The Onset Of Autism During Infancy
Insights From Sibling Studies

Ted Hutman, Ph.D.
Assistant Professor
Department of Psychiatry
David Geffen School of Medicine at UCLA

The Help Group Summit 2012
Autism Spectrum Disorders

A. Social interaction
   • Eye contact, facial expression
   • Peer relationships
   • Sharing interest and enjoyment
   • Social/emotional reciprocity

B. Communication
   • Language, conversation, echolalia
   • Play

C. Restricted & Repetitive Behaviors
   • Restricted interests/preoccupations,
   • inflexible adherence to routines, stereotypies
Autism Prevalence

- Nationwide: $1/88 = 1.1\%$ (CDC, 2012)
- Boys are 4-5 times more likely to be affected with autism than girls
### Age at Diagnosis

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Age at Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autistic Disorder (general population)</td>
<td>3.1 years</td>
</tr>
<tr>
<td>PDD-NOS</td>
<td>3.9 years</td>
</tr>
<tr>
<td>Asperger’s Disorder</td>
<td>7.2 years</td>
</tr>
<tr>
<td>Autistic Disorder (African American children)</td>
<td>7.9 years</td>
</tr>
</tbody>
</table>
Timing of Diagnosis

- Diagnoses are typically not made before the fourth year (Mandell et al., 2005)
- Outcomes are improved for children who receive early intervention (Bibby et al., 2002; Goldstein, 2002; Harris & Handleman, 2000; Lord, 2001; Rogers, 1998)
- Diagnoses conferred prior to 30 months are not as stable as those conferred after 30 months (Turner & Stone, 2007)
Reasons to Study Infants

• Early Detection
  • Channel children into treatment

• Treatment
  • What features, symptoms, skills to target

• Advance the study of autism
  • Characterize onset patterns
  • Inform genetic, neurobiological research
Studying Infant Siblings

- Autism is highly heritable
  
  (Bailey et al., 1995; Steffenburg et al., 1989)

- Recurrence rates within families estimated at 18.8%.  
  26.2% for boys.  32.2% in multiplex families.

  (Ozonoff et al., 2011)
## Recruitment Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-Risk Group</td>
<td>Infant siblings of children with autistic disorder</td>
</tr>
<tr>
<td>Low-Risk Group</td>
<td>Infants with no family history of developmental disabilities</td>
</tr>
</tbody>
</table>
"Outcome" Groups

<table>
<thead>
<tr>
<th>High-Risk Group (Infant Siblings)</th>
<th>Sibs-ASD</th>
<th>Sibs-Concerns</th>
<th>Sibs-TD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-Risk Group</td>
<td></td>
<td></td>
<td>Low-Risk TD</td>
</tr>
</tbody>
</table>
Initiating Joint Attention

(Rozga et al., 2011)
Response to Examiner’s Bids for Joint Attention

(Rozga et al., 2011)
Requesting

(Rozga et al., 2011)
• No differences in mother/infant behaviors at 6 mos.
  • Social gaze, vocalization, smiles

• 12-month non-verbal communication:
  • Pointing/showing
  • Response to pointing
  • Requesting
Joint Attention in the Eye-Tracker

Attention Getter

Baseline

Social Greeting

Opportunity for Gaze Following

Kristen Gillespie-Lynch
Response to Social Greeting

$F(1, 18) = 6.295; \ p = .008$
Response to Another Person’s Distress
Attention to Distress
(12, 18, 24, 36 months)

(Hutman, Rozga, DeLaurentis, Barnwell, Sugar, & Sigman, *JCPP*, 2010)
Affective Response to Distress
(12, 18, 24, 36 months)

(Hutman et al., 2010)
Awareness of change in social context
Attentiveness to examiner
Differences in duration of attention as well as number of gaze shifts
Early evidence of BAP?
Social Behavior During Cognitive Testing
Social Behavior During Cognitive Testing

(Ozonoff et al., *JACAAP*, 2010)

- Gaze to Face
- Social Smile
- Directed Vocalization

(Ozonoff et al., *JACAAP*, 2010)
How Early Do Parent Concerns Predict Later Autism Diagnosis?

(S Dev Behav Pediatr 30:367–375, 2009)

Sally Ozonoff, PhD,* Gregory S. Young, PhD,* Mary Beth Steinfeld, MD,* Monique M. Hill, MS,* Ian Cook, PhD,* Ted Hutman, PhD,† Suzanne Macari, PhD,‡ Sally J. Rogers, PhD,* Marian Sigman, PhD†

• Parents of children with autism are aware of the risk to later-born infants and report more general developmental concerns about the infants at study intake (6 months)

• At and after 12 months, parental concerns are more specific to ASD-related symptoms and are useful predictors of which high-risk infants will go on to receive a diagnosis at 36 months
Longitudinal Parent Report on Child Temperament

Activity
Adaptability
Approach
Mood
Intensity
Distractibility
Persistence
Sensory Reactivity
Rhythmicity

Age in Months
• Trajectories of Sibs-ASD differed from Sibs-TD
  • *Increasing* activity levels, negative affect, and intensity of affective responses
  • *Decreasing* adaptability and approach behaviors

• Links between parent-reported temperament at 12 months and parent behaviors during mother-child free play interaction at 18 months.
# Motor Skills Development

with Shafali Jeste, MD

(Geschwind, Ann Rev Med, 2009)

<table>
<thead>
<tr>
<th>Domain</th>
<th>Autism</th>
<th>Asperger</th>
<th>PDD-NOS</th>
<th>ASD</th>
</tr>
</thead>
<tbody>
<tr>
<td>social communication</td>
<td>required</td>
<td>required</td>
<td>required</td>
<td></td>
</tr>
<tr>
<td>language</td>
<td>required</td>
<td>–</td>
<td>variable</td>
<td></td>
</tr>
<tr>
<td>repetitive, restrictive behaviors</td>
<td>required</td>
<td>required</td>
<td>variable</td>
<td></td>
</tr>
<tr>
<td>sensory abnormalities</td>
<td>&gt;90%</td>
<td>80%</td>
<td>variable</td>
<td>94%</td>
</tr>
<tr>
<td>developmental regression</td>
<td>15%–40%</td>
<td>?</td>
<td>?</td>
<td>15%–40%</td>
</tr>
<tr>
<td>motor signs</td>
<td>60%–80%</td>
<td>60%</td>
<td>60%</td>
<td>60%–80%</td>
</tr>
<tr>
<td>gross motor delay</td>
<td>10%</td>
<td>?</td>
<td>?</td>
<td>5%–10%</td>
</tr>
<tr>
<td>sleep disturbance</td>
<td>55%</td>
<td>5%–10%</td>
<td>40%</td>
<td>50%</td>
</tr>
<tr>
<td>gastrointestinal disturbance</td>
<td>45%</td>
<td>4%</td>
<td>50%</td>
<td>4%–50%</td>
</tr>
<tr>
<td>epilepsy</td>
<td>10%–60%</td>
<td>0%–5%</td>
<td>5–40%</td>
<td>6%–60%</td>
</tr>
<tr>
<td>comorbid psychiatric diagnosis</td>
<td>70%</td>
<td>60%</td>
<td>&gt;25%</td>
<td>25–70%</td>
</tr>
</tbody>
</table>

(Geschwind, Ann Rev Med, 2009)
Motor Skills Development
with Shafali Jeste, MD

- Raw scores on Mullen Gross Motor Scale at 6 months are normally distributed.
- 6-month gross motor scores are correlated with the following measures at 12 months:
  - Receptive Language, $r = .31$, $p = .01$
  - Visual Reception, $r = .29$, $p = .02$
  - Requesting (ESCS), $r = .30$, $p = .04$
Motor Behavior at 12 months
Motor Behavior at 12 months
Combining the Warning Signs

- Using the following predictors at 12 months:
  - Response to name
  - Joint Attention
  - Language skills
  - Selective attention to social stimuli
- Selects a group for whom the estimated probability of ASD diagnosis is 47.1%
The Search for Early Biomarkers of ASD

6-week-old (passive fMRI)

- English > Rest
- Japanese > Rest
- English > Japanese

8-week-old (rs-fcMRI)

- Sensorimotor Network
- Auditory Network
- Visual Network
- Salience Network
Eye movement and pupillometry
Acknowledgements

Thanks to over 300 families who have participated in this study.

Investigators
Scott Johnson
Marian Sigman
Mirella Dapretto
Shafali Jeste
Daniel Geschwind
Susan Bookheimer
Connie Kasari
Agata Rozga

Graduate Students & Research Assistants
Lisa Christensen
Natalie Colich
Stephany Cox
Mari Davies
Angeline De Laurentis
James Earhart
Kristen Gillespie-Lynch
Lovella Gomez
Stephanie Marshall
Alia Martin
Joanna Mussey
Amanda Noroña
Mithi del Rosario
Nuri Reyes
Leigh Sepeta

Funding:
-NIMH Studies to Advance Autism Research & Treatment Grant #U54-MH-068172
-NICHD/NIDCD Autism Centers of Excellence Grant #1P50-HD-055784
NOW ENROLLING

• Infants < 6 weeks of age
  • 2 older siblings with ASD, OR
  • 1 older sibling + family history of ASD
  • Control group: NO family history of ASD

• Referral to **free treatment study** for eligible participants

(310) 825-3478

siblings@autism.ucla.edu