How low can you go?
A transdiagnostic perspective on early detection of neurodevelopmental risk

Grand Rounds
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Disclosures

• I have nothing to disclose.
Overview

• Early detection approaches
  – ASD as example

• Infant predictors of ADHD?

• Transdiagnostic early developmental pathways

• Questions
Early detection and diagnosis: Why?

• Early identification $\rightarrow$ early treatment $\rightarrow$ improved outcomes
• Decrease service utilization, economic burden
• Challenges: false positives, unnecessary treatment
Turning back the clock

• Infancy/early childhood: Ideal period in which to investigate phenomenology of childhood disorders
  – Improve accurate, earlier detection
  – Identify critical time points/domains to be targeted by intervention/prevention efforts
  – Investigate environmental/contextual and biological causal mechanisms
Early identification: How?

- Affected sibling
- High-risk infant
- Unaffected sibling
- Low-risk infant
Infant sibling design

Variety of eye tracking, behavioral, developmental, symptom measures

Diagnostic outcomes determined
What can we learn from infant siblings?

• Patterns of onset
• Early behavioral and biological markers
• Targets for intervention and prevention
• Intermediate phenotypes (i.e., broader autism phenotype) and endophenotypes
  – Critical for future genetic studies
Early behavioral markers of ASD

Social Communication

- Eye gaze
- Vocalizations
- Social smiles

Repetitive behavior

- Repetitive object play
Early social communication
Emergence of social communication behaviors

Ozonoff et al. (2010), JAACAP
Repetitive behaviors

• Repetitive behaviors in ASD present by 12 months in infant siblings who develop ASD (Elison et al., 2014; Ozonoff et al., 2008; Wolff et al., 2014)

• Little known about longitudinal course early in life, particularly not prior to 12 months

• How early are differences in directly-assessed repetitive behaviors with objects present in infants developing ASD?
Object exploration
Typical behaviors

Miller et al., in prep
Atypical behaviors

Unusual visual inspection of objects present, stable as early as 9 months of age in infants developing ASD

Unusual visual inspection per min.
Age (months)

Low-Risk TD (n=49)
High-Risk Non-ASD (n=64)
High-Risk ASD (n=15)

Miller et al., in prep.
Red flags for ASD in first 2 years

- Lack of appropriate gaze
- Lack of warm, joyful expressions with gaze
- Lack of sharing enjoyment or interests
- Lack of alternating to-and-fro vocalizations with parents
- Lack of response to name
- Delayed onset of babbling past 9 mos
- Decreased or absent use of pre-speech gestures (waving, pointing, showing)
- No single words by 16 mos
- No two-word utterances by 24 mos
- Repetitive movements or posturing of body, arms, hands, or fingers
- Loss of language or social skills at any age

(Dawson et al., 2000; Landa et al., 2013; Osterling & Dawson, 1994; Osterling et al., 2002; Ozonoff et al., 2008; Ozonoff et al., 2010; Ozonoff et al. 2011; Werner & Dawson, 2005; Werner et al., 2000; Zwaigenbaum et al., 2005)
What about everyone else?

- Broader autism phenotype; other developmental concerns
Differences persist

Miller et al. (2015), *Autism Research*
Early diagnosis of ADHD...

• **Careful, thorough** preschool diagnoses persist (Lahey et al., 2005; Riddle et al., 2013)

• Infant behavioral indicators suggested
  – Temperament (negative affect, inhibitory control)
  – Language, motor delays

• Capitalize on wide range of phenotypic variation inherent to high-risk infant sibling samples
Are differences detectable in infancy?

**Eye-tracking**

Miller et al., under review
Are differences detectable in infancy?

Eye-tracking

Parent /Examiner Report

Miller et al., under review
Are differences detectable in infancy?

• Measure early behaviors (12, 18, 24, 36 mos.) that may be associated with later ADHD:

<table>
<thead>
<tr>
<th>ADHD-related behaviors</th>
<th>Additional behaviors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inattention (off-task, distractible)</td>
<td>Negative affect</td>
</tr>
<tr>
<td>Hyperactivity</td>
<td>Vocalizations</td>
</tr>
<tr>
<td>Out of seat</td>
<td></td>
</tr>
<tr>
<td>Grab</td>
<td></td>
</tr>
</tbody>
</table>

• First 5 minutes of MSEL Fine Motor
Examples: 18 months

- Normative attention/activity
- Low attention/high activity
Transdiagnostic framework

• Focus on identifying processes shared across disorders that underlie and maintain symptoms, consistent with RDoC

• Increasingly utilized in study of adult psychopathology (e.g., Harvey et al., 2004)

• Potential for wide-reaching effects – treatments targeting shared impaired processes across diagnoses
ASD and ADHD

• Co-occur at rates well above chance (Rommelse et al., 2011; summarized in Davis & Kollins, 2012)

• Shared:
  – Genetics, familial transmission (Musser et al., 2014; Rommelse et al., 2010; Ronald et al., 2008)
  – Neuroimaging, neurocognitive findings (DiMartino et al., 2013; Geurts et al., 2004)

• Early ASD can “evolve” into behavioral phenotype more consistent with ADHD (Fein et al., 2005)

• Higher rates of ADHD in family members of those with ASD (e.g., Kanne et al., 2009; Nijmeijer et al., 2008)
  – ADHD concerns common among younger siblings of children with ASD (Miller et al., 2016; Miller et al., under review; Ozonoff et al., 2014)
Implications of transdiagnostic approach to ASD and ADHD

• Identification of general indices of atypical development
• Applications during period in infancy when child’s outcome still unclear
• Potential for prevention, more efficient use of early intervention funds
• How/when do similarities and differences first emerge in ASD and ADHD?
Transdiagnostic infant sibling study

Typically Developing

Heritability: ~0.9

ASD

Heritability: ~0.7-0.8

ADHD
Preliminary data: 12 months

Eye-tracking

- **Total looking time (ms)**:
  - **Low-Risk**: Height of the bar
  - **ASD-Risk**: Lower height of the bar
  - **ADHD-Risk**: Lowest height of the bar
Preliminary data: 12 months

Eye-tracking

Examiner ratings

- Low-Risk (n=33)
- ASD-Risk (n=57)
- ADHD-Risk (n=13)
Transdiagnostic factors?

• Behavioral coding?
• Temperament – effortful control, negative affect?
• Motor development?
• Language development?
• Objectively-measured activity level (accelerometer) or physiological variables?
Summary

• Much progress in early detection of ASD, longer-term outcomes of infant siblings
• Early differences in sustained visual attention, parent concerns, examiner observations may indicate later ADHD
• Familial risk for ADHD may be apparent in measures of sustained visual attention, examiner ratings by 12 months. Attention as shared process?
• Suggests potential for earlier detection of attention, behavior regulation problems than previously possible
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