Early Identification of Autism Spectrum Disorder

The HELP Group Summit
October 14, 2016

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Professor and Vice Chair
MIND Institute, UC Davis
Outline

- Early signs of ASD
- Stability of early diagnoses
- Other challenges in siblings
- Screening for ASD in infants and toddlers
- Working with families
Earlier Identification

- Median age of diagnosis = 50 months (CDC, 2016)
- Mean age of first parental concern = 18 – 19 months
  - 30–50% report concerns before 1st birthday

Earlier identification → Earlier intervention

![Bar chart showing median age of diagnosis for different conditions](chart.png)
Methods to Study Early Symptoms

- Retrospective
  - Parent report
  - Home video analysis

- Prospective
  - High risk samples
  - Longitudinal assessments of development

Infant Sibling Design
UC Davis – UCLA
Infant Sibling Study

Phase I  2003 - 2008  N = 350

- 6 Months
- 12 Months
- 18 Months
- 24 Months
- 36 Months
- 6 – 7 Years
- 9 – 12 Years

Phase II  2008 - 2013  N = 300

- 6 Months
- 9 Months
- 12 Months
- 15 Months
- 18 Months
- 24 Months
- 36 Months
- 6 – 7 Years

Phase III  2013 - 2017  N = 200

- 6 Months
- 12 Months
- 18 Months
- 24 Months
- 36 Months
UC Davis – UCLA
Infant Sibling Study

Goals

1. How early can we identify ASD in babies?
   - What are the earliest reliable markers?

2. How stable is early diagnosis?

3. What other developmental problems occur in infant siblings?
# Measures

<table>
<thead>
<tr>
<th>Category</th>
<th>Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Communication</td>
<td>ESCS, Mullen, MacArthur CDI, Language Use Inventory</td>
</tr>
<tr>
<td>Social-Emotional</td>
<td>Peek-a-boo, imitation, empathy, parent-child play, response to name</td>
</tr>
<tr>
<td>Face Processing</td>
<td>Eye gaze during still face paradigm</td>
</tr>
<tr>
<td>Autism Symptoms</td>
<td>AOSI, ADOS, ADI, SRS</td>
</tr>
<tr>
<td>Other</td>
<td>Cognitive, adaptive, motor, head circumference, object use/exploration, form and motion processing, smooth pursuit, audiovisual integration of speech</td>
</tr>
</tbody>
</table>
## Group Differences: ASD Outcomes v Low Risk Infants

<table>
<thead>
<tr>
<th></th>
<th>6 m</th>
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<th>24 m</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Mullen language</td>
<td></td>
<td>✔</td>
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<tr>
<td>MCDI vocabulary</td>
<td></td>
<td>✔</td>
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<tr>
<td>Vocalization freq</td>
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</tr>
<tr>
<td>Empathy</td>
<td></td>
<td>✔</td>
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</tr>
<tr>
<td>ESCS joint attention</td>
<td></td>
<td>✔</td>
<td>✔</td>
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</tr>
<tr>
<td>Response to name</td>
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<td>Parent-infant synchrony</td>
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<tr>
<td>Eye contact frequency</td>
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<tr>
<td>Examiner social ratings</td>
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<td>Repetitive object use</td>
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Declining Trajectories: Behavior with Examiners

Ozonoff et al 2010, JAACAP
Eye Contact

With Examiner

With Mother

Error Bars: +/- 1 SE
Response to Name
NCAST Feeding Scale

![Graph showing feeding scale for TD and ASD at 9 months and 12 months.](image-url)
Informant Ratings

Examiner Ratings, 2014

Parent Ratings, 2014
Informant Ratings

Examiner Ratings, 2014

Parent Ratings, 2014

Only 6 of 18 parents endorsed a regression retrospectively.
Prospective Tracking of Symptoms

$M$ age of diagnosis = 23.3 months

50% diagnosed by 18m
75% diagnosed by 24m
## Group Differences: ASD Outcomes v Low Risk Infants

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<td></td>
<td>✓</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>
| **Response to name**      |     | ✓    | ✓    | ✓    | ✓    | Gammer et al., 2015; Zwaigenbaum et al., 2005
| **Face processing**       |     |      |      |      |      | Jones & Klin, 2013
| **Imitation**             |     | ✓    | ✓    | ✓    | ✓    |
| **Parent-infant synchrony** | ✔  |      |      |      |      | Wan et al., 2013
| **Eye contact frequency** | ✔   | ✔    | ✔    | ✔    | ✔    |
| **Examiner social ratings** | ✔   | ✔    | ✔    | ✔    | ✔    |
| **Parent social ratings** | ✔   | ✔    | ✔    | ✔    | ✔    |
| **Repetitive object use** | ✔   | ✔    | ✔    | ✔    | ✔    | Wolff et al., 2014
Conclusions

- ASD *emerges* over the first 2 years of life
  - Not present at birth as Kanner suggested
- Most children developing ASD show declining trajectories
  - Regressive onset is the norm, not the exception
- Parents identify declining trajectories prospectively, but less so retrospectively
  - ADI-R report of regression is only the tip of the iceberg
- Promise for development of screening measures
Goals

1. How early can we identify ASD in babies?
   - What are the earliest reliable markers?

2. How stable is early diagnosis?

3. What other developmental problems occur in infant siblings?
Stability of Early Diagnosis

Ozonoff et al. 2015, J Ch Psychol Psychiat
Stability of Early Diagnosis

Ozonoff et al. 2015, J Ch Psychol Psychiat
Stability of Early Diagnosis

- Diagnosis before 36 months is very stable
  - Over 90% retain the diagnosis
  - If diagnosed early, intervene
  - No need to confirm diagnosis at older ages
- Very few “false positives”
- But… many children with ASD are not identified at 18 or 24 months
  - Symptoms emerge over time

Ozonoff et al. 2015, *J Ch Psychol Psychiat*
## Conclusions and Clinical Implications

<table>
<thead>
<tr>
<th>Few markers of ASD at 6 months or earlier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continued search for markers that identify risk before the onset of behavioral signs</td>
</tr>
<tr>
<td>Declining developmental trajectories that clinicians and parents can identify</td>
</tr>
<tr>
<td>Early diagnosis is very stable – if diagnosed, intervene</td>
</tr>
<tr>
<td>Screen early, screen often, screen later</td>
</tr>
<tr>
<td>Family history of ASD is a significant risk factor for later-born siblings</td>
</tr>
</tbody>
</table>
# Medical Risk-Prevention Model

<table>
<thead>
<tr>
<th>Cardiovascular Disease</th>
<th>Autism</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Undesired outcome</strong></td>
<td>heart attack, stroke</td>
</tr>
<tr>
<td><strong>Screening for risk factors</strong></td>
<td>family hx, hi chol, smoking, diabetes, hypertension</td>
</tr>
<tr>
<td><strong>Prevention/Monitoring</strong></td>
<td>lifestyle changes (e.g., exercise, diet)</td>
</tr>
<tr>
<td><strong>More intensive intervention as needed</strong></td>
<td>medication, stent, bypass surgery</td>
</tr>
</tbody>
</table>

Thanks to Wendy Stone PhD for sharing this slide
Primary care providers should …

- Be aware of early signs
- Perform developmental surveillance and elicit parent concerns at every visit
  - Administer standardized screening measure if indicated
- Perform formal screens for autism at 18 and 24 months for all children
Infant Social-Communication Milestones

1 month
- Gaze to Faces and Eyes

1-2 months
- Social Smile

3 months
- Cooing, Turn-Taking Vocals

6-9 months
- Consonant-Vowel Babbling

6-9 months
- Responds to Name

9-15 months
- Gestures & Pointing

12-15 months
- Imitation
Red Flags for Autism in Infancy

Babies should be referred who are not...

- **6 – 9 months**
  - Looking at faces
  - Smiling at others
  - Cooing

- **9 – 12 months**
  - Responding to name
  - Babbling
  - Playing social games
  - Displaying bright affect

- **12 – 18 months**
  - Pointing and showing
  - Using single words
  - Using gestures
  - Imitating
  - Interested in peers
Screening Tools

- Autism-specific screeners
  - Infant-Toddler Checklist *(ITC)*
    - 6 – 24 months
  - Modified Checklist for Autism in Toddlers *(M-CHAT)*
    - 16 – 30 months
    - [https://www.m-chat.org](https://www.m-chat.org)
Rapid video-referenced ratings of reciprocal social behavior in toddlers: a twin study

Natasha Marrus, 1 Anne L. Glowinski, 1 Theodore Jacob, 2 Ami Klin, 3,4,5 Warren Jones, 3,4,5 Caroline E. Drain, 1,6 Kieran E. Holzhauer, 1 Vaishnavi Hariprasad, 1 Robert T. Fitzgerald, 1 Erika L. Mortenson, 1 Sayli M. Sant, 1 Lyndsey Cole, 1 Satchel A. Siegel, 1 Yi Zhang, 1 Arpana Agrawal, 1 Andrew C. Heath, 1 and John N. Constantino 1

1Department of Psychiatry, Washington University, St. Louis, MO; 2Department of Psychology, Palo Alto University, Palo Alto, CA; 3Marcus Autism Center, Children’s Healthcare of Atlanta, Atlanta, GA; 4Division of Autism & Related Disabilities, Department of Pediatrics, Emory University School of Medicine, Atlanta, GA; 5Center for Translational Social Neuroscience, Emory University, Atlanta, GA; 6Department of Neurology, Washington University, St. Louis, MO, USA
Video Referenced Infant Rating System for Autism (VIRSA)

- Video-based screening instrument for 6, 9, 12, and 18-month-olds
  - Measuring social-communication behavior and repetitive, unusual use of objects
- Examine psychometric properties
  - Test-retest reliability
  - Inter-rater reliability
  - Convergent and discriminant validity
  - Predictive validity
• 20-second video segments
• Paired to contrast
• Babies playing socially with their parents
• Clips display varying degrees of sociability
## Completed VIRSA ratings

<table>
<thead>
<tr>
<th></th>
<th>6 mos</th>
<th>9 mos</th>
<th>12 mos</th>
<th>18 mos</th>
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<tbody>
<tr>
<td>Parent</td>
<td>81</td>
<td>111</td>
<td>136</td>
<td>87</td>
</tr>
<tr>
<td>Parent retest</td>
<td>62</td>
<td>85</td>
<td>90</td>
<td>48</td>
</tr>
<tr>
<td>Examiner</td>
<td>84</td>
<td>45</td>
<td>144</td>
<td>89</td>
</tr>
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</table>
**VIRSA Ratings: Parent**

Main effect for Group: $X^2 = 6.68$, $p < .05$

Group x Age interaction: $X^2 = 6.41$, $p < .05$

- ASD (n=16)
- Atypical (n=18)
- Typical (n=135)
VIRSA Ratings: Examiner

Main effect for Group: $X^2 = 55.4, p < .001$

Group x Age interaction: $X^2 = 20.7, p < .001$
VIRSA Screening Efficacy

<table>
<thead>
<tr>
<th>No differences among groups at 6 months, replicating other measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Declining trajectories over time, replicating other measures</td>
</tr>
<tr>
<td>By 9 months, the screening instrument can identify broad/general delays</td>
</tr>
<tr>
<td>By 18 months, it can differentiate which infants have ASD</td>
</tr>
<tr>
<td>This low-burden, video-based, informant-report screening measure is promising for earlier identification</td>
</tr>
</tbody>
</table>
Working with Families in the Face of Diagnostic Uncertainty

**PROMOTE:**
- Transparency and trust
- Monitoring

**AVOID:**
- Undue alarm
- Negative changes in relationship with child
What we see ≠ What parents see

- Inconsistent eye contact
- Flat affect
- Low facial tone

How to convey concerns to parents?

Independent
Strong-willed

Slide courtesy of Wendy Stone PhD
Communicating Concerns

- Acknowledge, do not dismiss, parent concerns
- Have open and honest discussions
  - Be willing to express uncertainty
  - Acknowledge range of outcomes, imperfection of prediction of severity
- Discuss repercussions of false negatives and false positives
  - Families will differ in their values
- Provide parenting strategies and practical advice

Caronna et al 2007, Arch Ped Adolesc Med
Resources


- [ASDetect.org](http://www.autismspeaks.org) – a video-based app for early identification of ASD


- [http://www.autismspeaks.org](http://www.autismspeaks.org)
  - First 100 Days kit
  - Learn the Signs campaign
  - Video Glossary