’ differences in restricted object use: ‘train,’ and ‘truck.’

Conclusion: Evidence supports qualitative differences in the words that toddlers with ASD and TD infants understand. Specifically, toddlers with ASD are less likely to understand words that are prompts for orienting, less likely to understand words that are labels for people, and more likely to understand words that represent their restricted interests.

Sponsor: Self-funded.

PS5.41

MORPHOLOGICAL PROCESSING IN AUTISM: EVIDENCE FROM PAST-TENSE PRODUCTION
Matthew Walenski, Stewart H. Mostofsky, Jennifer C. Giddley Larson, Michael T. Ullman, Department of Neuroscience, Georgetown University

Background: Pragmatic language deficits are commonly cited in autism, whereas grammatical and lexical abilities are less frequently studied. English past tense morphology offers a window into these latter two aspects of language. Dual-system models claim distinct neurocognitive underpinnings for grammar and lexicon: regularized past-tenses depend on rule-based grammatical computation (stem + -ed), while irregularized past-tenses depend on memorized word-specific (lexical) knowledge.


Methods: Eleven high-functioning boys with autism (HFA; ages 8-14) and 14 age-matched typically developing boys participated in a past-tense production task, containing regular (n=32; e.g., slip), irregular (n=32; sleep), and novel (n=32; splim) verbs.

Results: HFA subjects did not differ from controls in accuracy (percent correct) for regularized (rule-based: slipped, sleeped, splimmed) or irregularized (memory-based: slept, splam) past-tenses of real or novel verbs. In contrast, response time analyses revealed that HFA subjects were abnormally fast at producing regularized but not irregularized past-tenses relative to controls. This pattern is consistent with a recent study that also reports normal accuracy but faster-than-normal response times in autism for receptive grammatical processing (Just et al., 2004). Preliminary results from analyses examining the representation of lexical forms in memory suggest an apparently greater contribution from visual memory in the HFA subjects relative to controls, a pattern that appears consistent with previous findings (Kamio and Toichi, 2000).

Conclusion: HFA subjects are particularly fast at grammatical computation. Differences in lexical representations in memory may also be indicated.

Sponsors: NIH R01MH58189 (MTU); NIH R01NS048527 (SHM); NAAR (MTU, MW, SHM)

PS5.42

RELATIONS BETWEEN LANGUAGE LEVEL AND AUTISM SEVERITY IN YOUNG CHILDREN Linda R. Watson, Grace T. Baranek, Jane E. Roberts, Fabian J. David, Doanne L. Ward, University of North Carolina at Chapel Hill

Background: Previous research has explored the diagnostic overlap between language disorders and autism. There has been limited attention, however, to the relation between language level and autism symptom severity.

Objective: Examine the concurrent relations between observational and parent report measures of language and autism symptoms in young children with autism.

Methods: Developmental and diagnostic assessments of 23 children (ages 2:4 to 3:6) with autism were completed in conjunction with an ongoing study. Direct observation measures included the Preschool Language Scale-4 (PLS-4), Mullen Scales of Early Learning (MSEL), and Autism Diagnostic Observation Schedules, Module 1 (ADOS). Parent report measures included the MacArthur Communication Development Inventory-Words & Gestures (MCDI) and Autism Diagnostic Interview-Revised (ADI-R).

Results: Language age equivalent scores on the PLS-4 and the MSEL were negatively related to the ADOS communication algorithm scores. Receptive but not expressive language age scores on the PLS-4 and MSEL were also negatively related to the ADI-R algorithm scores for reciprocal social interaction. MCDI raw scores were negatively related to the ADI-R algorithm scores for communication, reciprocal social interaction, and stereotypic and restricted behaviors.

Conclusions: At young ages, there is a relationship between aspects of language development and autism.
SYNTAX (E.G. ‘DO YOU HAVE’ VS. ‘GIVE ME’) WHEN REQUESTING CANDY FROM A PUPPET REPRESENTING A LISTENER OF HIGHER SOCIAL STATUS (AN ‘OLD LADY’), BUT MORE DIRECT SYNTAX AND SEMANTIC AGGRAVATORS (E.G., ‘GIVE IT TO ME RIGHT NOW!’) WHEN REQUESTING CANDY FROM A ‘PEER’.

QUESTIONS: DO HIGH FUNCTIONING CHILDREN WITH AUTISM ADJUST THEIR LANGUAGE BASED ON THE LISTENER’S SOCIAL STATUS? IF SO, ARE THEIR ADJUSTMENTS SIMILAR TO APPROPRIATELY MATCHED CONTROLS?

METHOD: HIGH FUNCTIONING SCHOOL-AGED PARTICIPANTS WITH ASD WERE MATCHED TO GROUPS OF TYPICALLY DEVELOPING CHILDREN WITH AUTISM THE BASIS OF NONVERBAL COGNITIVE ABILITY AND LANGUAGE LEVEL. FIRST, PARTICIPANTS WERE INSTRUCTED TO ASK ‘OLD LADY’ AND ‘PEER’ PUPPETS FOR CANDY. SUBSEQUENTLY, PARTICIPANTS WERE PROMPTED TO ASK ‘NICELY’ AND THEN IN THE ‘NICEST’ WAY POSSIBLE (TO THE ‘OLD LADY’), AND IN A BOSSY WAY AND IN THE ‘BOSSIEST’ WAY POSSIBLE (TO THE ‘PEER’). RESULTS: ACROSS GROUPS, THE FREQUENCY OF SEMANTIC SOFTENERS FOR ‘NICE’ REQUESTS INCREASED WITH PROMPTED (F (2, 83) = 8.012, P < .001), AS DID FREQUENCY OF SEMANTIC AGGRAVATORS FOR ‘BOSSY’ REQUESTS (F (2,83) = 15.171, P < .0001). SYNTACTIC DIRECTIVENESS DID NOT CHANGE SIGNIFICANTLY. NO DIAGNOSTIC GROUP DIFFERENCES WERE FOUND ON ANY OF THE INDICES OF ‘POLITENESS/BOSSINESS’.

DISCUSSION: RESULTS SUGGEST THAT AT LEAST SOME HIGH FUNCTIONING CHILDREN WITH ASD ADJUST THEIR LANGUAGE STYLE IN RESPONSE TO A LISTENER’S SOCIAL STATUS. LIKE THEIR MATCHED CONTROLS, THEY ADJUSTED IN BOTH ‘NICE’ AND ‘BOSSY’ DIRECTIONS AND EXAGGERATED THAT ADJUSTMENT WHEN PROMPTED.

SPONSOR: SOCIAL SCIENCES AND HUMANITIES RESEARCH COUNCIL OF CANADA

PS5.44

VARYING LANGUAGE STYLE BASED ON SOCIAL STATUS Joannec Volden, Autumn Sorenson, University Of Alberta

INTRODUCTION AND RATIONALE: TYPICALLY DEVELOPING CHILDREN ADD SEMANTIC SOFTENERS (E.G., ‘PLEASE’), AND USE INDIRECT SYNTAX (E.G. ‘DO YOU HAVE’ VS. ‘GIVE ME’) WHEN REQUESTING CANDY FROM A PUPPET REPRESENTING A LISTENER OF HIGHER SOCIAL STATUS (AN ‘OLD LADY’), BUT MORE DIRECT SYNTAX AND SEMANTIC AGGRAVATORS (E.G., ‘GIVE IT TO ME RIGHT NOW!’) WHEN REQUESTING CANDY FROM A ‘PEER’.

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DISCUSSION: RESULTS SUGGEST THAT AT LEAST SOME HIGH FUNCTIONING CHILDREN WITH ASD ADJUST THEIR LANGUAGE STYLE IN RESPONSE TO A LISTENER’S SOCIAL STATUS. LIKE THEIR MATCHED CONTROLS, THEY ADJUSTED IN BOTH ‘NICE’ AND ‘BOSSY’ DIRECTIONS AND EXAGGERATED THAT ADJUSTMENT WHEN PROMPTED.

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PS5.45

OBSERVING THE SOCIAL COMMUNICATION OF CHILDREN WITH AUTISM IN THE CLASSROOM: THE IMPORTANCE OF CONTEXT Greg Pasco, Kate Gordon, Pat Howlin, Tony Charman, St. George’s, University Of London

BACKGROUND: THE INTENTIONAL COMMUNICATION OF NONVERBAL CHILDREN WITH AUTISM WAS OBSERVED AS PART OF THE EFFECTIVENESS OF PECS RCT (HOWLIN ET AL, UNDER REVIEW)

OBJECTIVE: TO INVESTIGATE THE EFFECT OF CHANGES IN CONTEXT ON THE FREQUENCY, FORM, FUNCTION AND DEGREE OF SPONTANEITY OF CHILDREN’S SOCIAL COMMUNICATIVE BEHAVIOUR

METHOD: NONVERBAL CHILDREN WITH AUTISM (N = 91, MEAN AGE 6 YEARS 10 MONTHS, SD 1:04) WERE VIDEOED DURING EVERYDAY ACTIVITIES IN THE CLASSROOM, INCLUDING SNACK, GROUP AND ONE-TO-ONE TEACHING SESSIONS AND FREE PLAY.

SESSIONS WERE RATED USING THE NEWLY DEVELOPED CLASSROOM OBSERVATION SCHEDULE TO MEASURE INTENTIONAL COMMUNICATION (COSMIC)

RESULTS: OVERALL RATES OF INTENTIONAL COMMUNICATION WERE SIGNIFICANTLY LOWER IN FREE PLAY SESSIONS THAN IN ALL OTHER CONTEXTS (Z = 2.73 TO 4.42, P < .01). THE PROPORTIONS OF DIFFERENT COMMUNICATIVE FUNCTIONS WERE ALSO SENSITIVE TO CHANGE IN CONTEXT, WITH GREATER PROPORTIONS OF IMPERATIVE REQUESTS IN SNACK (Z = 7.60, P < .001) AND GREATER PROPORTIONS OF COMMENTING IN NON-SNACK SESSIONS (Z = 3.13, P < .01). THE COMMUNICATIVE FORM, AND THE DEGREE OF SPONTANEOUS INITIATION WERE ALSO FOUND TO VARY.

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significantly across different contexts. 
Conclusion: All aspects of the social communication of children with autism are sensitive to the context in which they occur.
Sponsor: Three Guineas Trust

PS5.46
TEACHING SELF-INITIATIONS TO PREVERBAL CHILDREN WITH AUTISM Marie Louise Rocha, Laura Schriebman, University of California, San Diego
Background: Studies evaluating children with autism have specifically identified marked deficits in self-initiations, that is, spontaneous social initiations towards others. Developing interventions that effectively target early social communication behaviors in preverbal children with autism may minimize obstacles to the acquisition of language and social interaction skills. Previous research has identified that children with low social avoidance showed a modest increase in self-initiations during PRT (Pivotal Response Training), a naturalistic behavioral intervention for children with autism. Children in the same study identified as having high social avoidance did not show increases in self-initiations during PRT.
Objectives: The purpose of the present study is to: (1) develop and evaluate a self-initiation training (SIT) for preverbal children with autism with high levels of social avoidance, (2) assess which types of self-initiations increase after SIT, and (3) assess the generalization of self-initiations learned during SIT.
Method: Three children with a diagnosis of autism have participated in this intervention. Participants were between 2-5 years of age. Each participant’s behavior during a Structured Laboratory Observation (SLO) matched the behavior profile of children who did not learn to self-initiate during PRT. This study implemented a single subject multiple baseline design across subjects.
Results and Conclusion: Children with autism who do not learn to self-initiate from behavioral interventions targeting language, play and social skills can learn to do so with specific self-initiation training using behavioral techniques. Further data will be provided and discussed.
Sponsor: NIMH 5R01MH039434-16

PS5.47
USING EYE-TRACKING AND VIDEO REWARDS TO MODIFY FACE GAZE - PRELIMINARY DATA Cheryl Trepagnier, Marcm Sebrechts, Andreas Finkelmeyer, Jordana Woodford, Willie Stewart, Maya Coleman, The Catholic University of America
Background: Individuals with ASD have impairments in nonverbal attention and communication. It may be helpful to train increased face attention during preschool years.
Objectives: Develop and conduct preliminary trials of a computerized system that detects and rewards appropriate face gaze including gaze-following. The system is implemented in a children’s amusement-ride helicopter with a video display and concealed eye-tracking camera.
Methods: Families are recruited through area pre-schools and institutions that evaluate children 2-4. Clinical diagnosis is confirmed using the CARS, ADI and ADOS.
Portions of the Mullen and CSBS are administered. Two children were enrolled at the time of abstract submission.
Results: Data including a record of tracked gaze at specified regions of interest will be reported for dyadic attention training (almost completed) and joint attention training (about to begin) for S2, a boy, 3,5, with Autistic Disorder. Playroom behavior and response to probes showed little or no face gaze. S2’s gaze at the Buddy reveals interest in the face at the beginning of each session in the helicopter, with particular attention to mouth but also glance at eyes.
Conclusion: Preliminary findings support parents’ interest in participating, the need for flexible scheduling, the feasibility of the training procedure, its ability to garner attention to the face in the video environment, and the reward potency of video. Data acquisition and analysis is in progress.
Sponsor: NIMH

PS5.48
GESTALT PERCEPTION AND WEAK CENTRAL COHERENCE IN HIGH-FUNCTIONING AUTISM Sven Bölte, Armin Scheurich, Lutz Schmidt, Fritz Poustka, J.W. Goethe University Frankfurt, Germany
The objective of this study was to examine gestalt perception in high-functioning autism (HFA) and its relation to tasks assumed to indicate weak central coherence. Data on three principles of gestalt perception (similarity, closure, proximity) as well as on visual illusion susceptibility, local-global tasks, Block Design, the Embedded Figures Test (EFT) and overlapping figures tasks were collected in 15 adult male individuals with HFA, 15 with schizophrenia, 15 with depression and 15 normative controls. The group with HFA processed visual stimuli significantly less in accord with gestalt laws than the other samples, particularly in terms of grouping similar objects. Among other findings, gestalt processing correlated negatively with performance on the EFT and all three clinical groups did succumb less to visual illusions than the normative sample. Results suggest a considerably decreased tendency to process stimuli in terms of coherent meaningful units in autism, being associated with local processing of place relationships and enhanced visual disembedding.

PS5.49
TACTILE PERCEPTION IN ADULTS WITH AUTISM Carissa Cascio, Francis McGlone, Stephen Folger, Vinay Tannan, Grace Baranek, Kevin Pelphey, Gregory Essick, University of North Carolina
Background: There is evidence of sensory processing abnormalities in autism, but this is largely limited to clinical observations and self-reports.
Objectives: To determine using psychophysics whether somatosensory perception is altered in autism.
Methods: 7 high functioning adults with autism and 7 age and gender-matched controls were tested on both the forearm and palm for detection of touch, vibration, warmth, cool, heat pain, cold pain. Ratings of affect were obtained for textured surfaces stroked across the skin.
subjects completed the Adult Sensory Profile (ASP), which measures affective response to sensory stimuli experienced in daily life.

Results: Adults with autism scored higher on sensitivity and avoidance scales of the ASP than controls. When covarying for subject and group differences in ASP scores, group differences on the psychophysical tests emerged only for tests involving affectionately charged stimuli. The autism group exhibited greater sensitivity to noxious thermal stimuli and rated the pleasantness of surface textures differently than controls.

Conclusion: Adults with autism perceive many tactile stimuli similarly to controls; however, there is an intriguing relationship between self-reported affective response to ecologically valid sensory stimuli and performance on psychophysical tasks involving unpleasant and pleasant cutaneous stimuli.

Supported by National Institute of Mental Health (NIMH) grant K01-MH071284 and a grant from the Foundation of Hope for Research and Treatment of Mental Illness.

PS5.50
DOES ACQUIRED MEANING MODULATE THE EARLY PERCEPTUAL PROCESSING OF MEANINGLESS STIMULI IN PERSONS WITH AUTISM? Julie Coutya, Anthony Hosein, Caroline Langer, Jacob A Burack, Laurent Mottron, Bouthaina Jemel, Riviere des Prairies Hospital, & Concordia University

In a recent study, Bentin et al. (2002) recorded the N170 event related component to meaningless stimuli (dots, plus signs, etc.) before and after the subjects learned that these simple shapes might be perceived as being part of a face (e.g., eyes). The N170 amplitude to these stimuli enhanced after learning. Although the bottom-up information is not that of a face (e.g., dots), the N170 face-specific component was conceptually biased after learning.

Objectives: Investigate the extent to which perception in adults with high functioning autism (HFA) could be biased by prior knowledge and past experience as in typically-developing subjects.

Method: 12 adults with HFA and 10 age- and IQ-matched control participants were shown in the first block: pairs of dots, plus signs, or other simple shapes; in the 2nd block images of objects, in the 3rd block the same stimuli as in the 1st block, in the 4th block schematic faces with eyes made up of the simple shapes (the dots became then the eyes of a schematic face), and finally the simple shape block was presented again. A 59-channel EEG was recorded continuously while subjects detected rare target stimuli (flowers) randomly presented within each block.

Results: Both participants with HFA and control subjects showed the typical larger N170 component to faces than to objects. In both groups, the N170 to the meaningless stimuli (1st block) was smaller and delayed than that to faces. However, after being exposed to the dots in faces (5th block), these meaningless stimuli evoked a face-like ERP response equivalent to the N170 evoked by complete schematic faces in the control group while they did not evoke similar ERP responses in the HFA group.

Conclusions: The present data clearly show that perception in autism is mainly stimulus-driven, and is in a very least extent mapped by learning and past experience. This suggests a reduced influence of top-down processes on perception in autism.

Sponsor: NAAR to BJ.

PS5.51
PREFERENTIAL-LOOKING TO SOCIAL STIMULI IN ASD: AN EYE-TRACKING STUDY Sue Fletcher-Watson, Susan R Leekam, John M Findlay, Valerie Brown, University of Durham

Introduction: People with autistic spectrum disorder (ASD) show reduced looking to eyes and faces in eye-tracking research. Likewise, reduced orienting to faces, voices and other social cues has been observed in young children with ASD. It is possible that from a young age people with ASD fail to direct their attention to social elements of the environment, and that this is a crucial factor in the development of the disorder. In addition, people with ASD have been shown to be capable of using social cues and information under favourable conditions.

Objectives: To use a preferential-looking paradigm to investigate whether people with ASD prefer to direct their gaze to social or non-social stimuli when both are presented simultaneously. Method: Two images of everyday scenes were presented side-by-side. One contained a single person, the other contained no-one. Eye-movements were recorded using DPI eye-trackers and specially designed software. The first half of this study was a free-viewing task; in the second half participants were asked to decide the gender of the person in the images. Results: Preliminary data suggest that typically-developing (TD) people make the majority of their first eye-movements into the image containing a person and that they spend approximately 60% of the viewing time looking at this image. In contrast, people with ASD are expected to make fewer spontaneous fixations on the image containing a person. Conclusions: The social-attentional bias present in the TD population will be weaker in a group with ASD.

Sponsor: Economic and Social Research Council *

PS5.52
SENSORY SYMPTOMS AND SOCIABILITY IN AUTISM AND WILLIAMS SYNDROME Susan Rosemary Leekam, Michael D Burt, Bronia Arnott, University of Durham

Background: First-person autobiographical accounts often report that people with autism have unusual sensory experiences including atypical responses to auditory, visual, tactile and olfactory stimuli. Research studies comparing autistic individuals with developmentally delayed control subjects show that these sensory abnormalities are pervasive and multimodal.

Objectives: To compare patterns of sensory symptoms in individuals with autism with individuals with Williams syndrome, a genetic disorder in which hyperacusis and extreme sociability are typical symptoms.
Methods: Parents were interviewed using the Diagnostic Interview for Social and Communication Disorders. This interview elicits information on all symptoms of autistic spectrum disorder including information about responsiveness to a range of sensory stimuli. Data for 22 individuals with Williams Syndrome were matched and compared with data for 22 individuals with autism.

Results: Auditory symptoms were more common in the Williams syndrome group while proximal symptoms (touch, smell/taste, kinaesthetic, pain) were more common in the autism group. However multimodal symptoms were found in both groups. Additional analysis of sociability revealed that half the Williams syndrome group had atypical sociability that did not fit the characteristic pattern of overly chatty and indiscriminately friendly behaviour that is commonly associated with Williams syndrome. The relation between social symptoms and pattern of sociability is discussed.

Conclusion: These results add to previous research findings on sensory symptoms in autism and in Fragile X syndrome and may help us to understand better the profile of social and sensory atypicality found in these groups.

Sponsor: British Academy*

PS5.53
PITCH DISCRIMINATION ABILITY IN CHILDREN WITH AUTISM IS NOT HAMPERED BY MEANINGFUL SEMANTIC CONTENT Kristelle Hudry, Pamela Heaton, Elisabeth Hill, Goldsmith's College, University of London

Background: According to current theoretical accounts (weak central coherence, enhanced perceptual function), individuals with autism process perceptual or local information at the cost of higher-level information. Support for these theories exists in empirical data showing enhanced pitch perception in individuals with autism (e.g., Bonnell et al., 2003; Heaton, 2003)

Objectives: To assess the effect of meaningful semantic content on pitch discrimination in children with autism.

Methods: Children with autism (M age = 8y) and matched controls (with typical-development and learning difficulties), recruited through specialist and mainstream schools, completed a computerised pitch-discrimination task. Paired stimuli - real words, nonsense words, and tones - were either identical in pitch, or differed by small (2 semi-tone), medium (3 semi-tone), or large (tritone) intervals, and children indicated whether these sounded the same or different using a button box.

Results: While, for all children, accuracy in perceiving a difference increased with interval size, group effects were apparent. Children with ASD appeared better able than controls to detect small pitch differences. Furthermore, in making subtle pitch judgements, children with ASD did not appear adversely affected by the presence of semantically meaningful content, as did controls.

Conclusion: Children with ASD process the pitch and semantic aspects of auditory stimuli uniquely compared to controls.

Sponsor: Sixth Framework Program of the European Union, NEST-Pathfinder, SEDSU

PS5.54
CHARACTERISING AUDITORY PERCEPTUAL PROCESSING IN AUTISTIC SPECTRUM DISORDERS Catherine Jones, Anita Jayne Sarah Marsden, Jenifer Tregay, Francesca Happé, Gillian Baird, Emily Simonoff, Andrew Pickles, Jennifer Thomson, Usha Goswami, Tony Charman, Institute of Child Health, University College London

Background: Auditory perceptual processing is poorly understood in autism spectrum disorders (ASDs), despite sensory and perceptual abnormalities being commonly observed.

Objectives: Investigate the auditory perceptual processing profile of adolescents on the autistic spectrum.

Methods: Diagnosis of ASD was established using the ADI and ADOS. A battery of auditory tasks was administered to adolescents (14-15 years old) with and without ASD, ranging in symptom severity (autism, PDD) and IQ (40-136). Audiometric assessment was used to screen for hearing loss. Four auditory perceptual processing tasks were presented. In each task, the two tones were presented binaurally through headphones. Depending on the task presented, a decision was required as to which tone was 'higher' (Frequency Discrimination task), 'louder' (Intensity Discrimination task), 'longer' (Duration Discrimination task) or 'louder at the beginning' (Rise Time Discrimination task).

Results: Data collection is still in progress. We will report findings on the data collected so far, comparing both autism vs. PDD vs. non-PDD performance and that of high vs. low IQ individuals.

Conclusions: We anticipate that determining the profile of auditory perceptual processing abilities in autism may give insight into the sensory and perceptual strengths and difficulties that manifest at the behavioural level.

Sponsor: Medical Research Council, UK

PS5.55
AN ELECTROPHYSIOLOGICAL STUDY OF CONSCIOUS PERCEPTION OF FAMOUS AND UNFAMILIAR FACES IN AUTISM: EVIDENCE FROM A BACKWARD-MASKING EXPERIMENT Caroline Langer, Anthony Hosein, Julie Coutya, Jacob A Burack, Laurent Mottron, Boutheina Jemel, Riviere des Prairies Hospital & University of Concordia

Backward masking occurs when a briefly presented visual stimulus becomes difficult to see because of the appearance of a mask that follows the target. Current theories of visual masking emphasize the role of feedback and re-entry processes in conscious vision (Enns & Di Lollo, 2000). Studying re-entry process in autism is central to understanding in an integrative perspective visual cognition in persons with autism.

Objectives: Identify the neurophysiological correlates of conscious perception (and recognition) in adults with high functioning autism (HFA) in a backward masking experiment.

Methods: Event-related brain potentials (ERPs) were collected with 59 EEG channels while participants with...
HFA (N=12) and their age- and IQ-matched controls (N=10) performed a familiarity judgment on famous and unfamiliar faces. Each face picture was presented at 11 ms followed by a mask, at 22 ms + mask, 44 ms + mask, 121 ms+ mask, and 319 ms+ mask. 

Results: Both HFA and control subjects could hardly see the stimuli and discriminate between familiar and unfamiliar faces at 11 and 22 ms exposure durations. The behavioral results in the two groups of subjects were quite similar. However, the electrophysiological data at conscious recognition threshold (44 ms) revealed that while control subjects showed a N170 amplitude enhancement to famous than to unfamiliar faces, there was no N170 amplitude difference between famous and unfamiliar faces in HFA individuals. 

Conclusion: Our findings implicate conscious perception, and probably re-entrant feedback processes, in the amplitude enhancement of the N170 face component in typically developing subjects. In HFA individuals the absence of N170 effect concomitant with conscious recognition suggests a possible impairment of re-entrant feedback processes, and a reduced functional coupling between high and low order cognitive processes. 

Sponsor: NAAR to BJ.

**PS5.56**

 TEMPORAL REPRESENTATION OF SELF-INITIATED MOVEMENTS Cheryl M Glazebrook, Digby Elliott, James Lyons, McMaster University 

Background: Typically when individuals are asked to report the time they performed a finger tap they anticipate when the movement was executed. The time reported corresponds to preparatory activity in the motor areas of the frontal cortex.

Objectives: Given evidence that individuals with autism have abnormal frontal networks, we investigated their temporal perception of frontal activity related to self-generated movements.

Methods: Each trial began with a red dot moving around a circle on a monitor. After the first revolution, participants pressed the spacebar when they wished. The dot continued to move for a random time-period, and participants were asked to remember where the dot had been when they pressed the button. Next, an identical circle appeared and participants pointed to where they believed the dot was when they had pressed the button. In two other conditions participants also heard a ‘beep’ when the button was pressed and either reported when they pressed the button or when they heard the beep. In a final condition participants reported when they heard a beep generated by the computer.

Results: Analysis of the bias revealed no group differences between individuals with autism and their chronologically age matched peers (F<1). Participants reported they pressed the button ~100ms before they had, but were accurate when they reported the time of a computer generated tone.

Conclusion: The results demonstrate that individuals with autism exhibit the same biases as others when reporting self-generated movements. This suggests they have the same internal representation of voluntary movements as their peers. 

Sponsors: ASO, CRC, NSERC

**PS5.57**

 HOLISTIC PROCESSING OF FACES IN ADULTS WITH AUTISM Mayu Nishimura, MD Rutherford*, Daphne Maurer, McMaster University 

Background: There is conflicting evidence on whether individuals with autism process faces holistically (e.g. Teunisse & de Gelder, 2003; Joseph & Tanaka, 2003). Results may depend on whether the task requires attention to the eye or mouth region.

Objectives: To compare the ability of adults with and without an autism spectrum disorder (ASD) to process faces holistically when attending to the top vs. bottom halves of faces.

Methods: Composite faces were created by splitting digital photographs of faces horizontally, and then recombinining the faces using top and bottom halves of different individuals (Le Grand et al., 2004). Participants judged whether the top (or bottom) halves of two composite faces were the same. Typically developing individuals demonstrate a composite effect: poorer accuracy and longer reaction times on same trials when the top and bottom halves of faces are aligned (because alignment compels holistic processing, thus making it difficult to ignore the irrelevant half) than when holistic processing is broken by misalignment.

Results: Preliminary analyses of 9 adults with autism (Mean age = 19.2 years; 3 additional participants excluded for not following instructions) and 9 matched controls (Mean age = 20.0 years) revealed no group difference in the size of the composite effect in accuracy when matching top halves of faces, and neither group demonstrated a composite effect when matching the bottom halves of faces.

Conclusion: Preliminary findings suggest that high-functioning adults with autism can show normal holistic processing of faces. 

Sponsor: NSERC

**PS5.58**

 IS CONFIGURAL PROCESSING TO BLAME? INVESTIGATING THE DEVELOPMENT OF PERCEPTUAL PROCESSING BIASES IN AUTISM K. Suzanne Scherf, Marlene Behrmann, Jaime Doyle, Emily Dang, Nancy Minshew, Beatriz Luna, University of Pittsburgh School of Medicine 

One characteristic deficit in autism includes impaired face recognition. An inability to detect configural or global properties of faces, which describe differences in the relationships among the features, may contribute to this deficit. In order to evaluate whether individuals with autism have a general perceptual processing deficit or bias that impedes their ability to encode global characteristics of visual stimuli, we evaluated configural processing abilities in typically-developing (TD) and high-functioning autistic (ASD) children (8-13) and adolescents (14-17) using non-social hierarchical stimuli.
The stimuli included a global letter made up of either similar or different local letters (big H made up of little H or S). Participants identified the letter at the global or local level in separate blocks. Our results suggest that, similar to findings in the face recognition literature, the bias to encode global characteristics of visual stimuli continues to develop late into adolescence in TD individuals. TD children and adolescents demonstrated a strong bias to encode the local stimulus characteristics. They were more accurate and faster at identifying the local stimulus characteristics and experienced more interference from the local inconsistencies when identifying the global characteristics. Individuals with ASD did not follow this same developmental pattern of perceptual biases. Regardless of the kind of information that autistic children and adolescents were processing, they could not ignore interference from global or local information. This effect of interference was more extreme in ASD children and reduced by adolescence. These results suggest that individuals with ASD do not appear to have a selective deficit in encoding global characteristics of visual stimuli, but instead, may have a more general deficit in discriminating between relevant and irrelevant information at all levels of object processing.

SPONSOR: NIMH 2 RO1 MHS4246-010A

**PS5.59**

**ABNORMAL N1 / P1 RESPONSES IN CHILDREN WITH AUTISM ELICITED BY BOTH LOW AND HIGH SPATIAL FREQUENCY GRATINGS**

**Alison Scope, Elizabeth Milne, David Buckley, Olivier Pascalis, The University of Sheffield**

Background: It has been suggested that individuals with autistic spectrum disorder (ASD) may display abnormalities in low level visual perception. Objectives: To investigate low level visual perception in ASD by measuring visual evoked potentials elicited by a range of spatial frequency gratings.

Methods: High density visual evoked potentials were recorded from children and adolescents (aged between 9 and 18) diagnosed with ASD, and chronological and non-verbal mental age matched typically developing controls in response to sinusoidal gratings presented at 0.5, 1, 4 and 8 cycles per degree (cpd). The stimuli, which measured 7.5° x 7.5° of visual angle, were presented foveally and were visible for 500 msec.

Results: Analysis of EEG data at occipital leads indicated that the controls exhibited a typical N1 / P1 complex, with a clear N1 emerging between 80 and 95 msec in response to the higher frequency stimuli (4 and 8 cpd), and a P1 which increased in latency and decreased in amplitude with increasing spatial frequency. The ASD group however did not show a clear N1, and showed reduced P1 amplitude compared to the controls, at all four spatial frequencies.

Conclusion: These data suggest that early perceptual mechanisms, across a range of spatial frequencies, are abnormal in children with autistic spectrum disorder.

Sponsor: Bial Foundation

**PS5.60**

**PATTERNS OF SENSORY PROCESSING IN AUTISM AND RELATIONSHIPS TO DEVELOPMENTAL PERFORMANCE**

**Scott David Tomchek, Weisskopf Child Evaluation Center, University of Louisville School of Medicine, Department of Pediatrics**

Background: In addition to diagnostic features, aberrant sensory responding has been widely reported in the autism literature. Aberrant sensory processing has, however, been infrequently studied compared to communication and cognition in autism and existing studies have had multiple methodological deficiencies.

Objectives: Describe patterns of sensory processing found in children with an ASD to test the relationship(s) of these patterns to diagnostic and developmental variables.

Method: Retrospective data collection was used to collect developmental and sensory processing variables of 400 children with an ASD. Sensory processing abilities were measured by the Short Sensory Profile (SSP).

Results: The majority of the sample (80.5%) had a diagnosis of autism with a mean age 49.58 months. Some degree of sensory processing dysfunction on the SSP Total Score was noted in 89% of the sample with the greatest difficulties reported on the Underresponsive/Seeks Sensation, Auditory Filtering And Tactile Sensitivity sections. Exploratory factor analysis identified 6 parsimonious factors: Low Energy/Weak, Tactile and Movement Sensitivity, Taste/Smell Sensitivity, Auditory and Visual Sensitivity, Sensory Seeking/Distractibility, and Hypo-responsivity. These factor variables contributed to explaining the differences in five of six developmental variables of the sample that are associated with the diagnosis of autism. Most notably receptive language, adaptive and expressive language performance were significantly correlated with sensory processing factor scores.

Conclusions: Together, the sensory processing findings noted in this study describe a pattern of dysfunctional sensory modulation resulting in behavior regulation difficulties. These findings have significant implications for intervention programs involving individuals with an ASD, given the potential impact of these findings on a child’s ability to maintain active engagement.

**PS5.61**

**SPEECH-IN-NOISE PROCESSING IN AUTISM SPECTRUM DISORDERS: IMPAIRMENT IN PERCEPTION OF SENTENCES AND NONSENSE SYLLABLES IN NON-REVERBERANT LISTENING CONDITIONS**

**Jose I Alcantara, Emma J Weisblatt, Camilla Clark, Adele Lomax, Mawe McLaughlin, Neda Minakaran, Jerome Segal, University of Cambridge**

Background: Individuals with autism spectrum disorders (ASD) commonly report difficulties understanding speech in background noise (SIN). We have previously quantified these, which are particularly evident in background noises containing gaps or “dips”. However, the difficulties observed (1) could be due to difficulty in
understanding connected speech and (2) were measured in a non-reverberant, un-naturalistic acoustic environment.

Objectives: (1) To repeat speech in noise (SIN) testing using both sentences and nonsense syllables to investigate the effects of semantic information. (2) To investigate the effect of reverberation.

Design/Methods: (1) SIN perception was measured using speech reception thresholds (SRTs), for auditory stimuli in a non-reverberant chamber. Background noises varied in semantic content and in the "dips" present. Speech materials were standardised lists of everyday sentences and of vowel-consonant-vowel (VCV) syllables. 10 participants with ASD and 10 age- and IQ-matched typically-developing participants, aged 12 to 17 years, took part. (2) SRT measures were repeated in a reverberant room.

Results: (1) SRTs for the ASD group were significantly raised, meaning the ASD individuals required a higher SNR to understand speech, for both sentences and VCVs. (2) The ASD group did not show raised SRTs in the reverberant environment.

Conclusion/Discussion: The impairment is not due to a general difficulty understanding connected speech. The impairment was not found in reverberant conditions, possibly because some of the information in the "dips" was lost.

Funding: St Andrews Hospital

**PS5.62**

**INTERMODAL SPEECH PROCESSING IN CHILDREN WITH AUTISM: WHAT YOU SEE IS WHAT YOU HEAR**  
Jonathan A Weiss, James M Bebko, Nicole A Rahim, York University

**BACKGROUND:** Intermodal perception is the ability to coordinate information from various senses, leading to a unified perception of an event. The McGurk effect is an audiovisual illusion that demonstrates how we integrate the speech we see with the speech we hear. Children with autism may have increased difficulty in intermodal speech perception.

**OBJECTIVE:** To test whether children with autism perceive speech intermodally, compared to children with intellectual disabilities and typically developing children.

**METHODS:** Nineteen typically developing children, 19 children with autism, and 19 children with Down syndrome are participating in the study. Receptive and expressive language, IQ, and severity of autistic symptoms are assessed. Children are exposed to a video of a woman pronouncing vowel sounds and are asked to repeat the sounds that they perceive in a listening-only condition, speech-reading-only condition, and audiovisual McGurk effect condition.

**RESULTS:** Results to date have found that children with autism perceive the McGurk effect illusions significantly less than the children with Down Syndrome and typically developing children, even after controlling for speech reading and listening ability. As well, results confirmed a positive correlation among visual speech-reading skill and the McGurk effect, and a negative correlation among listening-only skill and the McGurk effect, across groups.

Additional analyses are currently being conducted.

**CONCLUSIONS:** Children with autism may have impairment in audiovisual speech processing compared to children without autism. That is, although children with autism are able to repeat the sounds that they heard and read the visual pronunciations with as much accuracy as the comparison groups, they do not appear to use the auditory and visual information present in the speech signal in a similar manner.

**SPONSORS:** OMHF*; Autism Society of Ontario*; CIHR*; ASD-Strategic Training Program*

**PS5.63**

**THE INTERMODAL PERCEPTION OF EMOTION IN CHILDREN WITH AUTISM**  
Kerry L. Wells, James M. Bebko, York University

According to the DSM-IV-TR, impairments in social interaction is one of the defining characteristics of autism and other pervasive developmental disorders. More specifically, emotional impairments are frequently seen among individuals with autism. Common among this population are inappropriate emotional reactions, a lack of any emotional display, and the inability to react to the affective state of others.

Why individuals with autism display impairments in emotional abilities has been a matter of debate among researchers, however, it has been suggested that perceptual impairments may underlie abnormalities in this area. Difficulties perceiving affect in others could lead to some of the social abnormalities characteristic of this disorder.

This study examined the ability of children with autism to perceive affect via the preferential looking paradigm, in which two side-by-side visual displays are presented to the participant along with a single soundtrack. These displays differ only in the affective content of the message, and are otherwise identical. The soundtrack matches only one of the visual displays. By preferring to look at one screen or the other, it is implied that the participants are able to detect a difference between the displays and therefore the emotional content of the message.

**PS5.64**

**EMPATHIC UNDERSTANDING IN CHILDREN WITH AND WITHOUT AUTISM**  
Susana Caló, Nia Tiltman, Jessica A. Meyer, R Peter Hobson, Institute of Child Health, UK

Background: Children with autism appear to show relatively little empathy towards the feelings of other people.

Objective: We tested whether children with and without autism would be sensitive to another (videotaped) person’s feelings, even when she showed no overt distress.

Methods: Twenty-three typically developing seven and eight-year-old children without autism, and matched high-functioning children with autism (currently being tested), watched a video vignette in which one woman was unresponsive when the other tore her drawing, and a child
looked on, concerned.

Results: There were six children without autism who did not understand that the second woman had torn the first woman’s drawing, three who showed partial comprehension, and 14 who understood this clearly. Of those who showed clear comprehension, 10 expressed empathy (e.g. ‘sad because Rosa ripped up her turtle and put it in the bin’ and ‘sad ‘cos her turtle got ripped up’). Data for the children with autism are being collected, and initial evidence suggests they may show little empathic understanding.

Summary and Conclusions: We shall consider the results in terms of participants’ capacity to feel for another person, from the perspective of developmental psychopathology.

Sponsor: Baily Thomas Charitable Trust & NHS R&D Levy

**PS5.65**

**INTENTIONAL ACTION UNDERSTANDING AND SHARING INTENTIONALITY IN CHILDREN WITH AUTISM** Livia Colle, Elisa Grandi, Cristina Becchio, Center for Cognitive Science, Department of Psychology, University of Torino, Italy

Background: Tomasello et al. (2005) have recently argued that social impairment in autism might be due to the lack of the fundamental motivation to share experience (emotions, attention, goals) with others, whereas the basic ability to understand others’ intentions should be intact.

Objectives: In order to better understand the relationship between these two early components of social-cognitive competence, understanding and sharing intentionality, we present 10 tasks involving different degrees of these two abilities to children with autism. We expected to find a significant impairment in children with autism in the sharing intentionality tasks.

Methods: 20 autistic children and 20 normally developing children, matched by mental age, were presented with 2 different play sessions. In each of them the experimenter proposed games respectively assessing: 1) the understanding of others’ intentions, using an experimental paradigm based on imitation at different level of complexity (finalized/unfinalized actions, object’s directed actions vs body movements, unfulfilled actions, pretended actions, funny actions); 2) sharing intentionality (empathy, joint attention, cooperation) in a playful and ecological situation.

Results: Children with autism performed as well as normally developing children in tasks requiring imitation of different actions, even if they showed some peculiarities and more difficulties than controls for pretended actions. They also performed as well as controls in simple shared activities (sharing emotions and cooperation) but revealed severe difficulties in more complex cooperative activities.

Conclusion: The discussion will be focus on the theoretical necessity to split into different levels the notion of shared intentionality.

**PS5.66**

**PREDICTORS OF COOPERATIVE BEHAVIOR IN CHILDREN WITH AUTISM** Costanza Colombi, Kristin Liebal, Michael Tomasello, Gregory Young, Felix Warneken, Sally Rogers, M.I.N.D. Institute/UC Davis

Background: Tomasello has recently suggested that sharing goals, or cooperative behavior, are a key human evolutionary landmark. Recent pilot research has demonstrated a specific pattern of cooperative abilities and difficulties in early autism.

Objective: To identify early social precursors to cooperative behavior in autism.

Design/Methods: Six cooperation tasks, four intentionality tasks, three different kinds of imitation tasks, four turn-taking games, and a response to joint attention task were administered to 14 young children with autism (mean CA=43.00, SD=10.07) and 15 young children with other developmental disabilities (mean CA=42.14, SD=8.12) matched on nonverbal abilities.

Results: Preschool children with autism showed worse performance than children with other developmental disabilities in the cooperation tasks (t=3.92; p<.001), imitation tasks (t=2.5; p<.05), turn-taking games (t=2.62, p<.05), and joint attention task (t=3.13; p<.01). The two groups did not differ in the intentionality task (t=.98; p<.33). Multiple regression analysis revealed that imitation skills (r=.34; p<.05) and response to joint attention (r=.40; p<.01) were the main predictors of cooperative behavior in both groups.

Conclusions: Cooperative behavior of preschool children with autism were impaired in comparison to the contrast group. Furthermore, performance in imitation and joint attention predicted cooperative behavior. Results are discussed within Rogers and Pennington’s (1991) intersubjectivity theory of autism.

Sponsor: This research was supported by a grant from NICHD #U19 HD35468-08.

**PS5.67**

**IMITATION OF GOALS BY 5-YEAR-OLD CHILDREN WITH AUTISM** Barbara Anne D’Entremont, Elizabeth L Seamans, University of New Brunswick

Background: Understanding people’s actions in terms of goals and intentions is thought to enable the development of joint attention. Since children with autism have difficulties with the latter, it is important to examine what they understand about the former.

Objectives: To determine if children with autism will imitate others’ actions in terms of goals.

Methods: Eight five-year-old children with autism were tested. An experimenter modelled hopping or sliding movements with a toy mouse. She either hopped/slid the mouse across a mat into a toy house (House condition) or hopped/slid the mouse across a mat to the same final resting location with no house present (No House condition; Carpenter, Call & Tomasello, 2005). The
number of trials where the child matched E’s actions or her location (in the house, on the mat) were recorded. Children matched her actions more often in the No House than the House condition (82% vs 53% of trials, respectively; t(7) = 2.12, p = .07, eta-square = .39). They matched the final location more often in the House than the No House condition (41 % vs 0% of trials, respectively; t (7) = 2.30, p = .05, eta-square = .43). Conclusions: Children saw the action itself as the goal in the No Houses condition, and responded by matching E’s actions whereas they saw the location as the goal in the House condition and responded by matching E’s location. Results will be interpreted in the context of Tomasello and colleagues’ recently proposed dual strands of ontogenetic development of social cognition. Funded by: Medical Research Fund of New Brunswick

**PS5.69**

**IMITATION IN AUTISM: PERFORMANCE ON SOCIAL VERSUS NON-SOCIAL IMITATION TASKS**

Brooke R Ingersoll, Lewis & Clark College

Young children with autism exhibit deficits in imitation skills. Previous research suggests that children with autism may have particular difficulty imitating for social purposes. To investigate this possibility further, children with autism and typically developing children matched for mental age were compared on a series of imitation tasks presented either in a structured elicited condition or in a naturalistic play condition. Tasks were balanced across conditions such that if one child received a modeled action in one condition, another child would receive the same action in the other condition. Preliminary results suggest that children with autism performed more poorly on the imitation tasks overall, and particularly poorly in the naturalistic play condition; the typical children did not exhibit this discrepancy. These findings support the hypothesis that children with autism are particularly impaired in the ability to imitate for social purposes.

**PS5.70**

**EXAMINING THE RELATIONSHIP BETWEEN SOCIAL SYMPTOMATOLOGY AND SOCIAL FUNCTIONING IN CHILDREN WITH AUTISM SPECTRUM DISORDERS**

Philip Lee, Jennifer Foss-Feig, Lisa Gilotty, Anne Della Rosa, Amy Schropp, Gregory Wallace, Lauren Kenworthy, Georgetown University

Background: The primary symptom in Autism Spectrum Disorders (ASD) is an impairment in reciprocal social interaction. To determine whether symptoms warrant a diagnosis of ASD, children are frequently administered the Autism Diagnostic Observation Schedule—General (ADOS-G), which contains a measure of reciprocal social impairment. In addition, the Vineland Adaptive Behavior Scales (VABS) is commonly used to evaluate adaptive social functioning.

Objective: To examine the relationship between the presence of social impairment symptoms and the level of social functioning in children with ASD. A significant relationship between social symptoms and social functioning was hypothesized, in that as symptom severity increased, functioning would decrease.

Methods: 54 children with ASD between 4 and 17 years were included; ADOS-G and VABS scores were used as measures of social symptomatology and functioning. The group was split based on VABS socialization scores into high (Scaled Score ≥ 70) and low (Scaled Score < 70) adaptive social functioning. Scores in the social domains of the ADOS-G and VABS were then compared separately for the high and low social functioning groups.

Results: There was no significant difference between groups on Full Scale IQ (F = 0.31, p = 0.58) or on the reciprocal social interaction domain of the ADOS-G (F = 0.001, p = 0.98). For the low group, there was a significant correlation between reciprocal social interaction ADOS-G scores and the socialization domain of the VABS (r = -0.43, p = 0.05). This indicated that as children showed higher levels of symptomatology on the ADOS-G, they also showed greater social impairment, as predicted. However, within the high group, there was no significant correlation between these two scales (r = 0.12, p = 0.25).

Conclusion: These results suggest that other factors may be influencing the relationship between social symptoms and functioning for children with ASD who show relatively good social functioning.

**PS5.71**

**ASSESSING THE DEVELOPMENTAL PATH OF PLAY ABILITIES IN CHILDREN WITH AUTISM: EFFECTS OF AN EARLY INTENSIVE INTERVENTION**

Carine Mantoulan, Bernadette Rogé, Kerstin Wittemeyer, Ghislain Magerotte, Université Toulouse le Mirail CERPP

Children with autism spectrum disorders (ASD’s) are known to have a major impairment in play behaviours. Early educational support must therefore provide strategies to improve play skills in order to improve long-term outcome for these children.

OBJECTIVE: Our early intervention program is based on recognised early intervention design criteria (age at which intervention is given; intensity of intervention; tailoring the program to the individual; generalisation of learnt skills; inclusion of a parental role; identifying neural correlates of changes in abilities) and includes structured and incidental play strategies.

METHOD: Over a period of two years (T0, T1, T2), our experimental group (N=15) received an intensive early intervention for at least 15 hours per week. We assessed a control group (N=10) who received no study intervention over one year (T0, T1).

After matching the groups on standardised measures, we did a monthly videotaped assessment of play behaviour (Single Case Protocol) during 2 years on our experimental group. The same assessment was conducted within the control group at T0 and T1.

RESULTS: Compared to the control group, the children in the experimental group showed a greater improvement in functional and symbolic play as well as a more
important decrease of sensori-motor play and stereotyped/repetitive behaviours between time T0 and T1.

The longitudinal study (T0-T2) of the experimental group shows an improvement in all the children and allows us to establish three different progression groups which can be linked to the children’s performance level.

The study has obtained financial aids from the Fond Social Européen and from the FNRS. A grant of the Fondation France Télécom has also been attributed in order to realize the intervention program.

**PS5.72**

**CONCERN FOR OTHERS IN CHILDREN WITH AND WITHOUT AUTISM**

Jessica Anne Meyer, Peter Hobson, Rosa Garcia-Perez, Ruth Harris, Institute of Child Health, UCL & Tavistock Clinic

**Background:** Young children with autism appear to be relatively insensitive to the feelings of other people.

**Objective:** We designed a novel experimental paradigm to test whether children would show empathy towards another person, even when she showed no overt reaction.

**Methods:** Participants were matched school-aged children with and without autism. Two investigators and the child each drew animals on cards. In one condition, the first tester’s drawing was torn by the second tester; in the second version of the same procedure, a blank index card was torn instead. The first tester did not respond overtly.

**Ratings:** Two independent judges rated the participants’ overall behavior for ‘concern’. Two new naïve judges rated every participant look to the first tester as falling into one of four categories: concerned, checking, orientating, and sharing positive affect. Inter-rater reliabilities were excellent.

**Results:** Children with autism showed less empathy, and as predicted, there was a group x task interaction for concerned looks in the Drawing vs. Blank Card condition. Control children but not those with autism showed more looks to the tester when her drawing and not a blank card was torn; in the former condition, the groups were similar for numbers of checking, sharing, and orientating looks, but significantly different for numbers of concerned looks (p < .01).

**Conclusion:** In contrast with control participants, children with autism showed little concern towards a person whose drawing was torn. We discuss the significance of a deficit in feeling for other people in the developmental psychopathology of autism.

**Sponsor:** Baily Thomas Charitable Trust & NHS R&D Levy

**PS5.73**

**AUTISM SPECTRUM DISORDERS: SEX DIFFERENCES IN AUTISTIC BEHAVIOUR DOMAINS AND COEXISTING PSYCHOPATHOLOGY?**

Fritz Poustka, Martin Holtmann, Sven Bölte, Dept. of Child and Adolescent Psychiatry J.W.Goethe University Frankfurt

**Background:** While gender differences are reported to be variable according to level of intellectual functioning, other differences are rarely studied.

**Methods:** A total of 23 females and 23 males (mean age 11y 9mo, SD 4y 5mo, range 5y to 20y 2mo) with an IQ above the mentally retarded range (mean IQ 88.8, SD 18.5, range 70 to 128) matched for age, IQ and ASD diagnoses were recruited and were compared using the ADI-R, ADOS and CBCL.

**Results:** We did not identify striking differences between males and females for the triad of autism core dysfunctions. However, parent report revealed significantly more symptoms in females than males, particularly social problems (t = 4.47, p < .01, d = 1.20), attention problems (t = 3.39, p < .01, d = .80), and thought problems (t = 3.24, p < .01, d = 0.84). Possible adjustment difficulties of ASD girls and interpreting bias by parents who may expect more social behaviour from daughters than from sons are discussed.

**Conclusion:** The severity of social and attentional problems in high-functioning females with autism emphasizes the need for thorough assessments and interventions in these domains. Future research should compare the cognitive phenotype of autism between genders.

**Sponsor:** Deutsche Forschungsgemeinschaft (German Research Foundation)

**PS5.74**

**SOCIAL UNDERSTANDING OF EYE GAZE IN CHILDREN WITH HIGH FUNCTIONING AUTISM (HFA)**

Adrienne H Rombough, Grace Iarocci, Simon Fraser University

**Background:** Spontaneous orienting in response to gaze direction is a prerequisite for healthy social development. Lack of spontaneous orienting in autism may indicate a failure to interpret the social relevance of eye-gaze.

**Objectives:** Investigate whether the tendency to spontaneously orient attention in response to eye-gaze cues is related to ability to understand social meaning of eyes.

**Method:** 20 children with HFA (x = 10.8 years), were MA matched to 20 TD comparisons. Children viewed static displays of deviated gaze and were asked to detect targets occurring in the periphery and instructed to ignore the eyes. A social situation was video-taped in order to determine the extent to which children spontaneously followed eyes in vivo. A modified version of Baron-Cohen’s (1995) candy task assessed ability to infer mental states from eye-gaze. A measure of line-of-sight following ability comprised a control condition.

**Results:** Children with HFA’s ability to orient spontaneously to gaze-direction was significantly correlated with their tendency to follow gaze in real social situations (r = .561). This was not found in controls. Interestingly, ability to track line-of-sight was impaired in the autism group relative to their TD peers.

**Conclusion:** Preliminary findings suggest that a lack of spontaneous orienting is associated with impoverished social gaze following in autism. Furthermore, children with autism’s ability to answer explicit questions about the social meaning of gaze is not associated with thier
tendency to follow gaze in social situations. 
Sponsors: ART, HELP

PS5.75
SOCIAL NETWORK STATUS AND PLAYGROUND OBSERVATIONS ON FULLY INCLUDED ELEMENTARY STUDENTS WITH AUTISM Erin Rotheram-Fuller, Connie Kasari, Amanda Gulsrud, University of California, Los Angeles
Background: Children with autism have poor peer relationships regardless of age or functioning level. Objectives: This project examined the relationship between playground observations of social interaction and the level of social network integration of children with autism in general education classrooms.
Methods: Participants were 25 children with autism in grades K-5 of diverse ethnic backgrounds (32% Caucasian, 8% African American, 32% Latino, 12% Asian, and 16% Other). Children were predominantly male (96%), and all were fully included in regular education classrooms. Participants were an average of 7.96 years old (sd=4.96), with an average IQ of 86.10 (sd=15.19). Measures included a social network assessment, playground observations of social interactions, and child ratings of loneliness.
Results: Children described approximately 60% of their classmates with autism as being socially included with peers. Despite this view of inclusion, 60% of the children with autism also received rejection nominations, and 21 of 25 children with autism (84%) spent time isolated on the playground. Paradoxically, children with autism who had greater engagement with peers on the playground also self-reported higher ratings of loneliness.
Conclusion: The involvement of children with autism in the social structures of regular classrooms reveals a mixed picture. While about half of the children with autism managed to avoid social isolation in the eyes of their classmates there seems to be a difference between observations of how children with autism spend their time in the presence of peers and perceptions of the class about their social situation.

PS5.76
CHILDREN WITH AUTISM SHOW DEFICITS IN RATIONAL IMITATION Elizabeth L Seamans, Barbara D'Entremont, University of New Brunswick
Background: Research has shown that typically developing infants will only copy the actions used to achieve a goal if they are seen as rational actions (Gergely, Bekkering & Kiraly, 2002).
Objectives: To investigate whether children with autism will limit imitation to rational actions.
Methods: Fifteen children with autism (M = 5.2 years, SD = 1.3 years) observed the experimenter activating a doorbell with her elbow and a tabletop light with her head (Meltzoff, 1988). When activating the objects, her hands were either occupied or free (Gergley et al., 2002).
Results: Significantly fewer children used their hands/elbows to activate the object when the experimenter’s hands were free (33%), than when her hands were occupied (60%), t(14) = 2.26, p < .05. A repeated measures ANOVA revealed a significant interaction between response type (head/elbow vs. head) and whether the experimenter’s hands were occupied or free, F(1, 14) = 4.85, p < .05. Children were more likely to use their hands to activate the object when the experimenter’s hands were unoccupied, but were equally likely to use their hands or heads/elbows to activate the object when the experimenter’s hands were occupied, p < .05.
Conclusion: Children with autism do not limit imitation to rational acts. Results will be discussed in terms of children’s abilities to determine others' intentions.
Funded by: Medical Research Fund of New Brunswick

PS5.77
CARDIORESPIRATORY REACTIVITY IN AUTISM: PRELIMINARY EVIDENCE OF RESPONSE THRESHOLD DIFFERENCES Stephen J Sheinkopf, A Rebecca Neal, Cynthia Miller-Loncar, Brown Medical School
BACKGROUND: Cardiorespiratory measures, including heart rate (HR) and vagal tone (VT), can be used to index physiologic reactivity to social stimuli in young children with autism.
OBJECTIVE: To test differences between children with autism and non-autistic comparisons on measures of HR and VT in response to a social behavioral assay.
METHOD: Young children with autism (AUT; n=21; ages 3-5 yrs) and non-AUT comparisons (n=16) were observed during a behavioral assay that included social events of increasing intrusiveness: [1] Baseline; [2] Distress Display; [3] Stranger Approach - Distal; and [4] Stranger Approach - Proximal. Mean HR and VT were calculated for each behavioral epoch. Initial findings are reported, with additional data available by May 2006.
RESULTS: Preliminary results indicated that the AUT group showed overall reduced VT and attenuated VT reactivity in response to distress displays and stranger approach (factorial repeated measures design). The AUT group showed HR deceleration during intrusive stranger approach. HR decelerations in controls were evident at less intrusive points in the assay. Neither AUT nor comparison groups showed HR increases during the stranger approach.
CONCLUSIONS: Autistic children show a different pattern of HR and VT reactivity during intrusive social events than do comparison children. This pattern of physiological reactivity could suggest an altered response threshold to social information in children with autism that could have implications for early identification and treatment.
SPONSORS: NIMH; NAAR
ABSTRACTS

REDUCED NEURAL SPECIFICITY FOR OBJECTS AND FACES IN THE FUSIFORM GYRUS IN AUTISM SPECTRUM DISORDERS Natalia Maria Kleinhans, Todd Richards, Clark Johnson, Keith C Stegbauer, Geraldine Dawson, Elizabeth Aylward, Department of Radiology
Background: Social emotional processing deficits are a distinctive, debilitating feature of autism spectrum disorders (ASD), yet links connecting clinical symptomatology to neurobiological defects remain unclear.
Objective: The purpose of this study was to identify the neural substrates of face and object processing in individuals with autism spectrum disorders.
Methods: We conducted an FMRI study of face processing; a primary component of social cognition, in 19 high functioning adults with ASD and 17 age and IQ matched controls. Perception and recall of neutral faces compared to houses was examined using a one-back working memory paradigm.
Results: Both ASD and control groups evidenced significant, bilateral activation in the fusiform gyrus and amygdala during face processing compared to house processing. However, control participants had significantly greater lateral fusiform activation than the participants with ASD in response to faces. In contrast, the ASD group evidenced significantly greater bilateral activation in the medial fusiform gyrus than the control group during face processing. (This region of the medial fusiform gyrus has been found to activate during viewing of houses and places in previous published studies.) No significant group differences were observed in the level of amygdala activation.
Conclusion: These results are consistent with previous FMRI studies of face processing in ASD, which posit that fusiform dysfunction is associated with the social deficits observed in this disorder. Reduced experience with faces, a clinical characteristic of this disorder, may result in diminished neural specificity of the medial and lateral fusiform gyrus for processing objects and faces, respectively, as was observed in the current study.
Funding source: NICHD (U19 HD34565) and NIMH (U54MH066399)

HEMISPHERIC DIFFERENCES IN RESOLVING LEXICAL AMBIGUITY IN HIGH FUNCTIONING AUTISM Rajesh Kumar Kana, Diane L Williams, Robert A Mason, Timothy A Keller, Nancy J Minshew, Marcel Adam Just, Center for Cognitive Brain Imaging, Carnegie Mellon University
Background: Studies have found that people with autism have difficulty in using context to disambiguate linguistic material. Considering this general difficulty, people with autism would have more problems in accessing the subordinate meaning of an ambiguous word (e.g. Sam ran...
from the bank when the huge alligator climbed out with a fish) than its dominant meaning (e.g. Sam ran from the bank when the angry robber hurried out with the money).

Objectives: Investigate the brain activation and functional connectivity in autism between neural systems participating in disambiguating ambiguous words in sentences.

Methods: This study examined the brain activation in 12 adult participants with autism and 12 age and IQ matched control participants while they read sentences containing words with dominant ambiguous, subordinate ambiguous, and unambiguous meanings.

Results: While the participants with autism showed ambiguity effect for both dominant and subordinate meanings of ambiguous words, the control group showed ambiguity effect only for the subordinate meanings. In addition, the participants with autism showed more right hemisphere activation than controls while processing the ambiguous sentences, whereas the control participants showed more activation in the left hemisphere language regions such as left inferior frontal gyrus. We also found reduced functional connectivity in autism between key participating cortical regions.

Conclusion: Brain activation and functional connectivity results reflect the processing differences between the autism and control participants.

Source of Funding: NICHD/CPEA

FACE PROCESSING IN AUTISM: FMRI/EEG SOURCE LOCALIZATION CORRELATIONS

Todd L Richards, Neva Oskin, Heracles Panagiotides, Sara Webb, Andrew Poliakov, Natalia Kleinhans, Elizabeth Aylward, Geraldine Dawson, University of Washington

Background: Face processing has been measured using event-related potential (ERP) component, N170, is faster and more robust for face stimuli than for other complex visual stimuli.

Objective: To correlate ERP source localization derived N170 latency and amplitude with fMRI derived brain activation in the fusiform during viewing of faces and houses in individuals with autism.

Methods: ERP data were acquired with an Electrical Geodesics 128-electrode system from six high-functioning adults with autism and six normal controls. Pictures of faces and houses were presented. Source localization was performed using dipole modeling with BESA software. fMRI data were collected from a 1.5 Tesla GE Signal scanner using a gradient-echo echoplanar pulse sequence (TR/TE 3000/50 milliseconds). Bivariate correlations were computed using SPSS between fMRI averaged z-scores within the right and left fusiform (defined on template brain) and BESA source localized N170 latency and amplitude.

Results: In controls, a significant correlation (p=0.056) was found between fMRI z-score and source-localized N170 latency in the right fusiform. No significant correlations were found for the autism group on either the left or right fusiform.

Conclusion: These results indicate that the autistic subjects may differ from controls in the correlation between fMRI and EEG source-location of the N170.

Funding source: NICHD (U19 HD34565) and NIMH (U54MH066399)

DO SIMILAR NEURAL PROFILES UNDERLIE SOCIAL COGNITIVE DEFICITS IN SCHIZOPHRENIA AND AUTISM? Amy E Pinkham, David L Penn, Joseph B Hopfinger, Kevin A Pelphrey, Department of Psychology, University of North Carolina - Chapel Hill

Background: Amygdala dysfunction may contribute to impairments in complex social judgments in both schizophrenia and autism.

Objectives: Compare amygdala activation in individuals with high-functioning autism (HFA), individuals with schizophrenia (SCZ), and healthy control individuals (HC) as they complete the Trustworthiness/Approachability task.

Methods: fMRI data was collected from 12 individuals with HFA, 12 with SCZ, and 12 HC as they made trustworthiness evaluations and age determinations of faces. Data was analyzed to examine differences in neural activation between trust and age judgments, between faces rated as trustworthy and trustworthy, and between groups.

Results: In contrast to previous reports of reduced amygdala activation in HFA, our sample showed significant activation while making social judgments and did not differ from HC. Individuals with SCZ showed reduced activation as compared to both HC and HFA groups, and neither the HFA or SCZ group showed differential amygdala activation to social vs. nonsocial judgments or to faces rated as trustworthy vs. trustworthy. In this respect, individuals with HFA and SCZ showed similar abnormalities in amygdala functioning.

Conclusions: This study is among the first to show activation of the amygdala in HFA during
complex social judgments. Additionally, individuals with SCZ and HFA may not differentiate between social and non-social judgments at the neural level and the amygdala may not be specialized for processing social stimuli in these disorders.

Sponsor: NARSAD
Oral Session #14
Early Development

Chair: Bernadette Rogé

Speakers:
Fiona S McEwen, Francesca Happé, Patrick F Bolton, Robert Plomin, Social, Genetic and Developmental Psychiatry (SGDP) Centre, Institute of Psychiatry, King’s College
Nola Watt, Amy Wetherby, Angie Barber, David McCoy, Lori Book, FIRST WORDS Project, Florida State University
Stacy Shumway, Amy Wetherby, Sally Kahn, Allison Plumb, David McCoy, FIRST WORDS Project, Florida State University
Kerstin Wittemeyer, Bernadette Rogé, Carine Mantoulan, Ghislain Magerotte, Université Toulouse Le Mirail CERPP

ABSTRACTS

EARLY IMITATION AND LATER AUTISTIC BEHAVIOUR: A LONGITUDINAL TWIN STUDY Fiona S McEwen, Francesca Happé, Patrick F Bolton, Robert Plomin, Social, Genetic and Developmental Psychiatry (SGDP) Centre, Institute of Psychiatry, King’s College

Background: Imitation impairments are common in young children with autism but the precise nature of the relationship between imitation and autism is unclear.

Objectives: Explore the relationship between imitation ability at two years and autistic symptoms at eight years using longitudinal data from a large, community-based twin sample.

Methods: Data were collected as part of the Twins Early Development Study (TEDS) in the UK. A measure of imitation was administered and scored by parents when twins were two years old. The Childhood Asperger Syndrome Test (CAST) was used by parents to rate twins at eight years, providing a continuous measure of autistic-like behaviour in social, communication and non-social (restricted and repetitive interests and behaviours) domains.

Results: Data from 2874 twin pairs were analysed (48.5% male; 34.6% monozygotic). Logistic regression showed that children who scored in the lowest 5% of imitation at two years were significantly more likely to score over the CAST threshold at eight years (Exp² = 3.75, p < .001). This was driven by high scores in the social domain (Exp² = 3.45, p = .004); poor imitation did not predict high levels of communication or non-social autistic-like behaviours.

Conclusion: In a population-based sample early imitation problems are related specifically to autistic-like behaviours in the social, but not communication or non-social domains.

Sponsor: MRC

REPETITIVE AND STEREOTYPED BEHAVIORS IN AUTISM SPECTRUM DISORDERS FROM 18 TO 24 MONTHS Nola Watt, Amy Wetherby, Angie Barber, David McCoy, Lori Book, FIRST WORDS Project, Florida State University

Background: Little is known about the presentation of repetitive and stereotyped behaviors (RSB) in children with autism spectrum disorders under two years of age.

Objectives: The purpose of this prospective, longitudinal study of the FIRST WORDS Project was to describe the types, rate, and proportion of RSB in children with ASD, developmental delay (DD), and typical development (TD) from 18 to 24 months of age, and to determine group differences and relationships between RSB and developmental level and later ADOS symptoms.

Methods: Videotapes of CSBS DP (Wetherby & Prizant, 2002) Behavior Samples for 123 children (50 ASD, 50 TD, and 23 DD) between 18 and 24 months of age were analyzed using the Noldus Observer 5.0 software to obtain precise measures of frequency and duration of RSB. Twenty-eight topographies of RSB were coded in 4 categories: repetitive movements with objects (RMO) and body (RMB), and unusual motor (UM) and unusual sensory (US) behaviors.

Results: The ASD group demonstrated a significantly higher proportion of RMO and higher proportion and rate of total RSB than both the DD and TD groups. The ASD group also
demonstrated more RMB and a significantly larger inventory of different RSB than the TD group. Proportion and rate of total RSB were moderately correlated with restricted and repetitive behaviors on the ADOS, and were negatively correlated with nonverbal developmental level in the third year.

Conclusion: RSB were evident between 18 and 24 months of age. These findings have implications for early identification and for understanding the role of RSB in the development of early symptoms of ASD.

Sponsor: USDOE, OSERS

COMMUNICATIVE ACTS OF CHILDREN WITH AUTISM SPECTRUM DISORDERS BETWEEN 18 AND 24 MONTHS OF AGE

Stacy Shumway, Amy Wetherby, Sally Kahn, Allison Plumb, David McCoy, FIRST WORDS Project, Florida State University

Objective: The purpose of this prospective study was to compare differences in the communicative acts of children between 18 and 24 months of age later diagnosed with ASD, matched with a group of children with developmental delays (DD) and typical development (TD).

Method: Archival videotaped CSBS DP Behavior Samples collected through the FIRST WORDS® Project were re-coded for 50 children with ASD, 23 with DD, and 50 with TD. Data were coded using the Noldus Observer® Video-Pro software, allowing for precise measurement of the frequency and co-occurrence of behaviors. Total communicative acts, acts directed with gaze, and acts directed with a vocalization and/or gesture were coded in relation to communicative function (behavior regulation, social interaction, joint attention).

Results: Children with ASD showed a significantly lower rate of total acts, acts with gaze, and acts with vocalizations than children with DD and TD. The ASD group used a significantly greater proportion of acts for behavior regulation and a significantly lower proportion of acts for joint attention than children with DD and TD. Children with ASD used a significantly lower proportion of acts with vocalizations when communicating for behavior regulation than children with TD. There were no group differences on the proportion of acts with gaze. The ASD group used a significantly lower proportion of deictic gestures, comparable proportion of representational gestures, and a higher proportion of other gestures (e.g., reach/touch adult) than children with DD and TD.

Conclusions: These findings demonstrate distinct patterns of communication in children with ASD between 18 and 24 months of age compared to children with DD and TD, consistent with those found with older children. This research will contribute to understanding the ontogeny of communication in children with ASD and help inform early identification efforts.

Sponsor: USDOE, OSERS

CAN CHILDREN WITH AUTISM SPECTRUM DISORDERS IMPROVE IN THE PRAGMATIC ASPECTS OF COMMUNICATION? - A COMPARATIVE EARLY INTERVENTION STUDY

Kerstin Wittemeyer, Bernadette Rogé, Carine Mantoulan, Ghislain Magerotte, Université Toulouse Le Mirail CERPP

Impairments in the pragmatic aspects of communication are the most salient in individuals with autism spectrum disorders (ASD’s), even at an early age. Previous studies have demonstrated the efficacy of early intervention in improving verbal and non-verbal behaviour in communicative interactions.

OBJECTIVE: We predicted that the children with ASD in our intervention program, which was based on accepted early intervention design criteria (National Research Council, 2001), would show improved pragmatic skills.

METHODS: Our study compared two groups of children with ASD’s, matched on the Griffiths Mental Scales and chronological age (age range: 30-70 months). The experimental group (N=15) received individualised intervention over a period of two years (1:1 sessions, varied teaching contexts, 15-20 hours intervention per week), whereas the control group (N=10) received no study intervention.

The children’s pragmatic skills were assessed using: the Early Social Communication Scales (ESCS); Shulman’s Test of Pragmatic skills; VABS; Theory of Mind tasks. A Single Case Protocol (SCP) was also used to assess the communicative forms and functions displayed by these children during standardized situations.

RESULTS: Our findings showed that the children of the experimental group improved on the composite pragmatic measures and were more able to use complex communication forms to regulate others, interact successfully and to share attention (ESCP, SCP). They also acquired greater conversational abilities (Shulman, SCP). Data from the control group does not show such
marked improvements.
CONCLUSION: Evidence was found to support the use of our early intervention program to improve the pragmatic aspects of communication.
The research program has obtained financial aids from the Fond Social Européen, the FNRS and France Telecom.
ABSTRACTS

SLEEP IN CHILDREN WITH AUTISM, DEVELOPMENTAL DELAY, OR TYPICAL DEVELOPMENT Beth Goodlin-Jones, A. Wu, K. Tang, T.F. Anders, M.I.N.D. Institute, UCDMC

Introduction: This project describes the sleep patterns in preschool (2-5 years) children with autism (Aut), developmental delay (DD), or with typical development (Typ) from objective measures (actigraphy, videosomnography) and parent diaries and questionnaires.

Methods: Preliminary results are available on the first half of the sample (n=101). Children are assessed 3 times for one week during a six-month time frame. These results pertain to the first week. Children wear the actigraphy monitor for one week, complete daytime functioning assessments, and have two nights of videotaping.

Results: At the time of consenting, 35% of families reported that their child had a sleep problem. The grand mean total sleep duration was 9 hours, 8 minutes (sd= 47) (range= 6.95 hrs to 10.9 hrs, n=83). For nighttime sleep duration, DD slept significantly less than Typ and Aut were intermediate (F 2,94 = 4.6, p<.05). In terms of time spent awake vs. awake while in bed, DD spent significantly more time awake (14%) than Aut (10%) (F 2,94 = 7.26, p <.05). Classification of sleep problems found no diagnostic group differences in terms of Sleep Onset problem (overall 34.7%). However, for night waking problems (overall 15%), DD (33%) have greater percentage of night waking problems than Aut or Typ. There were no associations on a PEP-R battery with sleep but significant associations were present with sleep duration and Teacher report.

Conclusions: Children with DD have greater difficulty with night waking and sleep duration than children with Aut orTyp.

Funding: NIH (RO1 MH068232)(TFA)

INCREASED PREVALENCE OF MATERNAL AUTOANTIBODIES AGAINST FETAL BRAIN IN AUTISM Daniel A Braunschweig, Paul Ashwood, Judy A Van de Water*, Irva Hertz-Picciotto, Robin Hansen, Lisa Croen, University of California, Davis

Background: While there presently is no clear etiology for autism, published reports have demonstrated associations between genetic factors, environmental toxins and abnormal immune responses with the development of autism. Transplacental passage of pathogenic maternal IgG antibodies from mothers with various systemic autoimmune disorders has been linked with the etiology of a number of fetal disorders including neonatal Lupus and Myasthenia Gravis. Thus, we propose that among a subgroup of susceptible individuals, transplacental transfer of maternal IgG antibodies may play a role in the etiology of autism.

Objective: We sought to analyze serum from the mothers of children with autism for the presence of IgG directed against human fetal brain proteins by of Western blot analysis.

Methods: Sera from more than 200 mothers of children with autism, aged-matched typically developing controls, and children with other developmental disabilities were analyzed by Western blot against human
fetal brain proteins.
Results: Significant differences in the prevalence and specificities of maternal IgG antibodies directed against fetal brain derived from mothers of autistic children compared with that from mothers of typically developing and disease controls was noted. Antibody reactivity was over two-fold more prevalent among mothers of autism patients compared with mothers of typically developing controls and could be separated into three distinct regions including bands at approximately 40kD, 57kD and a doublet of bands at approximately 70kD.
Conclusions: These preliminary findings suggest that serum antibodies from mothers who have children with autism may react against fetal brain proteins and may have detrimental effects during neurodevelopment.
[These studies were funded by NIEHS grant 1 P01 ES11269-01.]

ELEVATED LEVELS OF GROWTH-RELATED HORMONES IN AUTISM AND AUTISM SPECTRUM DISORDER James Louis Mills, Mary L. Hediger, Cynthia A. Molloy, George P. Chrousos, Patricia Manning-Courtney, Kai F. Yu, Mark Brasington, Lucinda J. England, NICHD, National Institutes of Health

Background: Autistic children are known to have larger head circumferences; whether they are also taller and heavier is less clear. Little is known about growth-related hormone levels in autistic children.
Objectives: To determine whether autistic children were taller, heavier, and have higher levels of growth-related hormones than control children.
Methods: Boys with autism spectrum disorder (ASD) or autism (n= 71) and age-matched controls (n= 59) had height, weight and head circumference measurements. Blood samples were assayed for IGF-1, IGF-2, IGFBP3, growth hormone binding protein (GHBP) and for DHEA and DHEAS.
Results: The autism/ASD cases had significantly (p=.03) greater mean head circumferences (z-score 1.24, SD 1.35) than controls (z-score 0.78, SD 0.93). Cases also had significantly (p=.01) greater weights (z-score 0.91, SD 1.13) than controls (z-score 0.41, SD 1.11). Heights did not differ significantly between groups (p=.65); however, cases had significantly (p=.003) higher body mass indices (z-score 0.85, SD 1.19) than controls (z-score 0.24, SD 1.17). The case group's levels of IGF-1, IGF-2, IGFBP3 and GHBP were all significantly higher (p<.0001), and cases were more likely than controls to have detectable levels of DHEAS (41% vs. 24%, p=.03).
Conclusion: Boys with autism/ASD had significantly higher levels of many growth-related hormones. These findings could help explain the significantly higher head circumferences, weights and BMIs we found. Future studies should examine the potential role of growth-related hormones in the pathophysiology of autism.
Funding: Intramural research program, NICHD, NIH.

BLOOD METAL CONCENTRATIONS IN THE CHARGE STUDY Irvia Hertz-Picciotto, Peter G Green, Lisa A Croen, Robin Hansen, Paula Krakowiak, University of California, Davis

Background: Adverse effects on neurodevelopment have been observed for lead and mercury. Previous reports of associations between body burdens of mercury and autism have been inconsistent or come from studies lacking rigorous quantitation of metals.
Objectives: To determine if blood levels of metals differ between children with versus without autism.
Methods: The CHARGE Study has been enrolling a population-based sample of 2-5 year old children with autism (AU), children with developmental delay (DD), and general population (GP) controls frequency matched on age, sex, and geographic region. Venous blood samples were drawn and metals were measured by inductively coupled plasma/mass spectrometry. Metals determinations were completed on 380 total children (261 AU, 40 DD, 79 GP). The AU cases were further divided into regressive (n=101) and early onset (n=119). ANOVA with unequal variances was used to compare means across groups.
Results: No significant difference in blood mercury was observed between the AU children (mercury mean±SD: 0.50±1.15 micrograms/dl) and either DD (0.41±0.51 micrograms/dl) or GP (0.51±0.74 micrograms/dl) children. Blood lead values were similar across AU, DD, and GP children (1.38, 1.30, 1.41 micrograms/dl, respectively). Similarly, children with a regressive trajectory versus early onset did not differ in their concentrations of circulating metals.
Conclusions: In 2-5 year olds, neither mercury nor lead concentration in peripheral blood of children with autism differs, on average, with that measured in population-based controls.
Sponsors: NIEHS, EPA, M.I.N.D. Institute
PS6.1
AGE OF PARENTS AND RISK OF AUTISM IN A LARGE CALIFORNIA BIRTH COHORT
Meredith Anderson, Gayle C Windham, Yinge Qian, Lisa A Croen, Judith K Grether, California Department of Health Services

BACKGROUND: Previous studies are inconsistent regarding autism risk and maternal or paternal age.
OBJECTIVE: To investigate the relationship between parental age and childhood autism in a large population.
METHODS: The California Department of Developmental Services (DDS) serves children with developmental disabilities, maintaining an electronic client database with diagnostic information. We identified 18,716 singletons born in California 1989-2001 with DDS-eligible autism and compared them to 7,039,330 singleton live births who survived to age one. Demographic characteristics, including maternal and paternal age, were obtained from birth certificates. We used Poisson regression to estimate the risk of autism in relation to parental age, adjusting for sex, birth weight, birth year, gestational age, parity, parental education and race/ethnicity, and a proxy measure of SES.

RESULTS: Maternal and paternal age were grouped as: <20, 20-24, 25-29, 30-34, 35-39, and 40+ years. In both maternal and paternal age crude models, risk of autism increased monotonically for each age group; compared to 25-29 year olds, the rate ratio (RR) for mothers 40+ was 1.85 (95% CI 1.71-1.99) and for fathers 40+ (separate model) was 1.90 (95% CI 1.80-1.99). In a model including both maternal and paternal age and covariates (above), risks for older maternal and paternal age were attenuated but still significant. The RR for the 40+ maternal age group was 1.48 (95% CI 1.35-1.62), and for the 40+ paternal age group was 1.38 (95% CI 1.29-1.47).

CONCLUSIONS: Our findings show that autism risk increases modestly with increasing maternal and paternal age.

SPONSOR: CA CADDRE, CDC U10/CCU920392-05

PS6.2
MATERNAL INFERTILITY HISTORY AND TREATMENT AND CHILDHOOD AUTISM SPECTRUM DISORDERS
Lisa A Croen, Daniel V Najjar, Roxana Odouli, Mary Croughan, Yvonne W Wu, Judith K Grether, Kaiser Permanente Division of Research

Background: Trends in infertility treatment parallel trends in autism prevalence, however data on a possible association is currently lacking.
Objective: To explore the association between maternal infertility history and treatment and childhood autism spectrum disorders (ASD).

Methods: We conducted a case-control study among children born at Kaiser Permanente Northern California (KP) from 1995-1998. Cases (n=377) were children with an ASD diagnosis (ICD-9-CM 299.0, 299.8) recorded in KP outpatient databases. Controls (n=1930) were randomly sampled from the remaining births without ASD, frequency matched to cases on gender, birth year, and birth hospital. Information on maternal infertility history, defined as evaluation at an infertility clinic, infertility diagnosis, or use of infertility medication was obtained from health plan databases. Odds ratios (ORa) adjusted for maternal age, education, race/ethnicity, child gender, and parity were estimated using logistic regression.

Results: Maternal history of infertility was more common among mothers of cases than controls (14% vs. 9%, p=0.01), as was conception on infertility medication (6% vs. 3%, p=0.004). Among singletons, the adjusted risk of ASD was similar for children of women with and without a history of infertility (ORa=1.0, 95% CI 0.7-1.5). Among multiple births, adjusted risk of ASD was significantly increased for children of women with a history of infertility (ORa=4.6, 95% CI 1.5-14.4), or who conceived during infertility clinic care (ORa=7.0, 95% CI 1.9-25.9) or while on infertility medication (ORa=5.4, 95% CI 1.7-16.9).

Conclusions: These data suggest that maternal infertility history and treatment are associated with ASD risk in multiple births.

Sponsor: CDC and KFRI

PS6.3
COMPARISON OF THE PREVALENCE OF AUTISM SPECTRUM BEHAVIOURS IN SINGLETON PRIMARY SCHOOL CHILDREN AND TWINS IN AN EPIDEMIOLOGICAL SAMPLE
Sarah Curran, Katharina Dworzynski, Robert Plomin, Angelica Ronald, Karrie Allison, Carol Brayne, Fiona Scott, Patrick Bolton, Institute of Psychiatry De Crespigny Park

This population based study of singletons focused on children in Cambridgeshire schools aged between 5 years and 9 years (all children in Years 1 - 4) at the distribution date of the screening questionnaire (Scott et al 2005). 155 schools (142 mainstream and 13 private schools) plus 7 special schools in Cambridgeshire. Woide geographical areas were chosen to represent broad cross-section including urban and rural areas across the county. The twin sample data came from the twins early development study (TEDS), a longitudinal, UK population study of twins born in 1994-96 (Trouton et al 2002). They were 7-9 years when their parents were approached. All families identified by the UK Office for
had ever expressed concerns about their child's diagnoses, and whether teachers or other professionals were sent questionnaires which included a screen for subtler presentations of autism spectrum disorder (the CAST, Childhood Asperger Syndrome Test, Scott et al., 2002; Williams et al., 2005), questions about existing diagnoses, and whether teachers or other professionals had ever expressed concerns about their child's development or behaviour.

The CAST scores analysed using linear multiple regression methodology. ANOVA to examine the effects of gender and grouping (twin or singleton group). ANOVAs to investigate how different zygosity groups (MZ, DZ or DZO) compared to the singleton group in each sex. Dunnett tests to follow up significant results to establish differences between individual zygosity groups and singletons.

**PS6.4 NO AUTISM AMONGST INUITS FROM NORTHERN QUEBEC?**

**Eric Fombonne, Johanne Morel, Judy Macarthur, Montreal Children's Hospital**

Background: Autism has been found in most population where it has been investigated. We have preliminary evidence that autism does not exist in the Inuit population of Northern Quebec.

Methods: The authors know extensively the Inuit population (N=12,000) of Northern Quebec. They have been responsible for more than 15 years for pediatric care and special education in the 14 villages of this huge territory. There is a universal free health care and educational system, with repeated periodic medical examinations from birth onwards, compulsory attendance to school, and excellent medical/educational tracking record system for each child. Results: No case of autism was ever reported in an Inuit child in this population in the last 15 years. A computer search of discharge medical and psychiatric diagnoses failed to identify an ICD-9 diagnosis suggestive of autism or one of its variant. No case was referred for psychiatric evaluation or special educational assessment that would be consistent with autistic developmental impairments. In order to develop a full epidemiological enquiry, we have conducted a pilot study in 2 villages that demonstrated the feasibility of this planned investigation. Conclusion: Autism appears to not exist amongst Inuits from Northern Quebec. If confirmed, it would have significant implications for the genetic understanding of autism. In addition, as Inuits are exposed through their fish-eating practices to high pre- and post-natal levels of mercury, it would also suggest that high mercury exposure in itself does not increase the risk of autism.

**PS6.5 NEONATAL ANTIBODIES TO INFECTIOUS AGENTS AND RISK OF AUTISM SPECTRUM DISORDERS (ASD)**

**Judith K Grether, Lisa A Croen, Karin B Nelson, Meredith C Anderson, Robert H Yolken, California Department of Health Services**

**BACKGROUND:** Infectious agents during pregnancy have been hypothesized to contribute to ASD. IgG antibodies measured in newborns are obtained transplacentally and are a marker for maternal exposure; IgM and IgA antibodies are generated by the fetus and correlate with active perinatal infection.

**OBJECTIVE:** To evaluate antibodies and immunoglobulins in newborn specimens in a population-based study.

**METHODS:** All subjects were born in 1994 in one of six SF Bay Area counties. Children with autism (n=258) were receiving services from California Department of Developmental Services or Kaiser Permanente of Northern California; controls (n=270) were selected randomly from birth certificate files within gender strata. Selected antibodies to infectious agents and levels of total class-specific immunoglobulins were measured in blood samples eluted from filter papers by enzyme immunoassays techniques.

**RESULTS:** The levels of IgG class antibodies measured in case and control groups did not differ for Herpes Simplex Virus Types 1 and 2, CMV, Epstein Barr, Human Herpes Virus Type 6, Varicella Zoster, Influenza A, Influenza B, and Toxoplasma gondii nor did IgM class antibodies to Toxoplasma gondii or Cytomegalovirus. Levels of total IgG were somewhat lower in cases (ORadj=0.97 (95% CI 0.95, 0.996), but no difference was seen for total IgM or IgA class immunoglobulins

**CONCLUSION:** Perinatal exposure to these or other infectious agents which generate increased levels of fetal immunoglobulins are unlikely to be major causes of autism in a US population.

**SPONSOR:** California CADDRE CDC U10/CCU920392-05 and Stanley Medical Research Institute.

**PS6.6 INCREASED AUTISM RISK AND PRENATAL EXPOSURE TO HURRICANES IN NEW ORLEANS**

**Denis Kenneth Kinney, Andrea Maxwell Miller, David Crowley, Emerald Huang, Erika Gerber, McLean Hospital**

**BACKGROUND:** Previous studies have found that autistic children are more likely than controls to have prenatal exposure to either maternal medical complications or stressful life events. Those findings, however, could potentially have been due to biased maternal reports or to effects of genes for autism. Objective: To investigate whether exposure to stress during certain gestational periods is associated with increased risk for autism, using a research design that is less subject to artifacts that were potentially present in previous research.
Methods: Hypothesis: autism risk will increase with increasing severity of exposure to hurricanes and tropical storms during vulnerable months of gestation. National Weather Service data were used to identify severe storms that affected Louisiana from 1980-1995 and the parishes (counties) hit by the eyes (centers) of storms. To calculate autism prevalence rates for cohorts that were exposed to storms during different gestation periods, we used de-identified data on birth dates and birth parishes for children who were born in Louisiana and diagnosed with Autistic Disorder by state mental health facilities, together with corresponding census data on all live births in Louisiana.

Results: Cohorts exposed prenatally to storms in New Orleans or in parishes hit by eyes of storms had significantly higher prevalence rates if exposure occurred in months near the middle or end of gestation, rather than other months. Prevalence was particularly high for the cohort exposed in those months to hurricane eyes in New Orleans.

Conclusion: The results complement other studies that have found that prenatal stress induces hypersensitivity to postnatal stress in laboratory animals, and that such hypersensitivity makes children especially vulnerable to developing autism.

Sponsor: Cure Autism Now Foundation*

PS6.7
THE PREVALENCE OF AUTISM ON STATEN ISLAND Jennie K Kline, Tina Rovito-Gomez, Ira L Cohen, Mailman School of Public Health

Background: Although the etiology of autism is unknown, there has been heightened concern that the prevalence of autism on Staten Island is abnormally high.

Objectives: To assess the prevalence of autism in children aged 6-12 years who attend schools on Staten Island.

Method: Children suspected of having autism are referred to the Board of Education’s (BOE) Multi-Disciplinary Committee on Preschool Special Education or Committee on Special Education, depending on age. Cases meeting committee criteria for autism enter public or private special education programs. On Staten Island, the majority of such children, aged 6-12, attend special public school programs, while the remainder attend a large private school. Approximately 50% of children attending public school programs and 80% attending the private school were assessed with the ADI-R and ADOS-G. In the remaining cases, DSM-IV based record reviews were done.

Results: Ninety-eight percent of children attending public school programs and 100% attending the private school met ADI-R or ADOS-G criteria for autism. Agreement between classification based on record reviews and school criteria was 91%. Agreement was 100% in 25 cases in which an ADI-R was completed. The overall prevalence of autism was 43 cases per 10,000 (90% CI: 37-50 per 10,000); prevalence varied with grade level (17 to 72 cases per 10,000) and with sex, with younger children and males having higher rates.

Conclusion: Taking account of age, the prevalence of autism on Staten Island is comparable to that in other samples.

PS6.8
INCREASED RISK OF INJURY AND ACCIDENT IN CHILDREN WITH AUTISM Brian K Lee, Li-Ching Lee, Jen J Chang, Craig J Newschaffer, Center for Autism & Developmental Disabilities Epidemiology, Bloomberg School of Public Health, Johns Hopkins University

Background: Some evidence indicates that children with autism are at a higher risk for injury or accident due to sensorimotor deficits and difficulties in responding appropriately.

Objectives: To report injury and accident in children aged 3-5 with autism, ADHD/ADD, and selected typical controls from a US national survey.

Methods: This study analyzed data from the National Survey of Children’s Health (NSCH). NSCH was conducted by CDC to collect self-report data from parents who had children aged 0-17 across the US. A total of 82 children were identified as having an autism diagnosis, and 191 ADHD/ADD. Typical controls were 13,398 children without known disabilities or other medical conditions. Regression analysis was performed to compare the risk of injury and accident in children with autism against children with ADHD/ADD, and typical controls.

Results: The prevalence of injury that required medical attention in the past 12 months was 19.5%, 18.3%, and 10.6% for autism, ADHD/ADD, and typical controls, respectively. The prevalence of either injury or accident was 20.7%, 23.0%, and 12.2% for autism, ADHD/ADD, and typical controls, respectively. Results from multivariate analysis indicated that the autism group was twice as likely (95% Confidence Interval of Odd Ratio: 1.16, 3.65) to experience injury that needs medical attention than typical controls but was not different from the ADHD/ADD group.

Conclusion: The findings confirmed that young children with autism are at a higher risk of injury. This study is supported by CDC cooperative agreement U10/CCU320408-05

PS6.9
STUDY OF PREVALENCE OF AUTISTIC SPECTRUM DISORDERS IN CHILDREN WITH DOWN SYNDROME Rosane Lowenthal, Sabrina Ribeiro Sabadini, Marcos Tomanić Mercadante, Cristiane Silvestre de Paula, Universidade Presbiteriana Mackenzie

Although autism is said to occur rarely with Down syndrome, it may be more common in those persons with Down syndrome who also show superimposed behavioural problems. There are no epidemiological studies of the prevalence of autistic spectrum disorders in a large population of children with Down syndrome in Brazil. The aim of the study was to identify the comorbidity of autistic spectrum disorders in a population from APAE- Paraná. (Association of parents and friends by mentally retarded children. 531 parents of children
with Down syndrome, between 5 and 19 years old, were asked to complete the Questionnaire on Behavior and Social Communication (ASQ). The questionnaire items provide an operational diagnosis which is based on the behavioural item scores in the three areas of functioning: reciprocal social interaction; language and communication; and repetitive and stereotyped patterns of behaviours. Right now, we are proceeding the research. By the occasion of the congress, it will be concluded. It is important that autism is recognized, identified, and fully assessed in individuals with Down syndrome in order for them to receive appropriate education and support.

**PS6.10**

**MATERNAL AND PATERNAL AGE AND RISK OF AUTISM SPECTRUM DISORDERS**

*Daniel V Najjar, Bruce Fireman, Judy K Grether, Lisa A Croen, Kaiser Permanente Division of Research*

Background: Advanced maternal age has been associated with risk of autism spectrum disorders (ASD) in many previous studies, but the role of paternal age has rarely been studied.

Objective: To explore the association between maternal and paternal age and ASD.

Methods: We examined ASD risk in all singleton children born at Kaiser Permanente Northern California (KP) from 1995-1999. We identified 593 children who had at least two ASD diagnoses (ICD-9-CM 299.0 or 299.8) recorded in KP outpatient databases before May 2005. They were compared to all 132,251 remaining singleton KP births. Maternal and paternal age and other characteristics were ascertained from KP and birth certificate files.

Proportional hazards regression was used to evaluate ASD risk in relation to maternal and paternal age adjusted for sex and birth date of the child, parity, maternal and paternal education, and whether these results remain consistent in a larger sample, and the role of paternal age has rarely been studied.

Conclusions: These data suggest that advanced maternal and paternal age across ASD severity strata were not statistically significant.

Results: Risk increased significantly with each 10-year increase in maternal age (HRa=1.31, 95% CI 1.07-1.62) and paternal age (HRa=1.28, 95% CI 1.09-1.51). Adjusted hazard ratios were elevated within the subgroups of children with autistic disorder (maternal age: HRa=1.18, 95% CI 0.87-1.60; paternal age: HRa=1.34, CI 95% 1.06-1.69) and PDD-NOS/Asperger’s (maternal age: HRa=1.45, 95% CI 1.09-1.93; paternal age: HRa=1.24, 95% CI 0.99-1.55). Differences in risk associated with parental age across ASD severity strata were not statistically significant.

Conclusions: These data suggest that advanced maternal and paternal age are independently associated with ASD risk.

SPONSOR: CDC and KFRI

**PS6.11**

**EVALUATING THE PERFORMANCE OF SEVERAL PARENT AND TEACHER SCREENING QUESTIONNAIRES FOR AUTISM SPECTRUM DISORDERS**

*Helene MJ Ouellette-Kuntz, Helen Coo, Nathalie Garcin, Ira L Cohen, Garth Smith, Jeanette JA Holen, Queen’s University, Kingston, Ontario*

Background: Use of gold-standard tools to confirm the diagnosis of autism spectrum disorder (ASD) in large epidemiology studies is unfeasible.

Objective: To investigate the feasibility of using parent- and teacher-completed questionnaires to confirm case status among children clinically diagnosed with an ASD.

Methods: Parents in Southeastern Ontario who are participating in a national epidemiology study were asked to complete the Social Communication Questionnaire (SCQ), Childhood Asperger Syndrome Test (CAST), Autism Spectrum Screening Questionnaire (ASSQ), PDD Behavior Inventory (PDDBI), and Autism Diagnostic Interview-Revised (ADI-R). Teachers were asked to complete the ASSQ and the PDDBI. The Autism Genetic Resource Exchange’s (AGRE) Broad Spectrum (A) cutoff for the ADI-R was used to determine case status, and the sensitivity of the questionnaires was examined.

Results: Fifty-six of 137 families (40.9%) consented to participate. To date, 41 ADI-Rs have been done for families who completed questionnaires. All children met or exceeded the AGRE Broad Spectrum (A) cutoff, and were therefore considered cases. Sensitivity of the 3 parent questionnaires analyzed to date was 73.2% (ASSQ), 87.8% (CAST) and 90.2% (SCQ). The collective sensitivity for children who met the cutoff on at least 1 of the 3 questionnaires was 97.6%. Twenty-three of 41 teachers (56.1%) returned questionnaires.

Conclusion: Inclusion of data from teachers would reduce the sample size considerably, with little potential in this group for an increase in sensitivity. We will examine whether these results remain consistent in a larger sample, and will also measure specificity and other properties of these questionnaires using a control group.

Sponsor: Queen’s University Developmental Disability Program

**PS6.12**

**INFECTION IN THE FIRST TWO YEARS OF LIFE AND AUTISM SPECTRUM DISORDERS (ASD)**

*Nila J Rosen, Cathleen K Yoshida, Lisa A Croen, Kaiser Permanente Division of Research/ California Department of Health Services*

Background: Little is known about the relationship between postnatal infections and ASD.

Objective: To investigate the association between infections in the first two years of life and subsequent diagnosis of ASD.

Methods: We conducted a case-control study among children born at Kaiser Permanente Northern California (KP) from 1995-1999 who remained KP members for at least two years following birth. Cases (n=420) were children with an ASD diagnosis recorded in KP databases. Controls (n=2100) were randomly sampled from the remaining births without ASD, frequency matched to cases on gender, birth year, and birth hospital. Information on clinicians-diagnosed infections in the first two years of life and on several covariates was obtained from KP and birth certificate databases.

Results: In the first 30 days of life, the frequency of infection was higher among children with ASD compared to those without ASD.
PS6.13
PREVALENCE OF PERVASIVE DEVELOPMENTAL DISORDERS IN ICELAND IN A COHORT BORN 1994-1998
Evald Saemundsen, Pall Magnusson, Solveig Sigurdardottir, Vilhjalmur Rafnsson, Division of Autism and Communication Disorders, State Diagnostic and Counseling Center


Objectives: Report for the first time on the prevalence of all pervasive developmental disorders (PDDs) as defined by the ICD-10 in a new cohort.

Method: The cohort of the study consisted of 21,883 children born in the period 1994-1998. The data were collected from the records of the State Diagnostic and Counseling Center, a tertiary service charged with the surveillance of serious neuro-developmental disorders in the whole country. Diagnoses were based on evaluations with the ADI-R, and the ADOS and/or the CARS, and a consensus of an interdisciplinary team of clinicians. All the children were tested for cognitive level. Most of the children diagnosed during their early preschool years were reevaluated before entry to elementary school.

Results: One hundred twenty-eight children were diagnosed with PDDs. The prevalence per 10,000 for all PDDs was 58.5 (95% CI: 48.3 ; 68.6), for childhood autism 22.4 (95% CI: 16.1 ; 28.7), for other PDDs 29.7 (95% CI: 22.4 ; 36.9), and for Asperger's syndrome 6.4 (95% CI: 3.0 ; 9.7). The sex ratio for all PDDs was 3.3 boys for every girl. Of the children diagnosed with PDDs, 48.8% had IQ/DQs below 70.

Conclusion: There is a continued increase in the number of diagnosed cases of PDD in Iceland. The prevalence found in the present cohort parallels findings from recent population-based studies.

PS6.14
RISK OF AUTISM AND BIRTH CERTIFICATE DATA: A UTAH POPULATION BASED STUDY
Robert Satterfield, Judith P. Zimmerman, Shaheen Hossain, Lynne M. MacLeod, Judith Miller, William McMahon, Utah Department of Health, University of Utah Medical Center, the Utah Registry of Autism and Developmental Disabilities, Epidemiologist

Background: Identification of risk factors related to autism may facilitate early identification and prevention of autism.

Objectives: To investigate the association between selected maternal complications and obstetric procedures and the autism population.

Methods: Data were collected from the population of eight year olds in Utah during 2002 across 3 urban counties. The Utah Registry of Autism and Developmental Disabilities queried 33 medical sources and 8 school districts with autism exceptionality or ICD-9 codes 299.0 or 299.8, which resulted in 185 autism cases. These cases were merged to 1994 Vital Records. Results: The 185 autism cases were matched (62% matching rate) to the 1994 birth certificate records (26,830), resulting in the identification of 114 children with autism. Significant differences were found in mean birth weight for children with autism (3192 versus 3338 grams, p-value <.005) compared to the birth cohort. Autism cases experienced significantly higher rates of breech presentation (9.7% versus 4.1%, p-value <.007), cesarean section (20.2% versus 9.2%, p-value <.0001), and significantly higher rates of assisted ventilation > 30 minutes (4.4 versus 1.3, p-value <.005), compared to the birth cohort. The matched autism cases resulted in 82.5% male compared to 51.8% male in the birth cohort (p-value <.0001). Slightly increased differences were found in mother's age (27.2 years versus 26.5 years) and mother's education (13.8 years versus 13.3 years), however these were not statistically significant. Mothers of children with autism were more likely to be married, have slightly more prenatal care visits, and entered prenatal care earlier than their birth counterparts.

Conclusion: This multi-source linked population based study provided new findings that have not been reported by other studies. The results indicate the need for further investigation into potential risk factors during pregnancy and birth.

PS6.15
SERUM LIPID PROFILES IN AUTISM: THE CHARGE STUDY
Michelle M. Wiest, Lisa A. Croen, Robin L. Hansen, Steve M. Watkins, Irva Hertz-Picciotto, University of CA, Davis

Background: During development, lipids are integrated into brain tissue to provide essential cell structure and play key roles in cell signaling throughout life. Abnormal enrichment or depletion of serum lipids can reflect faulty metabolism throughout the body and may reveal underlying causes of symptoms associated with autism.

Objective: To determine if levels of serum lipids are associated with autism.

Methods: The study population comprised 138 autism cases and 49 general population controls selected from the CHARGE (Childhood Autism Risk from Genetics and the Environment) study. Autism diagnoses were confirmed using the ADI-R and the ADOS-G. Detailed data on medical, developmental and exposure history were collected and aliquots of blood samples taken from index
children (age range: 24-68 months) were sent to Lipomics Technologies Inc. for gas chromatography-based lipid profiling.

Results: Preliminary results indicate that age and sex adjusted differences in lipid concentrations are not consistently present between cases and controls. There was significantly more variation in certain lipids among cases than controls. For instance, docosahexaenoic acid (22:6n3) was significantly more variable within autism cases than controls, particularly in phosphatidylycholine (SD cases = 2.30; SD controls = 0.70).

Conclusions: Serum lipid concentrations, on average, do not differ between children with autism and children from the general population. Greater variability was observed within autism cases and requires further investigation.

PS6.16
PREDICTORS OF THE DEGREE OF IMPAIRMENT ASSOCIATED WITH AUTISM SPECTRUM DISORDERS Lisa D. Wiggins, Catherine E. Rice, Jon Baio, Centers for Disease Control and Prevention

Study Objectives: This study examines predictors of the degree of impairment associated with autism spectrum disorders (ASD). Predictors of interest included cognitive impairment (CI), DSM-IV diagnostic domains, and the presence of autism discriminator behaviors (ADB).

Methods: The study sample constituted 285 ASD surveillance cases defined by the Centers for Disease Control and Prevention. Trained clinicians applied a standardized coding scheme to abstract surveillance records to code the presence or absence of predictors of interest. CI was measured as IQ d 70. ADB were defined as behaviors that most distinguish children with ASD from children with other developmental disabilities.

Degree of impairment was coded as mild, moderate or severe and was based on all information contained in the source record.

Results: CI accounted for 35.2% of the variance in degree of impairment (p < .001). After controlling for CI, the number of criterions present in the stereotyped behaviors domain significantly predicted degree of impairment ($\hat{r}^2 = .13$, $p = .01$), whereas the number of criterions present in social and communication domains did not.

Preoccupation with parts of objects (where sensory dysfunction is coded) uniquely predicted degree of impairment ($\hat{r}^2 = .16$, $p = .003$). Sensory dysfunction was also one of the ADB that offered unique predictive ability ($\hat{r}^2 = .12$, $p = .02$).

Conclusions: Degree of impairment associated with ASD can be predicted by the presence of CI, the frequency of stereotyped interests and behaviors, and the level of sensory dysfunction. Our analyses suggest that sensory dysfunction is an especially robust predictor of degree of impairment associated with ASD that may provide clues to the various phenotypic expressions of the autism spectrum.

AUTISM SPECTRUM DISORDERS IN RELATION TO PARENTAL OCCUPATION: PURSUING THE "GEEK" HYPOTHESIS Gayle C Windham, Karen Fessel, Lisa A Croen, Judith K Grether, Ca Dept. of Health Services

Background: Previous studies suggested that fathers of children with autism spectrum disorders (ASD) are more likely to work as engineers or in other "geek" occupations, but findings may be affected by selection biases.

Objective: To explore whether fathers or mothers of children with ASD are over-represented in fields requiring "systemizing skills", in a population-based sample accounting for SES.

Methods: Subjects included 284 children with ASD and 659 gender-matched controls, born in 1994 in the San Francisco Bay Area. Parental occupation and industry were abstracted from birth certificates and coded according to the Bureau of Labor and Statistics. The main occupations of interest, engineering, computer programming and science, were grouped as "technical" occupations. An association with occupation may be related to parental SES, so we tried to define a referent group that was professionally similar. Odds ratios (ORs) were calculated by logistic regression, adjusting for parental age, education and child race.

Results: Mothers of cases were more likely to work in technical occupations (11.6%) than mothers of controls (6.7%), with little difference among fathers. Compared to parents in other white collar occupations, the adjusted OR for technical occupations among mothers was 2.5 (95% CI 1.2-5.3) and among fathers was 1.3 (95% CI 0.79-2.1), which were slightly attenuated when compared to all others employed.

Conclusions: Our results do not support previous findings about occupation of fathers of children with ASD and suggest that maternal occupation (particularly before an affected child's birth) may be associated with increased risk.

Sponsor: CA CADDRE CDC (#U101CCU920392-05)

PS6.18
VARIATION IN INCIDENCE OF AUTISM AND OTHER NEURODEVELOPMENTAL DISORDERS WITH SEASON OF BIRTH: AN EVALUATION OF FOUR CHILDHOOD-ONSET NEUROPsychiatric CONDITIONS Hjördis Osk Atladottir, Erik T Parner, Søren Dalsgaard, Diana E Schendel, Per Hove Thomsen, Poul Thorsen, Department of Biostatistics, Institute of Public Health, University of Aarhus, Denmark.

Background: The etiologies of Autism Spectrum Disorder and many neurodevelopmental disorders are largely unknown. The detection of a seasonal variation of birth of children diagnosed with a certain disorder could suggest etiological factors that follow a seasonal pattern.

Objectives: Examine the seasonal variation of births of children diagnosed with one of four common childhood neuropsychiatric disorders: Autism Spectrum Disorder, Hyperkinetic Disorder, Tourette's syndrome, and
Obsessive Compulsive Disorder.

Methods: The study cohort consisted of all children born in Denmark from 1990 through 1999 identified in the Danish Medical Birth Register (N=669,995). Outcome data consisted of both inpatient and outpatient diagnoses reported to the Danish National Psychiatric Registry from 1995 through 2004 using the ICD-10 diagnostic coding system (Autism Spectrum Disorder N= 1860, Hyperkinetic Disorder N=2033, Tourette's syndrome N=259, Obsessive Compulsive Disorder N=485).

Logistic regression combined with spline (a smoothing method) was used to estimate the variation with season of birth for each disorder and estimates of risk from season of birth were adjusted for the difference in follow-up time and change in incidence over time of each disorder.

Results: No statistically significant variation in season of birth was observed for any of the four disorders, or the ASD subdiagnoses (Hyperkinetic Disorder: p= 0.06; Tourette's Syndrome : p=0.14; Obsessive Compulsive Disorder: p=0.71; Autism Spectrum Disorder: p=0.83; childhood autism: p=0.52; atypical autism: p=0.27; Asperger syndrome: p=0.55; and PDD-NOS: p=0.83). Conclusion: The lack of a seasonal variation of birth, per se, cannot exclude the possibility that one or more seasonal environmental factors, such as infection, could be related to these disorders.

Sponsor: Danish Research Agency, Centers for Disease Control and Prevention

PS6.19
DISPARITIES IN HEALTH CARE AMONG CHILDREN WITH AUTISM
Gregorys Liptak, Lauren Benzoni, Daniel W Mruzek, Karen W Nolan, Melissa A Thingvoll, Christine M Wade, Edgar Fryer, University of Rochester Medical Center

Background: Racial and ethnic disparities affect health care in the United States.

Objectives: Determine if disparities exist in the prevalence of autism among children of disadvantaged populations, and if disparities exist in utilization of and access to care for families of children with autism.

Methods: Secondary analysis of data obtained from the National Survey of Children’s Health, a nationally representative sample (CDC, 2003-4). Data were analyzed using SUDAAN statistical software.

Results: 473 children (weighted sample size 309,793) were identified by their families as having autism. The prevalence of autism per 1,000 was 2.60 for Latinos and 4.98 for non-Latinos (p<0.000). Families of Latino children with autism reported difficulty getting primary medical care or advice, problems accessing specialists, and getting care in a timely fashion (all p<0.003). The prevalence of autism per 1,000 in African-American children was similar to that for non-African-Americans (4.65 v. 5.15). Families of African-American children with autism were significantly less likely to identify someone as their child's personal doctor, get care in a timely fashion, and receive preventive medical care (all p<0.003).

Conclusions: Latinos have a significantly lower reported prevalence of autism than non-Latinos. This may be due to genetic differences or to a lower rate of diagnosis due to disparities in care. Both Latinos and African Americans are less likely than white non-Latinos to utilize or have access to specific aspects of healthcare.

Sponsor: DHHS: LEND*

PS6.20
VALIDATION OF THE SOCIAL COMMUNICATION QUESTIONNAIRE (SCQ) IN 'AT-RISK' AND NORMAL POPULATIONS
Susie Chandler, Gillian Baird, Tony Charman, Emily Simonoff, Andrew Pickles, Tom Loucas, David Meldrum, King's College London

Objective: To examine the diagnostic validity of the SCQ in at risk and normal populations.

Methods: SCQ data was collected from three samples: a cohort of children at risk for PDD (n=1066, mean age=10.3 years); children from mainstream schools (n=411, mean age=12.0) and a group of children living in one postcode (n=247, mean age=11.5). Diagnostic assessments were subsequently completed on a stratified sub-sample (n=255) of the at risk group; cases were assigned autism, PDD or non-PDD diagnoses on the basis of ADI-R and ADOS information, and ICD-10 criteria. Diagnostic status of cases in the mainstream and normal population samples were established through examination of Child Health records.

Results: Mean SCQ scores for the at risk, mainstream, and normal samples were 15.2 (SD=8.6), 4.1 (SD=4.7) and 4.7 (SD=5.0) respectively. A ROC analysis for the at risk sample showed strong discrimination between PDD and non-PDD diagnoses. SCQ score was independent of IQ. When the same cut-off was applied to the mainstream and normal samples, proportions of cases classified correctly were 95.9% and 96.8%. False-positive cases tended to have other neurodevelopmental diagnoses (e.g. ADHD).

Conclusion: A statistical weighting procedure will be used to confirm the diagnostic validity of the recommended SCQ cut-offs (Berument et al, 1999) within an at risk population, and to test whether the SCQ also has validity as a screening measure within the general population.

Sponsor: Wellcome Trust, Department of Health

PS6.21
COMPARING THE MODIFIED CHECKLIST FOR AUTISM IN TODDLERS (M-CHAT) AND THE SOCIAL COMMUNICATION QUESTIONNAIRE (SCQ) IN CHILDREN REFERRED TO CHILD HEALTH SERVICES
Abigail C Davison Jenkins, Gillian Baird, Emily Simonoff, Andrew Pickles, Tony O'Sullivan, Ajay Sharma, Susie Chandler, Victoria Bird, Elizabeth Ireland, Fiona May, Tony Charman, Institute of Child Health, University College London

Objectives: To evaluate whether the use of screening instruments would improve the accuracy of referral to specialist paediatric services for autism spectrum disorders (ASDs) for pre-school children (18-48 months)
with developmental problems referred to community child health services. To compare the accuracy of the M-CHAT and SCQ.

Method: In the first phase, the SCQ and M-CHAT were administered, either over the telephone or by post, to parents of 540 children referred to 2nd tier child health services. Results (from the first phase only): The SCQ and M-CHAT have very different distributions in this population. There is no correlation between age and score on either measure, 92 (17.0%) of the sample scored above the suggested SCQ cut-off for ASD (15). The M-CHAT has 2 suggested cut-offs and the proportion of the sample above cut-off were 200/540 (37.0%) and 78/540 (14.4%) for the ‘total score >3’ and the ‘fail 2 of 6 critical items’ cut-offs, respectively. Correlation between total scores for the two screens is moderate ($r^2 = 0.45$). However, at the level of previously published cut-offs for ASD agreement between the 2 screens was lower.

Conclusion: The screen parameters will be determined in the second phase when a stratified random subsample of ~120 of children will be seen for a research diagnosis.

Sponsor: The Health Foundation (formerly PPP Healthcare Trust)

**PS6.22**

**COMPARING REVIEW OF HISTORICAL RECORDS AS CASE ASCERTAINMENT IN AUTISM SPECTRUM DISORDERS**

*Vanessa Gonzalez, Marygrace Yale Kaiser, University of Miami*

Background: It is thought that the number of children with Autism Spectrum Disorders is on the rise, however the cause of this rise is still unknown.

Objectives: This study proposed to determine the best method of case ascertainment by comparing two common procedures used in surveillance research.

Methods: Participants included 89 families who have a child 4-9 years old who have been previously diagnosed with Autistic Disorder. Participants were recruited from the University of Miami Center for Autism and Related Disabilities and from the Miami-Dade County Public Schools. The SCQ was completed by caregivers to obtain information about core diagnostic features of autism.

Review of historical records was also performed for all participants, where trained abstractors reviewed each evaluation and scored them using the DSM IV criteria for ASD.

Results: It was found that the record review consistently identified more children than the SCQ using any criteria. It was found that children identified as not having ASD via record review had a significantly lower proportion of social manifestations than those identified as ASD. It was also found that the most influential criteria in deterring children from being identified as Autistic was the delay before 3 years of age.

Conclusion: Delays in social interaction may be harder to identify than behavioral or communication deficits. These results have significant implications for the interpretation of current prevalence figures.

Sponsor: CDC

**PS6.23**

**USE OF A TEACHER NOMINATION STRATEGY TO SCREEN FOR AUTISM SPECTRUM DISORDERS**

*Kristina Kaparich, Susan L. Hepburn, Carolyn DiGuiseppe, Steven Rosenberg, Cordelia Robinson, Lisa Miller, University of Colorado at Denver and Health Sciences Center*

Background: There is a need for a quick, reliable method for identifying school-aged children who need further assessment for autism spectrum disorders.

Objectives: The goal of this project was to develop a nomination strategy to identify children likely to have high-functioning autism spectrum disorders, for use in general education classrooms.

Methods: Teachers were asked to complete two measures: (1) a previously validated screening tool for high-functioning ASD - Autism Spectrum Screening Questionnaire (ASSQ) on every child in the class; and (2) a teacher nomination tool for identifying children with social and communicative difficulties. Teacher nomination strategies were compared with ASSQ scores. An ASSQ score of 17 or higher, a cut-point previously shown to identify children with ASD, was considered to be a positive test.

Results: A total of 60 teachers were included in the study. The mean ASSQ score for the 1354 children who were scored was 4.31 (range 0-47). Ninety-five children (7%) scored at least 17 on the ASSQ. Asking the teacher to nominate up to two children had a sensitivity of 61% compared to the ASSQ, while also maintaining high specificity (96%). Specificity increased to 99% when teachers were allowed to nominate only one child (or none), but sensitivity declined to 42%. Scoring the ASSQ required an estimated 3.5-5.5 hours per class, compared to 15 minutes per class for the nomination strategy.

Conclusion: The results of this study support the use of a teacher nomination strategy as a cost-effective way to identify children at risk for autism spectrum disorders in general education classrooms.

Sponsor: CDC* #UI0/CCU820391

**PS6.24**

**SCREENING CHILDREN WITH DEVELOPMENTAL DISABILITIES FOR AUTISM SPECTRUM DISORDERS**

*Cory Shulman, Keren Meshulam, The Hebrew University of Jerusalem*

Background: Because early diagnosis and individualized intervention are associated with improved outcome for most children with autism, screening children with developmental disorders (DD) who are at risk for autism, is crucial.

Objectives: The major goal of this research was to assess the feasibility of routinely screening children with DD, suspected of having autism with a battery of checklists, completed by their teachers, in order to ascertain which children should be referred for comprehensive diagnostic evaluations.

Methods: Teachers of 70 children with DD from a special education program in Jerusalem identified a subgroup of children suspected of ASD. The teachers completed the
working alliances. Among mothers who reported low problem behaviors, parenting self-efficacy was high and working alliance was not associated.

Conclusion: Strong working relationships between mothers and intervention providers may enhance maternal parenting self-efficacy, especially when children present with problem behaviors that can negatively influence self-efficacy.

Sponsors: NIH and BUMC General Clinical Research Center

PS6.27
STRESS IN PARENTS OF PRESCHOOL-AGED CHILDREN WITH AUTISM, DEVELOPMENTAL DELAY, AND TYPICAL DEVELOPMENT Annette Estes, Geraldine Dawson, Elizabeth Koehler, University of Washington

Background: Stress levels are generally higher for parents of children with autism compared with parents of typically developing children.

Objective: Identify specific child factors that relate to stress in parents of children with autism to assist in providing effective strategies for reducing stress in families.

Methods: Participants are from a longitudinal study on the neurobiology and development of children with autism (ASD), developmental delay (DD), and mental-age matched children with typical development (Typ).

Children were evaluated for general cognitive ability using the Mullen Scales and for ASD using the ADI, ADOS, and DSM-IV. Language, adaptive behavior, behavior problems and social abilities were also assessed in children. Parents reported their own level of parenting stress, depression, and anxiety.

Results: Data are reported for 51 children with ASD, 20 with DD, and 27 Typ children (Mean ages; ASD = 43.9 months, DD = 44.2 months, Typ = 28.1 months).

Parenting Stress in the ASD group was significantly higher than in the DD and Typ groups. Anxiety was higher in the ASD group than in the Typ group. Depression scores did not differ between groups.

Analyses are planned to investigate the relationship between specific child factors and parenting stress in this sample.

Conclusions: Preliminary findings indicate elevated stress levels in parents of children with ASD compared with parents of children with DD and typically developing children. Results of analyses aimed at identifying the specific factors, including child factors, that play a role in increasing parenting stress will be presented.

Funding source: NICHD (U19 HD34565) and NIMH (U54MH066399)

PS6.28
PARENT SUBSTANCE USE AND MOOD CONCERNS AS A RISK FOR AUTISM SPECTRUM DISORDERS Rachel Jane Hundley, Lindsay Jackson, Elizabeth Baroni, Ellen Hanson, Janice Ware, Children's Hospital Boston; Developmental Medicine Center

Background: Literature has documented the role of parental mood disorder as a risk factor for autism.
Although mood concerns may often be associated with increased risk for substance use, parental substance use has not been directly explored as a risk for having a child with an autism spectrum disorder (ASD).

Objectives: Examine association of mother’s and father’s substance use (prior to birth of child) as a risk for ASD.

Method: Patients with a clinical diagnosis of ASD were recruited from Children’s Hospital, Boston. As part of a larger study, participants were assessed with the ADI-R andADOS, resulting in a confirmed diagnosis of ASD. Each of the child’s parents completed the Family History Interview (Bailey, A.) about themselves and the child’s other parent, as well as case report forms detailing mental health and substance use history.

Results: Data are collected on 35 children with ASD and their parents (anticipated n = 60). Initial findings indicate concern for mood disorder as well as early experimentation with alcohol, particularly in fathers. Additional analyses will investigate consistency of self-report and other-report of substance use and mood concerns.

Conclusion: Preliminary findings support the need for additional controlled investigation on the prevalence, type, and intensity of substance use, in the context of parental mood concerns, as a risk factor for ASD.

PS6.29 MATERNAL SYNCHRONIZATION: EVALUATING THE CONVERGENT VALIDITY OF AN INNOVATIVE MEASURE OF RESPONSIVE MATERNAL BEHAVIORS DURING PLAY. Elia I. Jimenez, Michael Siller, Cynthia Zierhut, Agata Rozga, Marian Sigman, Department of Psychology UCLA

Background: Two longitudinal studies in autism (Siller & Sigman, 2002, submitted) have demonstrated a predictive link between maternal synchronization and children’s subsequent language development. In these studies, maternal synchronization was measured using a microanalytic coding system focusing on maternal responses to children’s ongoing attention/activity.

Objectives: Evaluating concurrent correlates of maternal synchronization, focusing on (a) maternal involvement within children’s natural environment, and (b) global ratings of maternal sensitivity.

Methods: 28 children with autism (CA=45 months) and their mothers participated in child assessments and the in-home videotaping of an episode of mother-child interaction. Interactions were coded by independent research teams for (a) maternal synchronization and (b) maternal sensitivity (Ainsworth et al., 1978). In addition, children’s mothers were instructed to carry a signaling device for one week. Mothers were signaled at 20 random times and asked to report on their children’s ongoing activities/experiences. Maternal responses were coded for the degree of maternal involvement in children’s activities.

Results: Results showed significant correlations between the measure of maternal synchronization and (a) global ratings of maternal sensitivity, r=.38, p<.05, and (b) the level of maternal involvement in children’s natural activities, r=.56, p<.05. These findings expand the validity of the measure of maternal synchronization introduced by Siller & Sigman (2002).

Funding: Program Project Grant HD-DCD35470; STAART Grant U54-MH068172

PS6.30 IMPACT OF A FAMILY-CENTERED EARLY INTERVENTION PROGRAM FOR CHILDREN WITH AUTISM ON IMPROVING ACCESS TO SERVICES AND DECREASING PARENTAL STRESS Myriam Chrétien, Suzanne L. Kennedy, Katherine Moxness, Lee Tidmarsh, West Montreal Readaptation Centre

While an increasing number of early intervention programs for children with autism have been surfacing, access to services continues to be a trying experience for families given multiple and lengthy waiting lists. In response to this situation a pilot project was developed that aimed at reducing waiting times from the initial referral for diagnostic evaluation to the beginning of intensive intervention services and decreasing parental stress. Children aged 0 to 5 years and their families referred to the hospital’s autism clinic for diagnostic evaluation were placed on parallel waiting lists and completed the Parental Stress Index (PSI) upon beginning their participation in the study and 6 months later. Indicators such as time delays as well as parental satisfaction and the efficacy of family interventions were also measured. Parents of 52 children participated in this study. Preliminary results indicate a considerable reduction in the time required for beginning intensive intervention services, from approximately 24 months to an average of 9 to 11 months. The PSI results show that the majority of parents have a clinically significant level of parental stress (82% of mothers and 65% of fathers). Qualitative results indicated that for many parents the development of the child and behavioral problems are important concerns. Areas of parental satisfaction included acceleration of the process to access services and feeling appreciative of the assistance received. In conclusion, the preliminary findings suggest that families benefit from being placed on concurrent waiting lists and obtaining support while awaiting a diagnosis and beginning intensive intervention.

PS6.31 BELIEF SYSTEMS OF FAMILIES OF CHILDREN WITH AUTISM SPECTRUM DISORDERS Gillian Alison King, Lonnie Zwaigenbaum, Peter Rosenbaum, Susanne King, Anita Bates, Donna Baxter, Thames Valley Children’s Centre

Background: Priorities, values and worldviews affect how families adapt to their experiences and to the world around them. These belief systems have rarely been studied in ASD.

Objectives: To assess the belief systems of families of children with ASD as they navigate key transition points (i.e., their child’s entry into elementary or high school).

Methods: We conducted in-depth interviews with 16
families of children with ASD or Down syndrome (as a contrast), recruited through parent organizations. Interviews were audio-taped and transcribed. Study investigators discussed observations about main ideas and recurring themes. A list of 85 code words was generated, divided into 9 categories, including beliefs, supports, coping, hopes, expectations, and insights. Inter-rater coding agreement was 83%.

Results: There was an overarching theme of parents doing their best to help their child, their families and themselves fit into the larger world of schools and communities. Parents adopted worldviews that generated a sense of ‘fit’ (or coherence), including a sense of optimism, acceptance and appreciation (e.g., of their child’s unique strengths and contributions), and an emphasis on actively working towards change. Some differences in strategies were identified between families of ASD and Down’s children.

Conclusions: Despite struggles and challenges, parents adopted positive worldviews that brought meaning to their experiences and a sense of belonging for their children.

PS6.32
MATERNAL SYNCHRONY IN PLAY IS ASSOCIATED WITH COGNITIVE ABILITIES AMONG TODDLERS WITH AUTISM Jennifer Chantal Kuhn, Megan H. Pesch, Stacy E. White, Alice S. Carter, University of Massachusetts Boston and Boston University School of Medicine

Background: Siller and Sigman (2002) found that maternal synchrony, a measure that quantifies the extent to which mothers follow their children’s lead in play, predicted later language and joint attention gains among school-age children with autism.

Objectives: To explore concurrent associations between maternal synchrony and toddler cognitive abilities.

Methods: Participants were recruited to a study of toddlers with autism and their families. Diagnosis of an autism spectrum disorder was confirmed with the ADOS-G, ADI-R, and clinical impression. Scores for mothers’ verbal and gesture synchrony were calculated based on microanalytic coding of videotaped mother-child play interactions. Child cognitive abilities were assessed via the Mullen Scales of Early Learning.

Results: The sample included 36 toddlers between 18 and 33 months of age (21 boys, 15 girls; mean age 28±4 months) and their mothers. Maternal gestural synchrony was positively correlated with child non-verbal IQ (r=0.40, p<0.05) and showed a trend level correlation with child verbal IQ (r=0.32, p=0.09). In a subsample of 18 children coded so far, verbal synchrony showed a trend towards predicting child receptive language when percent of child attention to toys was entered as a covariate (R-squared change =0.19, p=0.08).

Conclusion: These data suggest associations between maternal synchrony in play and toddlers’ cognitive abilities. Data on 60 children has been gathered and will be coded and analyzed for presentation at IMFAR. Greater understanding of these constructs may enhance family-based interventions.

Sponsor: NAAR & NIH

PS6.33
QUALITY OF LIFE IN CHILDREN WITH AUTISM AND THEIR FAMILIES Li-Ching Lee, Rebecca A Harrington, Brian B Louie, Craig J Newschaffer, Center for Autism & Developmental Disabilities Epidemiology, Bloomberg School of Public Health, Johns Hopkins University

Background: Research on the quality of life (QOL) of children with autism is limited.

Objectives: Examine differences in QOL by comparing children with autism (AUT) to children with ADHD and to typically developing children in the domains of social activity, family burden, family activities, and parental concerns about their children’s QOL.

Methods: Data were derived from the National Survey of Children’s Health. Two case groups, autism (n=483) and ADHD (n=6,319), were compared against typical controls (n=58,953) by three age strata (3-5, 6-11, and 12-17).

Results: Children with AUT were significantly less likely than children with ADHD (adjusted OR=0.40, 0.48 for age 6-11, 12-17, respectively) and typical controls (adjusted OR=0.32, 0.28 for age 6-11, 12-17, respectively) to participate in any organized social activities. Families of AUT reported significantly higher childcare burden than both families of ADHD and controls, across the three age strata. Parents’ concerns about their children’s achievement, self-esteem, stress coping, learning difficulties, and being bullied by classmates, were all significantly higher in the AUT group than the other two groups.

Conclusion: Children with autism face numerous challenges that might have impact on family’s QOL. Caring burden on families could be substantial and parental concern over their children’s QOL is significant. This study is supported by CDC cooperative agreement U10/CCU320408-05

PS6.34
ADOLESCENT SIBLINGS OF INDIVIDUALS WITH AUTISM: A DIATHESIS STRESS MODEL OF THE IMPACT OF BROADER AUTISM PHENOTYPE CHARACTERISTICS ON SIBLING WELL-BEING Gael I Orsmond, Marsha Mailick Seltzer, Boston University

Background: Research has examined sibling well-being from either a family stress model or a family genetics perspective. We combine these two approaches.

Objectives: Using a diathesis-stress model, we examine the contribution of broader autism phenotype (BAP) characteristics in siblings and mothers to the well-being of adolescent siblings.

Methods: Data were collected through telephone interviews and mailed surveys completed by 57 siblings ages 12-18. Sibling and mother BAP characteristics were rated using the Development, Social Interaction, and Mood Questionnaire (DSIM). Other measures included sibling depressive and anxiety symptoms, sibling life events and coping style, and maternal support and
depressive symptoms. Results: One-third of adolescent siblings reported depressive symptoms suggestive of clinical depression and 10% reported clinically relevant anxiety symptoms. Siblings were at greater risk of depressive and anxiety symptoms when they used greater emotion-focused coping strategies (e.g., venting, denial), if they had a higher number of BAP characteristics and experienced a higher number of life events in the last year, and if their mother had a higher number of BAP characteristics and reported greater depressive symptoms.

Conclusion: Findings support a diathesis-stress model of sibling well-being wherein the presence of BAP characteristics in siblings or mothers presents a vulnerability that interacts with other environmental factors to put siblings at risk.

Sponsors: NICHD and NIA

**PS6.35**

**NATURE AND AMOUNT OF INTERVENTIONS UTILIZED BY YOUNG CHILDREN WITH AUTISM: CONCURRENT RELATIONS TO CHILD CHARACTERISTICS AND SOCIOECONOMIC STATUS.** Nuri M Reyes, Michael Siller, Marian Sigman, The Semel Institute for Neuroscience and Human Behavior

Objective: Examine concurrent relations between the nature/amount of children’s intervention programs (intensity of school programs and after school interventions) and a) children’s developmental characteristics (chronological, language, mental age), and b) families’ socioeconomic status (SES, parental education, income).

Method: Twenty-eight children with autism (mean age=45, mean language age=16.6 months) and their families participated in two testing sessions to confirm children’s diagnoses and to assess global developmental characteristics, such as language abilities and mental age (Mullen, 1995: Reynell, 1977). Questionnaire measures were used to evaluate the amount/ nuture intervention programs (Bono, Daley, & Sigman, 2004) and the families’ SES.

Result: Findings showed that the amount/ nature of intervention programs was closely related to the families’ SES but unrelated to child characteristics such as language or mental age. For example, we found a positive correlation between family income and the intensity of after-school programs, r=.42, p<.05. Interestingly, years of paternal education were negatively associated with the intensity of school programs (r=-.51, p<.01) but positively with the intensity of after school programs (r =.42, p<.05).

Conclusion: This research advances our understanding of factors that influence parental access to intense intervention programs for young child with autism.

Funding: Program Project Grant HD-DCD35470, STAART Center Grant U54-MH068172

**PS6.36**

**RESOLUTION WITH THE CHILD’S DIAGNOSIS AMONG PARENTS OF CHILDREN WITH AUTISM SPECTRUM DISORDERS** Shahaf Salomon, Nurit Yirmiya, David Oppenheim, Nina Koren-Karie, Cory Shulman, Shlomit Levi, Department of Psychology, The Hebrew University of Jerusalem, Mount Scopus.

Background: Coming to terms with the diagnosis of autism and reaching resolution regarding its emotional impact is a challenging process for most parents, with important possible implications for the parent-child relationship.

Objectives: To assess resolution of the diagnosis of an ASD among mothers and fathers of children with autism and To explore whether child characteristics (e.g., age, IQ) and parental characteristics (e.g., age, education) are associated with resolution or lack of resolution.

Methods: Thirty children (Mean CA= 8 years, 1 month, Mean IQ=64) diagnosed with the ADOS-G and the ADI-R and their parents participated. IQ (Mullen, K-ABC, WISC-III or WAIS) and level of functioning (The Vineland Adaptive Behavior Scales) were assessed. Both parents were interviewed with the ‘Reaction to Diagnosis Interview’ (RDI; Pianta & Marvin, 1993) and parental IQ was assessed by four subtests of the WAIS III.

Results: Twelve of the 30 mothers and 14 of the 30 fathers were classified as being resolved with the diagnosis of autism. Parental age, and education as well as child’s age, IQ, child’s level of functioning and the duration since receiving the diagnosis did not differ significantly between resolved unresolved mothers and fathers. However, a trend was found for maternal IQ (t 28= 1.947, p= 0.06), with resolved mothers (M= 110.42, SD= 11.47) scoring higher then unresolved mothers (M= 100.14, SD= 11.93). The same trend was found for fathers (t 28= 1.83, p= 0.07) with resolved fathers (M= 110.55, SD= 1.53) scoring higher then unresolved fathers (M= 100.52, SD= 1.57). Nonsignificant differences were also yielded when we explored possible differences among children whose parents were both resolved (6), both unresolved (10) or one was resolved whereas the other was not (14).

Conclusion: About half of the parents in our sample were resolved. Resolution was not associated with child’s IQ and daily living skills or with time since receiving the diagnosis.

**PS6.37**

**EXAMINING A ‘GOODNESS-OF-FIT’ MODEL BETWEEN CHILDREN WITH HIGH FUNCTIONING AUTISM AND THEIR PARENTS**

Caley B Schwartz, Heather A Henderson, Nicole E Zahka, Anne Pradella, Peter C Mundy, Nicole Kajkowski, Camilla Hileman, Albert Buchman, University of Miami

The concept of ‘goodness-of-fit’ between children and their environment has been examined as a predictor of outcome variability among children with disabilities. It is thought that a good fit between children and their environment leads to more positive mental health outcomes, while a lack of fit leads to less adaptive functioning (Chess & Thomas, 1986).

Objective: To examine the interaction, or goodness-of-fit, between children with high-functioning autism (HFA) and...
their parents on measures of internalizing symptoms as a predictor of variability in functioning.

Design/Methods: Symptomatology for 49 HFA children (8-15 years, 94% male) was measured by parent report on the Autism Spectrum Screening Questionnaire and emotional functioning was assessed using the self-report form of the Behavior Assessment Scale for Children. A similar self-report measure, the Symptom Checklist-90, was used to assess 49 parents’ (83% mothers) emotional functioning. Scores on anxiety and depression scales were combined to form one measure of internalizing symptoms (IS).

Results: Children reporting higher IS reported fewer deficits in interpersonal relations, but poorer parent relations compared to low IS children. This effect was qualified by an interaction with parent IS indicating that high IS children with low IS parents had the lowest levels of autistic symptomatology and the strongest interpersonal relationships.

Conclusions: The results indicate that variability in autistic symptomatology and emotional profiles among HFA children can be accounted for in part by examining the interaction, or goodness-of-fit, between child and contextual/familial factors.

Sponsor: NIMH, grant # MH-71273

PS6.38
PARENTS' VIEWS OF ONTARIO HEALTHCARE SERVICES FOR THEIR CHILDREN WITH AUTISM, DOWN SYNDROME, OR FRAGILE X SYNDROME Patricia Minnes, Karin G Steiner, Patricia Minnes/Queen's University

Background: Although medical problems of persons with ID have been increasingly recognized in the literature, less attention has been given to the particular needs of different diagnostic groups, or to perceptions of the quality of care received by persons with a developmental disability.

Objectives: We are comparing parent perceptions of Ontario healthcare services to inform providers of the diverse needs of special populations, and to support further research on enhancing healthcare for these groups.

Methods: Three sets of parents, each with a son or daughter from the same diagnostic group, were recruited to participate in focus group interviews. Three mothers of children with autism, six parents of persons with Down syndrome, and eight caregivers of individuals with Fragile X syndrome shared their views on: (a) quality of care; (b) challenges and successes in obtaining care; and (c) enhancement of health services.

Results: Qualitative analyses yielded a range of emergent themes that highlighted barriers to care, dilemmas in accessing and delivering care, the role of parents in securing services, and that of family practitioners in regulating access to a wide range of services. Parent reports differed significantly on challenges in accessing care, but parents expressed overlapping ideas for enhancing the healthcare system. Parents in all groups called for expansion of syndrome-specific education for medical students and support for themselves in obtaining health- and system-related information.

Conclusion: Healthcare for persons with ID could be enhanced by educating all stakeholder groups about syndrome-specific needs and by linking services to ease transitions in care.

Sponsor: CIHR/Health Equity in Intellectually Disabled People (HEIDI) Research Team, Queen’s University*

PS6.39
AUTISM AND MIGRATION : A COMPARATIVE AND DESCRIPTIVE STUDY Sylvie Viaux, Pascal Lenoir, Dominique Sauvage, Groupe Hospitalier Universitaire Pitié-Salpêtrière

Background: Different epidemiological studies show an increase of prevalence in autism, both in the general population and in a population of children born of foreign parents

Objectives: study of population of autistic and TED-NOS children born of migrants descriptive and comparative

Methods: semi-prospective study in a child population

Results

156 autistic and TED-NOS children, including 28 children born of foreign parents Age : 2-14 Sex ratio : 5.25/1 (migrant) ; 3.16/1 (non-migrant)

Children born of foreign parents : Daycare Unit : 16.3%, 68% of these couples are from « mixed » nationalities 83% bilingual environment.

DSM IV-R: Infantile autism (69.6%) Early progressive disorder onset 80% Autism intensity mean scoreGlobal Developmental Quotient 45

Socio-economic factors no significative differences ,Abnormal psychosocial situations (p<0.009)

Follow-up : Age of parents/discovery 1-2 yrs. Curve is shifted compared to non-migrants.Age when first health care was given 3-4 yrs] (60%) Health care follow-up : peak at 3 years.

Delay in care higher in migrant children.

Conclusion Important proportion of migrants at the daycare unit (16.3%) compared to the region’s migrant population (6.24%)

The main factor seems more to be migratory than the ethnic factor. Children have a classic autism profile. Health care follow-up is different between migrant and non-migrant population. Parents and professionals should be sensitized to this atypical follow-up for an early care.

PS6.40
USE OF THE ADI-R AND ADOS WITH CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDER
(FASD): IMPLICATIONS FOR THE DIAGNOSIS OF AUTISM SPECTRUM DISORDER (ASD) Somer Lauren Bishop, Catherine Lord, University of Michigan Department of Psychology
Background: Children with fetal alcohol spectrum disorders (FASD) are described as having many of the same types of impairments as children with autism spectrum disorders (ASD), including communication and social difficulties, and strong sensory interests.
Objectives: To examine the validity of the ADI-R and ADOS in classifying children with FASD, and to determine whether children with FASD follow a similar symptom profile as children with ASD. Methods: Families were recruited through 2 FASD diagnostic clinics. Parents completed the ADI-R, Vineland II, and various questionnaires. Children completed the ADOS and the Differential Ability Scales, and were given a clinical diagnosis.
Results: Preliminary analyses were conducted on 24 children with FASD, ages 3 to 11 years. The ADI-R and the ADOS each correctly classified 17 out of 23 (74%) children with FASD as non-spectrum. Only 1 child was incorrectly classified as ASD by both instruments. One other child with FASD who received a clinical diagnosis of PDD-NOS met cut-offs on both instruments. Results of the ADOS indicated that though many children with FASD exhibited impairments in the quality of their social initiations and responses, the frequency with which they engaged in social interactions was more typical than children with ASD.
Conclusion: This study emphasizes the importance of using both the ADI-R and ADOS together in order to correctly classify children. Results also suggest that though many children with developmental difficulties may exhibit impairments in the quality of their social interactions, a low frequency of social interaction may be more specific to children with ASD.
Sponsor: NIH, NIAAA

PS6.41 FACTOR STRUCTURE EVALUATION OF THE CHILDHOOD AUTISM RATING SCALE Vincent Pandolfi, Caroline I Magyar, Rochester Institute of Technology
Background: Since the Childhood Autism Rating Scale (CARS; Schopler et al., 1980) was developed, many newer measures of autism spectrum disorders (ASD) have gained widespread acceptance. It is important to assess the relative contribution of CARS data in the context of more contemporary measures of ASD. A literature review suggests favorable psychometric properties for the CARS; however, a consistent factor structure has not been identified.
Objectives: To determine whether the CARS measures separate but related clusters of impairments that characterize the broad autism spectrum and to evaluate empirically derived factor models.
Methods: Maximum-Likelihood confirmatory factor analysis (CFA) and exploratory Principal Axis factor analyses (PAF) evaluated archival data from 164 children presenting to a university clinic with suspected autism spectrum disorders.
Results: CFA and PAF failed to support DiLalla & Rogers’ (1994) 3-factor and Stella et al.’s (1999) 5-factor models. PAF generated a reliable 8-item scale reflecting a composite of items assessing social, communication, and stereotyped behaviors.
Conclusions: Results are consistent with Schopler et al.’s (1980) assertion that the CARS measures a unitary phenomenon. This one-dimensional scale has limited utility in the differential diagnosis among ASDs and for generating individualized symptom profiles. However, previous psychometric research supports the CARS’ use for screening and distinguishing between children with and without ASDs.
*Sponsor: NIH

PS6.42 EVALUATION OF COGNITIVE DEVELOPMENT IN YOUNG CHILDREN WITH AUTISM USING THE DIFFERENTIAL ABILITY SCALES Lonnie L Sears, Andrea King, Lisa Ruble, University of Louisville School of Medicine
The Differential Ability Scales is a test of cognitive ability providing comparisons of strengths and weaknesses in verbal and nonverbal problem solving areas. The lower preschool level items assess visual motor construction, verbal comprehension, nonverbal reasoning, and expressive picture naming. To determine the potential clinical and research benefits of the DAS for young children with autism, 27 preschool children (aged 2.5 to 6.0 years) were administered lower preschool level subtests using the extended norms. The extended norms provide the opportunity to assess development of cognitive skills over an extended age range. Results of the study indicated that the Verbal Comprehension subtest was difficult for this age group and 23 subjects refused all subtest items (85% refusal). In contrast, the other DAS subtests had fewer than 22% of children refusing subtest items. For those children participating in testing, lowest scores occurred on Verbal Comprehension (T=24.2) compared to Picture Similarities (T=36.9). T-scores for cognitive subtests measuring visual-motor construction, nonverbal reasoning and expressive picture naming were negatively correlated with social and play impairments and stereotypical behavior as assessed by the Autism Diagnostic Observation Schedule (ADOS) and the Childhood Autism Rating Scale (CARS). These findings indicate that the DAS is a useful measure of cognitive development in young children with autism. Although many do not complete verbal comprehension items, the Block Building, Picture Similarities and Naming Vocabulary subtests engage most young children with autism and provide cognitive measures that are associated with behavior and the emergence of social, communication, and play skills.

PS6.43 CONCURRENT AND PREDICTIVE VALIDITY OF THE MACARTHUR-BATES COMMUNICATIVE
DEVELOPMENT INVENTORY FOR CHILDREN WITH AUTISM SPECTRUM DISORDER Veronica Smith, Pat Mirenda, University of Alberta
Among individuals with developmental delays, children with autism spectrum disorder (ASD) present unique challenges in language assessment to both researchers and clinicians because of the varied spectrum of cognitive, linguistic, social, and behavioural functioning associated with the condition. The current study was undertaken with the goal of using evidence from standardized measures of language/vocabulary to better understand the concurrent and predictive validity of a parental report measure, the MacArthur Communication Developmental Inventories (CDI), both Words and Gestures (n= 40) and Words and Sentences (n = 39) forms, for children with ASD. Concurrent validity was examined by comparing parent report data from each form of the CDI and standardized measures of vocabulary and the normative data published in the inventory manual on children with mental ages from 12 to 30 months. Significant correlations between .50 and .62 were obtained for both forms of the CDI. Predictive validity was examined with parent report data from the CDI for children with mental ages below 12 months, between 12-24 months, and above 24 months across three time points, baseline, 12 months, and 24 months beyond the initial parent report. Significant correlations of between .47 and .72 were obtained between the CDI and standardized language measures at 12 and 24 months for all but very young children who demonstrated limited vocabulary skills at baseline. These results establish the validity of parent report using the MCDI of vocabulary development for children with ASD and confirm their utility with some minor exceptions with developmentally very young children for researchers and clinicians who attempt to evaluate language skills of children with severe delays.

PS6.44
SCHOOL PREPARATION PROGRAM MARTINE BEAURIVAGE, SYLVIE DESCHAMPS, JESSICA BOISSELLE-LADOUCEUR, C.R. Lisette-Dupras and West Montreal
School Preparation Program
The goal of the program is to teach the children the necessary skills required for integration into regular classrooms. The program is offered to children who have been diagnosed with an autism spectrum disorder. Typically developing school aged children are also participate in the program activities to demonstrate appropriate social interactions normally found in school settings.
The specific objectives of the program are largely found to derive from the preschool teaching program from the Ministry of Education of Quebec. Individual objectives are equally determined with the help of an evaluation grid which is part of a developmental inventory and kindergarten pedagogical objectives (MEQ).
The school preparation program is offered during the summer months, three days a week, for 8 weeks. The groups are composed of 8 to 10 children, a teacher and two specialized educators.
A report indicating the mastered skills and recommendations for the school year is given to the parents at the end of the program.

PS6.45
A GROUP, RANDOMISED CONTROLLED TRIAL OF THE PICTURE EXCHANGE COMMUNICATION SYSTEM (PECS) FOR LANGUAGE DELAYED CHILDREN WITH AUTISM SPECTRUM DISORDER Kate Gordon, Greg Pasco, Pat Howlin, Tony Charman, St. George's, University of London
Objective: To investigate the effectiveness of PECS training for non-verbal children with autism spectrum disorder (ASD), delivered in the specialist school setting
Participants: 84 children aged 4 to 10 years (mean 6.8, SD 1.3) in 17 classes, all with formal diagnoses of ASD and little/no functional language
Procedure: Classes were randomised to receive immediate, delayed or no PECS training. Teachers attended a 2-day PECS workshop and over the following 2 terms classes received 6 half-day consultation visits. All children were observed 3 times: at baseline and at the end of the immediate and delayed treatment phases
Outcome measures: Children were observed in the classroom during snack-time. Primary measures of outcome were rates of spontaneous communicative initiation and rates of PECS use. Rates of speech and scores on standardised language tests were also measured
Results: Analysis of the dataset is currently being conducted. We aim to report findings using an adjusted hierarchical ordinal regression analysis on the observation and standardised measures. The model will also test for maintenance of any treatment effects 12 months after the end of the training period.
Conclusions: This study is the largest fully randomised psychoeducational trial for children with ASD conducted to date. We hope that the findings will contribute to our understanding of whether PECS is an effective programme for promoting communication and which children with ASD it benefits
Sponsor: Three Guineas Trust

PS6.46
USING TELEHEALTH TECHNOLOGY TO PROVIDE TRAINING ON EVIDENCED-BASED PRACTICES FOR CHILDREN WITH ASD Brian R Lopez, Sandy Heimerl, Debra Hall, Patricia Osbourn, Center for Development and Disability, University of New Mexico School of Medicine
Background: Providers located in rural communities frequently have less access to training on evidence-based practices for children with ASD.
Objectives: To determine the feasibility of telehealth technology to provide evidence-based training to providers in rural communities.
Methods: We conducted seven interactive telehealth seminars on best practices for children with ASD. The trainings were provided to a live audience (n=61) and to
participants in four rural locations across New Mexico (n=54). The average attendance for each training session across the four rural locations was 7.5 attendees (SD=4.1). Satisfaction was measured via 5-point Likert scale questionnaires.

Results: The groups did not differ on satisfaction with training content, t(113)=1.67, p=.09 , but the live audience group expressed more concerns about the telehealth technology than the rural group, t(113)=5.39, p<.001. Despite technical difficulties, rural participants approved of the training platform as it saved them time and money while allowing them to obtain the same information as they would have received in person. The rural groups also reported telehealth technology caused minimal interference with the content of the presentations. Despite the technological difficulties, 83% of the rural attendees were willing to participate in future telehealth trainings.

Conclusions: Participants found the telehealth platform a useful bridge to accessing information on specialized populations and were willing to participate in future telehealth trainings.

Research funded by HRSA-OAT

PS6.47
HOW TO IMPLEMENT EVIDENCE-BASED EDUCATIONAL PRACTICES IN SERVICES FOR PERSONS WITH DEVELOPMENTAL DISABILITIES ? Ghislain Magerotte, Universite de Mons-Hainaut

Background: ‘Research-based or evidence-based practices’: it is now the ‘must’ in education of persons with developmental disabilities. But the current practices in the French speaking countries seem to be far away of these ‘good practices’.

Objectives: Identify how these ‘good practices’ are know by the French speaking services and parents - Identify ways to disseminate these practices and to make the educational practitioners, who always want to ‘reinvent the wheel’, more aware of these practices and to stimulate these professionals to contribute to the research-based practices ?

Methods :? We’ll review some ‘evidence-based practices’ in different kinds of services (mainly in early intervention and in special schools) - based upon our earlier researches and upon questionnaires, interviews and focus groups. A special attention will be paid to the Positive Behavior Support practices and the use of the Functional Assessment, and to the visual structuring of the educational environment.

Results: The transfer of new competencies acquired by professionals after training sessions to the current practice is not quite easy. We’ll discuss some reasons of this situation and make some suggestions to reduce the research-practice gap.

Conclusion: This information will make both researchers and providers of professional development more able to transfer research results into the professional practice.

Sponsor: Marguerite-Marie Delacroix Foundation

PS6.48
SEXUALITY, PUBERTY, AND GROWING UP: ADDRESSING THE NEEDS OF YOUTH WITH AUTISM SPECTRUM DISORDERS Shana Nichols, Audrey Blakeley-Smith, Judy Reaven, Susan Hepburn, North Shore-LIJ Health System

Sponsor: Autism Coalition/Autism Speaks; JFK Partners; Society for the Scientific Study of Sexuality

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.

Study Objectives: 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: Focus groups (N = 7), and a questionnaire study (N = 50) were conducted to better understand parents perspectives and learning needs. Parents (N = 17) of high-functioning youth (VIQ > 80) ages 10-15 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: Preliminary analyses demonstrate increased comfort with the topic for parents both within group (p < .03) and in discussions with their child (p < .05). Goal attainment ratings (0-5 scale) were high for all parents (M = 4.33, SD = .12) though 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.

PS6.49
TRAINING TEACHERS TO USE PIVOTAL RESPONSE TRAINING - FROM WORKSHOP TO CLASSROOM Jessica Suhreinich, Laura Schreibman, University of California, San Diego

Background: Teachers who are certified in special education often do not receive specific training in teaching children with autism. Pivotal Response Training (PRT) is a naturalistic behavioral intervention that has been shown to increase the language, play and social skills in children with autism in individual settings. This study investigated the effectiveness of a training model for instructing teachers to use PRT in the classroom setting.

Objectives: To assess the effectiveness of a PRT training model for teachers.

Methods: Participating teachers attended a 6 hour training workshop and received follow-up visits to their classrooms. Teachers in condition 1 (n = 8) received two
30 minute follow-up visits. Teachers in condition 2 (n = 5) received 30 minute follow-up visits until each teacher met a standard criterion for fidelity of implementation (FI). FI of PRT in a classroom setting was measured at baseline and at each classroom visit. Results: None of the participants in condition 1 met a standard criterion for FI. However, specific components of PRT were more likely to be correctly implemented by all teachers. Teachers in condition 2 received a range of two to five follow-up visits before meeting a standard criterion for FI. Conclusions: These findings support the effectiveness of a training model that included both a workshop and follow-up visits in each teacher’s classroom. Teacher characteristics that may be helpful in predicting the amount of time required to train a teacher to use PRT and issues in translating PRT to group settings will also be discussed.

PS6.50
USING SELF-DETERMINATION TO PROMOTE SUSTAINED PHYSICAL ACTIVITY FOR ADOLESCENTS WITH ASD Teri Todd, Gregory Reid, McGill University

Background: Physical activity, an important part of a healthy lifestyle, is often overlooked for people with severe disabilities, including those with autism spectrum disorder (ASD). Sustained, regular physical activity has many health benefits but it is a challenge to motivate individuals with ASD to engage in 30 minutes of exercise, which is required to meet recommended fitness guidelines.

Objectives: To investigate the effectiveness of instructional strategies which purport to promote self-determination on engagement in sustained physical activity of adolescents with severe ASD.

Methods: Three adolescents, two male and one female, participated in a school-based 30 minute cycling program which began in March and continued through June. A single subject changing criterion design with multiple baselines was used to evaluate the effectiveness of the instructional strategy. The program was divided into four phases: baseline, instruction, self-monitoring and goal-setting, and maintenance. Edible reinforcers were given at a set rate for 12 sessions following which participants regulated the reinforcers, encouraging self-reinforcement.

Results: Two participants increased the duration and distance cycled over the course of the program, usually completing a full 30 minutes during the final 7 weeks. The duration and distance cycled did not increase for one participant; nonetheless he did participate on a regular basis. Self-reinforcement resulted in fewer edible reinforcers being consumed during the activity for all 3 participants.

Conclusion: The self-determined instructional strategy which included self-monitoring, goal-setting, and self-reinforcement, was effective in promoting sustained engagement in a cycling activity.

PS6.51
JOINT ATTENTION OF CHILDREN WITH AUTISM IN THE PRESCHOOL SPECIAL EDUCATION CLASSROOM Connie Wong, University of California at Los Angeles

Young children with autism have specific deficits in joint attention and research has shown that joint attention skills are predictive of later language and social development. Given its importance, targeting joint attention is an especially important goal for early interventionists. However, research is limited in describing the joint attention behaviors of young children with autism in the preschool classroom.

The objectives of this study were to determine the extent children with autism initiate joint attention behaviors in their everyday classroom environment and the extent teachers target and respond to those joint attention skills at school.

In the study, fifty-five children were observed in their preschool special education classroom for approximately two hours over three separate days in structured, unstructured, and caregiving activities. Participants were analyzed in two groups: children with a clinical diagnosis of autism (N=27) and children with mental retardation or other developmental delays, MR/DD (N=28). The children ranged in age from three to five years old and their mental ages ranged from 18.5 to 59 months. Child characteristics and demographics were not significantly different between the two groups.

Results show that compared to children with MR/DD, children with autism displayed fewer responses to and initiations of joint attention. Additionally, findings indicate that although teachers seldom focused on joint attention in their teaching, when they did, it was rarely for the purposes of increasing joint attention skills.

These findings suggest the importance of teachers targeting joint attention skills in their preschool special education classes, specifically for children with autism.

PS6.52
STABILITY OF AUTISM ELIGIBILITY IN SPECIAL EDUCATION: A PROSPECTIVE ANALYSIS Marygrace Yale Kaiser, Jennifer Durocher, Vanessa Gonzalez, Christine Hughes, University of Miami

Background: Evidence suggests that increasingly more children with Autism are receiving special services from the public schools.

Objectives: To monitor the disability status of a group of children first receiving special education services as 4-year olds as they move through elementary school.

Methods: Participants included 258 children born in 1992 who were receiving special education services under an Autism eligibility in 1996. Disability status was examined in subsequent school years and compared to other children from the same birth cohort also receiving special education services.

Results: A majority of the sample were still receiving special education services under an Autism eligibility in subsequent school years (92% as 5-year olds, 84% as 6-year olds, 79% as 7-year olds, and 73% as 8-year olds). Children no longer eligible for special services as Autistic
were likely to no longer be public school, with approximately 1% in general education classrooms and between 4-7% receiving services under another disability category. When compared to other children from the same birth cohort in later school years, the sample accounted for 63% of Autism cases in 1997 but only 37% of Autism cases in 2000.

Conclusion: These results suggest that an Autism eligibility is fairly stable when first received as early as four years of age. However, it also appears that a majority of children who are receiving services as Autistic as 8-year olds were not identified as Autistic during that pre-kindergarten period. Implications on prevalence estimates will be discussed.

Sponsor: Florida Department of Education.

PS6.53
TEACHERS' ATTITUDES AND RELATIONSHIPS WITH INCLUDED SPECIAL NEEDS STUDENTS
Aimée Andrea Yazbek, Barbara Anne D'Entremont, University of New Brunswick

Background: Various individual child and teacher characteristics have been implicated in relationships between teachers and typically developing students. However, it is unknown whether these are similarly important for the relationships between special needs students and their teachers. Thus, it is necessary to study these relationships among special needs students.

Objective: Investigate the importance of one child characteristic, disability type, and one teacher characteristic, attitude towards inclusion, as predictors of the relationship between teachers and their special needs students.

Methods: Forty-eight general education teachers of special needs students (K-3) rated their attitudes towards inclusion and the quality of their relationships with one special needs student currently in their class. Special needs students represented the following disability types: autism, behavioural disabilities, intellectual disabilities, physical and perceptual/sensory disabilities, communication disorders, and comorbid disabilities.

Results: Direct associations were demonstrated between child's disability type and a) teacher-child relationship and b) attitude towards inclusion. Attitude towards inclusion did not mediate the association between disability type and teacher-child relationship, nor did disability type moderate the association between attitude towards inclusion and teacher-child relationship. The prospect of including students with behavioural disabilities generated the most negative attitudes. Current students with behavioural disabilities had the poorest relationships with teachers.

Conclusions: Child's disability type appears to an important predictor of teacher-child relationship quality, while attitude towards inclusion does not. The findings are discussed in terms of the need for providing external supports to teachers in order to improve their attitudes and relationships with students.

PS6.54

FACTORS AFFECTING THE ACADEMIC ACHIEVEMENT AND ADAPTIVE LIFE SKILLS OF CHILDREN WITH AUTISM Deborah K. Anderson, Amy N. Esler, Catherine E. Lord, University of Michigan Autism and Communication Disorders Center (UMACC)

Background: Research has documented considerable difficulties in the acquisition of academic and adaptive life skills among children with autism. To date, the most consistent predictors of outcome for children and adults with an ASD are early language abilities and verbal IQ. Hence, research has focused largely on developmental level, while the role of autistic behaviors and symptoms remains mostly unexplored. Yet numerous studies find that high-functioning children with autism, whose progress is not substantially limited by IQ, report a wide range of outcomes, perform significantly worse than typically developing controls on complex academic tasks, and have worse adaptive skills than their IQ would suggest. The question addressed by this study is how behaviors that often co-occur with autism might interfere with adaptive skills and learning in the classroom.

Objective: To investigate the relationship between various predictors (such as diagnosis, IQ, treatment received), behavior problems, and academic and adaptive outcomes.

Methods/Procedure: Academic and adaptive outcomes were assessed at approximately 9-years of age in a sample of 128 children with a clinical diagnosis of autism (n=72), PDD-NOS (n=27), or nonspectrum disabilities (n=29). Academic achievement scores in reading, writing, spelling, and math were obtained through normed instruments administered to the child. Adaptive behavior (daily living skills) and behavior problems (lethargy, hyperactivity, stereotypies, irritability) were assessed through standardized parent report measures. General Linear and Structural Equation Models were used to explore potential main, interactive, and indirect effects of behavior problems on academic achievement and adaptive behavior.

Results: There was a negative relationship between behavior problems and adaptive/academic outcome variables. Implications for interventions are discussed. This research was funded through grants MH6865 and HD35482.

PS6.55
SENSORY PROBLEMS IN AUTISM: INCIDENCE, SYMPTOM PATTERNS, AND CORRELATES
Michael E Behen, Robert R Rothemel, Emily Geenen, Claire Stano, Diane Chugani, Children's Hospital of Michigan-PET Center

Background: Despite widespread recognition of increased incidence of sensory problems in children with autism, few studies have examined the relationship between problems in one sensory modality to problems in others, as well as correlates of sensory problems in autistic children.

Objectives: Examine the incidence of problems in each sensory modality, the relationship of sensory problems across modalities, and determine correlates (e.g., age,
symptom severity, IQ) of differential sensory profiles in autistic children.

Methods: Fifty-seven school-aged children (45 males/22 females, mean age=96.2+ 34.2 months) were included in the study. All children had diagnoses of autism from a neurologist, confirmed by semi-structured interview (ADI-R). Caregivers completed the Symptom Profile Scales for Developmental Disabilities, a caregiver-report measure developed by the authors that quantifies symptoms diagnostic of and/or associated with developmental disabilities, including autism.

Results: Sixty percent of the children exhibited sensory problems in at least one modality, with 38% showing problems in multiple modalities. The incidence by modality was 35% auditory, 22% visual, 16% tactile, 14% each for vestibular and olfactory, and 29% gustatory.

Hierarchical and K-means cluster analyses based on scores for the six sensory modalities yielded four groups: no problems, auditory/visual/vestibular, and multiple-modality. One-way ANOVAs revealed between-group differences on overall autistic symptomatology and adaptive behavior, sleep problems, and several subject variables (age walked, birthweight).

Conclusion: A majority of the children in the study presented with sensory problems. Several symptom clusters were identified that differed on overall autistic symptomatology, developmental level, and other indices of developmental pathology.

Sponsor: R01 HD34942

PS6.56
SYMPTOM OVERLAP BETWEEN BIPOLAR DISORDER AND AUTISM SPECTRUM DISORDER
Jeremy Blank, Felicia Widjaja, Gerald Voelbel, Gahan Pandina, Marsha Bates, Robert Hendren, University of California, Davis Department of Psychiatry and Behavioral Sciences and the M.I.N.D. Institute

Background: A subset of children with autism spectrum disorder (ASD) present with emotional dysregulation that resembles the affective instability symptoms common in bipolar disorder (BD). A growing literature suggests co-occurring disorders and possible morbidity or etiologic overlap. However, this overlap has not been well defined.

Objective: To use standardized measures to study BD symptoms in children with ASD and the extent of ASD symptoms in children with BD.

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 of affective instability from the K-SADS and eight symptoms from the DSM-IV Asperger’s/Autism Checklist were selected. The ASD and BD groups were compared for symptom presence (mild or greater) frequency.

Results: As expected, the K-SADS symptoms of affective instability were more prevalent in the BD group; however, 1/3-1/2 of children with ASD also demonstrated mood symptoms, suggesting a subgroup of children with ASD may have an overlapping disorder. From the Asperger’s/Autism Checklist, the ASD group had a higher symptom frequency. However, a high percentage of BD patients expressed several symptoms suggesting that individuals with BD may also have an overlapping disorder with ASD.

Conclusion: Symptom overlap in ASD and BD suggest co-occurring symptomatic disorders (DSM) and possibly overlapping morbidities. Further definition of this affective instability overlap will be necessary for biomarker research. Clinical implications include more accurate diagnosis and effective treatment matching.

Sponsor: New Jersey Governor’s Council on Autism; Stanley Foundation Research Award

PS6.57
AGGRESSIVE BEHAVIOR AND TEMPERAMENT IN CHILDREN WITH AUTISM SPECTRUM DISORDER
Beth Craven-Thuss, M Mary Konstantareas, University of Guelph/Department of Psychology

Background: Children with Autism Spectrum Disorder (ASD) are prone to aggressive behavior that is detrimental to their integration in school settings. Few studies have examined relationships between individual differences and aggressive behavior in this population. Past studies of aggressive behavior in children with ASD have either failed to measured individual differences or only considered symptom severity and/or cognitive functioning.

Objectives: The current investigation examines the relationship between aggressive behavior and individual temperament profiles.

Methods: Participants were interviewed and required to fill out questionnaires gathering information on these topics. The Childhood Autism Rating Scale (CARS) provided a current measure of autistic symptom severity. The Behavior Problem Inventory measured the frequency of each child’s aggressive behavior. Estimates of cognitive functioning were gained by employing the Developmental Profile II. The Children’s Behavior Questionnaire was used to measure temperament. Average levels of individual temperamental dimensions were compared to previously published data from a sample of typically developing children.

Results: Data are collected on 40 parents of children with ASD (mean age in years = 8.1, age range = 3.5 years to 13.0 years). Findings indicate that children with ASD may have a temperament profile with higher reactivity and lower self-regulation, compared to typically developing children. Aspects of temperament accounted for significantly more variance in frequency of aggressive behavior when compared to other predictors (i.e., symptom severity, cognitive functioning).

Conclusion: It seems important to consider temperament as an individual difference relevant to aggressive behavior in children with ASD.
ATYPICAL BEHAVIORS IN CHILDREN WITH AUTISM AND CHILDREN WITH A HISTORY OF LANGUAGE IMPAIRMENT Kelli C Dominick, Naomi O Davis, Janet Lainhart, Helen Tager-Flusberg, Susan Folstein, Boston University School of Medicine

Background: Children with autism display atypical behaviors that, while not essential to the diagnosis, cause marked distress for both the child and the family. Among these behaviors are: unusual eating habits, abnormal sleep patterns, self-injurious behavior, aggression, and temper tantrums.

Objectives: The first goal was to investigate the frequency, course, and inter-relationships of these atypical behaviors in children with autism (ASD) and children with a history of language impairment (HLI). Our second goal was to determine the relationship of these behaviors to language, IQ, and autistic symptoms.

Methods: Children with ASD and HLI were recruited through a program project. Autism diagnoses were confirmed using ADI-R and ADOS. Children's language (PPVT and EVT) and IQ (DAS) were assessed and parents completed the Atypical Behavior Patterns Questionnaire, an interview developed for this project.

Results: Matched groups included 54 children with ASD (47 males, 7 females) and 38 children with HLI (27 males, 11 females). Atypical eating behavior, abnormal sleep patterns, temper tantrums and self-injurious behavior were more common in the ASD group. Within the ASD group, children with more atypical behaviors had a lower NVIQ, lower levels of expressive language, more severe social deficits and more repetitive behaviors. Conclusion: These atypical behaviors are more common in children with ASD and are related to cognitive and language disability.

This research was funded by grants from the NIDCD (U19 DC 03610, Boston University School of Medicine; PO1 HD35476, University of Utah) which are part of the NICHD/NIDCD Collaborative Programs of Excellence in Autism, and by the NINDS (F30 NS048615).

PS6.59
ASSESSING CARDIOVASCULAR REACTIVITY TO ENVIRONMENTAL STRESSORS IN INDIVIDUALS WITH AUTISM SPECTRUM DISORDERS Matthew S Goodwin, June Groden, Wayne F Velicer, Lewis P Lipsitt, M Grace Baron, Stefan G Hofmann, Gerald Groden, The Groden Center/Research Coordinator

It has been suggested that neurophysiological factors implicated in ASD can contribute to arousal modulation problems that interfere with this population’s ability to attend to, process, and interact with the environment. Despite this hypothesized link, there is a lack of idiographic research that directly assesses arousal responses to novel stimuli or social situations in this population. The current presentation will report on a series of three studies conducted at the single-subject level that: (1) assess the feasibility of telemetrically recording heart rate (HR) as a measure of sympathetic arousal in 15 persons with ASD, (2) determine a wide sample of potentially stressful situations involving novel stimuli and social situations that can elicit significant physiological arousal in this population, and (3) compare arousal responses to these environmental stressors in five persons with ASD and five age- and sex-matched typically developing individuals. All of the participants were found to tolerate the telemetric devices and the dependent variable HR proved to have measurement characteristics that suggest sensitivity to the stress-induced experimental conditions. It was hypothesized that the group with ASD would show significant (p<.05) cardiovascular responses to a greater number of stressors than the typically developing control group. However, results revealed just the opposite. The group with ASD showed significant (p<.05) responses only 22% of the time compared to the typically developing group who showed significant (p<.05) responses 60% of the time. Also, on average, the participants with ASD had mean HR responses 20 bpm higher during baseline and nearly every potentially stressful situation compared to the typically developing group. Interpretation of these results and methodological considerations for future research that employs telemetric measures of HR as a direct measure of arousal in persons with ASD will be discussed.

PS6.60
ADHD SYMPTOMS AS A FUNCTION OF SPEECH, RACE & GENDER IN INDIVIDUALS WITH AUTISTIC DISORDERS Alicia Hall, Ruth Abramson, Harry Wright, Sarah Ravan, Heidi Cope, Michael Cucarro, Margaret Pericak-Vance, University of South Carolina School of Medicine

Approximately 12% of children with Autism Disorder (AD) are treated with stimulant medication, in order to reduce symptoms of Attention Deficit/Hyperactivity Disorder (ADHD) (Aman, etal.,1995). Little is known about the influence of speech, race and gender on parent perception of ADHD symptoms.

Objective: To determine if there are significant differences in ADHD behaviors based on level of speech (verbal/nonverbal), race (Caucasians/African-Americans), and gender in AD children.

Design/Methods: Participants (n=146) were drawn from a molecular genetic study of AD. Diagnoses were confirmed using medical records and/or clinical evaluation and the Autism Diagnostic Interview-Revised (Lord, 1994). The SNAP-IV has been frequency used in research as a measure of ADHD behaviors. (Solante, et.al., 2001, Swanson, etal, 2001). The subscales used in this study were ADHD- Inattention, ADHD-Hyperactivity and ODD.

Results: Many participants scored in the clinically significant range on the ADHD-Inattention Scale (48.8%), the ADHD-Hyperactivity Scale (31.4%) and the ODD Scale (12.5%). Speech was significant on the ADHD-Inattention (F(1,134)=4.124,p=.044), ADHD-Hyperactivity (F(1,192)=4.765,p=.031) and ODD (F(1,192)=6.960,p=.009) scales, verbal children scoring higher. Race was significant on the ADHD-Hyperactivity (F(1,192)=3.907,p=.050) scale, Caucasians scoring higher.
than African-Americans. Gender was significant on the ADHD-Inattention (F(1,134)=5.026, p=.027), males scoring higher. Interaction effects on the ADHD-Inattention scale for Speech*Ethnicity (F(1,134)=7.311, p=.044) and Gender*Ethnicity (F(1,134)=4.270, p=.041) were present.

Conclusions: This study suggests the report of ADHD symptoms in children with AD are influenced by speech, gender and race. Children with fluent speech have more ADHD symptoms than nonverbal children. Caucasians reported more Hyperactivity symptoms than African-Americans. Males have more Inattention symptoms than females.

**PS6.61**

**ANXIETY SYMPTOMS IN SCHOOL-AGED CHILDREN WITH AUTISM SPECTRUM DISORDERS**

Susan Lynn Hepburn, Judy Reaven, Erin Flanigan, Kristina Kaporich, Corry Robinson, Lisa Miller, Dept. of Psychiatry, University of Colorado at Denver Health Sciences

Background: Phenotypic description of comorbid anxiety and autism is needed, and should incorporate multiple assessment approaches, including: parent report, self-report, and direct observation.

Objectives: The main goal of this project is to describe how anxiety symptoms manifest in school-aged children with ASD, utilizing multiple assessment methods.

Methods: Twenty-seven parent-child dyads participated in this study. All of the children (20 males, 7 females, mean age of 9 ½ years) received a clinical diagnosis of autism (n = 18) or Asperger syndrome (n = 9), and obtained scores within the autism ranges on both the ADOS and SCQ. Parents and children completed several measures of anxiety symptoms, including the K-SADS, SCARED, CY-BOCS, and NIH Obsessive Compulsive Scale.

Behavioral coding is on-going.

Results: Fifteen children (56%) met diagnostic criteria for specific phobia, 8 (30%) for obsessive-compulsive disorder, and 8 (30%) for generalized anxiety. Reliability between child and parent report appears to differ as a function of symptom type. Form of anxiety symptoms and child characteristics (e.g., gender, age, developmental level, symptom severity) will be explored.

Conclusion: This study provides information from multiple assessment methods concerning the presentation of anxiety symptoms in school-aged children with autism. Implications for research and intervention will be discussed.

Sponsor: CDC* #UI0/CCU820391, Organization for Autism Research (OAR)

**PS6.62**

**OBSSESSIONS AND COMPULSIONS AS REPORTED BY PARENTS OF CHILDREN WITH AUTISM SPECTRUM DISORDERS**

Alison Herndon, Celeste St. John-Larkin, Judy Reaven, Susan L. Hepburn, Department of Psychiatry, University of Colorado Health Sciences Center

Background: Individuals with an autism spectrum disorder often present with obsessive and compulsive behaviors. Previous work examining the content of obsessions and compulsions in adults with autism suggests that the forms of the behaviors are distinctly different from those seen in adults with obsessive-compulsive disorder.

Objectives: This study is an extension of previous research and focuses on the content and form of obsessions and compulsions in school-aged children with autism.

Methods: Forty parents of children with autism (n = 31) or Asperger syndrome (n = 9), mean age of 9 years (range = 7 - 14 years) completed the Children’s Yale-Brown Obsessive-Compulsive Scale and reported the absence of presence of a specific list of target behaviors.

Results: Results demonstrated that children with autism tend to demonstrate a different set of obsessive and compulsive behaviors than has been reported in the literature on persons with OCD and not autism. Furthermore, symptoms were rarely dystonic for the children with autism, suggesting a potentially important diagnostic distinction.

Conclusions: Implications for comorbidity of OCD and autism, as well as implications for treatment and further research will be discussed.

Sponsors: National Institutes of Child Health and Human Development U19 HD35468-07, Collaborative Programs of Excellence in Autism (CPEA); Program Project PI = Rogers/Hepburn.
developmental level and language ability on behavioural and emotional problems will be considered and the role of family functioning, parental mental health problems and stress will also be explored. Data on change over time will also be presented.

Conclusions: As research has shown that behavioural and emotional problems in autism persist into adolescence and young adulthood, understanding of these issues in very young children will have important implications for intervention and long term outcome.

Sponsor: National Health and Medical Research Council of Australia (NHMRC), and the Australian Research Council (ARC)

**PS6.64**

**SELF-REGULATION AND COMPLIANCE IN CHILDREN WITH AUTISTIC DISORDER AND HYPERACTIVITY**

Laudan B. Jahromi, Lisa Lee, Connie Kasari, James T. McCracken, University of California, Los Angeles

Background: Children with autism often show hyperactivity, distractibility, and impulsivity. Methylphenidate hydrochloride is often an efficacious treatment, yet little information exists on whether medications affect social behavior.

Objectives: Examine the effect of methylphenidate on observational measures of children’s self-regulation and compliance/defiance behaviors.

Methods: Participants were 21 children with pervasive developmental disorders and moderate to severe hyperactivity. Children were predominantly male, and between the ages of 5 and 14 years. Measures included the Vineland Adaptive Behavior Scale (VABS), the Aberrant Behavior Checklist (ABC), and observational coding of self-regulation and compliance/defiance during caregiver-child interactions.

Results: Preliminary analyses at baseline indicated that children who made more bids for their parents’ attention rather than self-regulating were rated as more irritable (r = .47, p < .05) and more hyperactive (r = .45, p < .05) on the ABC, and scored lower in the socialization domain of the VABS (r = .45, p < .05). Children with greater observed compliance during the clean-up task were rated by their parents as more lethargic (r = .53, p < .05), suggesting that compliance may be related to less emotional reactivity. Further analyses will be conducted to assess change in social behavior as a function of methylphenidate.

Conclusion: Preliminary findings suggest that children’s baseline measures of social behavior were related to parent-report measures of their adaptive and aberrant behaviors.

Sponsor: NIMH

**PS6.65**

**EXACERBATION OF AUTISTIC FEATURES DURING EPISODES OF KLEINE-LEVIN SYNDROME IN A CASE WITH OVERGROWTH SYNDROME AND PDD-NOS**

Ayse Kilincaslan, Nahit Motavalli Mukaddes, Rizbeh Fateh, Istanbul Medical Faculty, Child Psychiatry Department

Background: Kleine-Levin syndrome (KLS) is a rare disease characterised by recurrent episodes of hypersomnia, cognitive and behavioral disturbances, compulsive eating behavior and hypersexuality. The disease is predominantly described in adolescent males and otherwise normal people. The present case study will focus on symptom expression and differential diagnoses during and between episodes in a girl with PDD-NOS and overgrowth syndrome.

Method:

Case description: 15 years old girl was referred to our clinic due to her hypersomnia, lack of interest in the surroundings, irritability, eating unusual things just as uncooked rice and pasta and increase in stereotyped behavior. A total of 5 episodes with similar behavioral features, all starting after a flu-like condition, lasting for 3 to 15 days were being described in the last 3 years. Her psychiatric interview revealed a premorbid diagnosis of PDD-NOS (according to DSM-IV criteria) with her social deficit and stereotyped behavior. She was above 97th percentile for height, weight and head circumference and had a dysmorphic face. She had moderate mental retardation and a history of epilepsy. She was evaluated in our genetic department where she was clinically diagnosed with Sotos syndrome. Her MRI and EEG findings revealed no abnormality but human lymphocyte antigen analysis indicated HLA-DRB1*0415 and HLA-DQB1*0306 compatible with KLS.

Conclusion: Cognitive and behavioral symptoms frequently appear in KLS but when the episodes occur on the basis of an autistic spectrum disorder, they demonstrate some distinct behavioral characteristics such as decrease in speech, sociability and increase in stereotyped behavior and interests.

**PS6.66**

**MODERATORS OF DEVELOPMENT IN AUTISM**

Peter Mundy, Heather Henderson, Nicole Zahka, Caley Schwartz, Nicole Kojkowski, Anne Pradella, Camilla Hileman, The Center for Autism & Related Disabilities, University of Miami

Children with Autism display individual differences in social development. These differences are very clear among higher functioning children with autism (HFA) and are often complicated by emotional disturbance such as anxiety and depression. The study of variability in social impairments and comorbidity in autism is important because it may assist in understanding phenotypic differences that complicate diagnosis, research and treatment. Moreover, since the broader phenotype for autism is marked by its association with depression and anxiety disorders, the study of the interplay between individual differences in comorbidity and social impairments in HFA children may reveal fundamental features of the underlying pathophysiology of autism. Research on social impairments and comorbidity is essential to understanding the specific intervention needs of HFA children.
This presentation illustrates a new approach to research designed to identify processes that may moderate the expression of autism. Two studies are described that indicate EEG measures of asymmetry in anterior brain activity are significantly associated with differences in social symptoms, the presence of comorbidity and the age of parents first concerns among HFA children. These data suggest that motivation processes associated with anterior asymmetry may moderate the course and expression of autism. A third study is described that indicates that an EEG/ERP measure of task performance error monitoring is related to individual differences in intelligence as well as social symptoms in HFA children. This suggests that the supervisory attention functions and self-regulation processes associated with anterior cingulate activity may also moderate symptom presentation and intellectual achievement in children with autism. The latter observation may help to explain previous observations from imaging studies of significant relations between anterior cingulate activity and symptom presentation in autism.

**PS6.67**

GROUP COGNITIVE BEHAVIORAL THERAPY FOR CHILDREN WITH HIGH-FUNCTIONING ASD AND ANXIETY

Judith Ashkanazi Reaven, Shana Nichols, Audrey Blakeley-Smith, Susan Hepburn, JFK Partners - University of Colorado at Denver and Health Sciences Center

Background: Children with ASD are at greater risk for developing anxiety disorders than typically-developing children and those with other developmental disabilities. Objectives: Conduct a pilot study to assess the effectiveness of an original, manualized group cognitive behavior intervention package (with parent participation) designed to reduce anxiety symptoms in children with high-functioning ASD.

Methods: Children ages 8-14 were recruited from the Autism and Developmental Disorders Clinic of JFK Partners, UCDHSC and through word of mouth in the Denver community. Criteria for inclusion: 1) current clinical diagnosis of autism, 2) exceeding criteria for ASD on the ADOS, 3) exceeding criteria for ASD on the ASQ, 4) presenting with clinically significant symptoms of anxiety on the K-SADS-PL, and 5) Verbal IQ of 80 or higher. Children and their parents participated in the 12 week group treatment. The SCARED was administered pre-, post-treatment, and at 3 and 6 month follow-up.

Results: Ten children with ASD (mean age of 12.25 years; age range 11-14 years) and their parents participated in the study. Preliminary analyses indicated that parent report of social anxiety symptoms decreased after treatment, t (1,9) = 3.42, P = .014 and parent report of the severity and interference associated with targeted fears also decreased significantly, t (1,9) = 1.82, p = .041. Conclusions: Preliminary findings suggest that group CBT treatment, with parent participation, may be effective in decreasing anxiety symptoms in children with ASD.

**PS6.68**

FACTORs ASSOCIATED WITH PRESENCE OF DEPRESSIVE SYMPTOMS IN ADULTS WITH AUTISM SPECTRUM DISORDER

Lindsey J Sterling, Geraldine Dawson, Jessica Greenson, Annette Estes, University of Washington

Background: Previous research has suggested that adolescents and adults with autism often exhibit symptoms of depression (e.g. Ohaziuddin et al., 2002). Objectives: Investigate whether specific characteristics, such as severity of autism symptoms, cognitive functioning, and related psychopathology are associated with presence of depression in adults with autism.

Methods: Participants were assessed as part of the STAART Center of Excellence Study or the NICHD CPEA Family Study of Autism 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 symptoms and associated psychopathology. Participants were also assessed with the ADOS and ADI-R in order to confirm the autism spectrum diagnosis. Cognitive functioning was evaluated using the Wechsler Adult Intelligence Scale (WAIS).

Results: Psychiatric history data were collected on 39 adults with autism. Fourteen of these individuals endorsed depressive symptoms. Of this group, 9 individuals (64%) also reported symptoms related to obsessive-compulsive disorder, and 7 (50%) reported symptoms related to anxiety. Preliminary results suggest that individuals endorsing depressive symptoms tend to exhibit higher levels of cognitive functioning (as expressed by verbal and full scale IQ scores) and higher levels of social functioning (according to ADOS social domain scores) than individuals without depression.

Conclusions: Investigation of the correlates of depression will help identify risk factors for depressive symptoms in adults with autism. Elucidation of these factors will have important clinical implications for screening and treating individuals with autism who suffer from depression.

Funding source: NIMH (U54MH066399) and NICHD (U19HD34565)

**PS6.69**

USING CLUSTER ANALYSIS TO GROUP CHILDREN WITH ONE OR MORE OF SIX DEVELOPMENTAL DISORDERS

Murray James Dyck, Jan Patricia Piek, Griffith University, Gold Coast, Queensland

Background: Developmental disorders seldom occur in isolation: any given disorder is typically accompanied by some other disorder.

Objectives: To identify groups of children who share an ability profile and to assess whether these groups also share clinical diagnoses.

Methods: 163 children with confirmed diagnoses of
Autistic Disorder or Asperger’s Disorder, Mixed Receptive-Expressive Language Disorder, mild Mental Retardation, Developmental Coordination Disorder, ADHD inattentive or combined subtype and 449 typical children were assessed with age-standardised measures of perceptual organisation, verbal comprehension, receptive and expressive language, fine and gross motor skills, theory of mind, emotion understanding and recognition abilities, response inhibition, and verbal working memory.

Results: In our cluster analysis, we specified a 7-cluster solution to correspond with the 7 different samples. The empirically derived groups did not closely correspond to the diagnostic groups. Rather, there were 2 clusters that mainly consisted of typical children with average or above average ability, 2 clusters that consisted of both disordered and typical children with markedly poorer motor coordination or language abilities, and 3 clusters that mainly consisted of children with a disorder. These clusters grouped children with very low scores on all abilities (Mental Retardation), markedly low motor coordination and markedly high response inhibition scores (Autistic Disorder), and moderately low scores on all abilities, but with especially low language scores (Mixed Language Disorder).

Conclusion: Ability profiles of children with a developmental disorder mainly do not correspond to the profiles used to define disorders. Relatively poorer language or motor skills in children with low average general ability are associated with increased risk of disorder.
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Autism Speaks was founded in 2005 by Suzanne and Bob Wright and is committed to aggressively funding biomedical research, raising public awareness about autism, and bringing hope to all who deal with the hardships of autism spectrum disorder. In 2006, Autism Speaks merged with the National Alliance for Autism Research (NAAR), creating the largest non-profit organization in the nation dedicated to accelerating the pace of autism research. In its ten year history, NAAR has committed nearly $30 million to fund over 270 autism research projects, fellowships and collaborative programs worldwide. This investment has been leveraged to attract more than $53 million in autism research awards by the National Institutes of Health (NIH) and other funding sources. For more information, please visit www.AutismSpeaks.org.

Cure Autism Now is an organization devoted to accelerating research to prevent, treat and cure autism. In its ten year history, Cure Autism Now has provided more than $31 million for autism research programs. This includes the establishment and ongoing support of the Autism Genetic Resource Exchange (AGRE), the largest open-access repository of genetic and clinical information for autism. In addition, Cure Autism Now advocacy and funding have resulted in an overall leveraged investment of autism that exceeds $170 million. Granting programs include Young Investigator, Pilot Project, Treatment and Innovative Technology awards, as well as support of various targeted initiatives and conferences. Cure Autism Now has 18 chapters across the country with national headquarters in Los Angeles. More information about Cure Autism Now can be found at www.cureautismnow.org.