Autism Spectrum Disorder in Young Children: An Overview

Katarzyna Chawarska, PhD
Emily Fraser Beede Professor of Child Psychiatry, Pediatrics, and Statistics
Yale School of Medicine
Child Study Center
Overview

• Core features of ASD

• Comorbid conditions

• Broader Autism Phenotype

• Prodromal signatures of ASD
Autism Spectrum Disorder

- Complex neurodevelopmental disorder
- Prevalence in 8 year olds: 1 in 68 cases (14.7 per 1,000)
- Lack of biological markers
- Marked heterogeneity
- Developmental disorder
- Early onset (< 3 years)
Core characteristics
Symptoms of ASD in toddlers

• Core social and communication symptoms
  – Limited attention to faces and voices
  – Limited drive to share experiences with others (joint attention) and to reference others for social and affective information (social referencing)
  – Atypical nonverbal communication
  – Stereotypical/idiosyncratic use of language (e.g., echolalia)

• Core Restrictive and Repetitive Behaviors Symptoms
  – Seeking/avoiding specific sensory inputs
  – Interest in details of objects (e.g., wheels, dials)
  – Hand and finger mannerisms
Emergence of behavioral manifestations of autism
What are the behavioral signatures of autism at 18 months?

Classification and regression tree analysis

Behavioral signatures of autism at 18 months

- Low functioning infants more likely to show ‘prototypical’ signs of autism
- In higher functioning infants, early signs may be less prototypical
- Implications for screening and diagnostic practices:
  - Different combinations of behaviors at the same age level may be diagnostic of ASD

Stability of early ASD diagnosis and predictors of outcome

• Short term stability (2 to 4 years)
  – Very good for ASD diagnosis (80-90%) \((Chawarska\ et\ al.\ 2007;\ 2009;\ Kim\ et\ al.\ 2016;\ Guthrie\ et\ al.,\ 2014)\)
  – Changes expected within spectrum due to shifts in type and intensity of symptoms

• Long term stability (2 to 4 to 9 years) \((Lord\ et\ al.,\ 2006)\)
  – High stability of ASD diagnosis (90%)

• Predictors of outcome:
  – Severity of social impairment
  – Verbal and nonverbal skills
  – Rate of skills acquisition
  – Presence of comorbid disorders: EF dysfunction, ADHD, Anxiety

\textit{Kim, Macari, Koller, \& Chawarska, 2016. JCPP}
Risk for ASD: Familial factors

- Recurrence of ASD in younger siblings of children with ASD:
  - Prospective studies of younger siblings of children with ASD: 18-25% (Ozonoff et al, 2011)
  - Epidemiologic studies: 10.1% (Risch et al., 2014)

- Factor affecting recurrence rates:
  - Number of affected siblings in the (Ozonoff et al, 2011)
  - Sex of the younger sibling (Palmer et al., 2017)
  - Sex of the affected sibling (Palmer et al., 2017)

![Graph showing probability of recurrence by sex and sibling status]

Palmer et al., 2017 JAMA Pediatrics
Broader Autism Phenotype in younger siblings of children with ASD

• Presence of Broader Autism Phenotype features in younger siblings of children with ASD: ~20% - 30%

• Delays in language and social skills and emotional difficulties in early childhood

• Increased likelihood of affective disorders, anxiety, ADHD, and other disorders later on

• Increasing accuracy of early detection of ASD and BAP amongst younger sibs
  – Screen early and often using ASD-specific screeners
  – Monitor development in other areas (e.g., attention, anxiety)
  – In case of identified delays, implement targeted intervention even if diagnosis is still unclear
Risk for ASD: Prematurity and Genetic Syndromes

- Prevalence of ASD in premature infants (7.1%)
  - 15.0% for 23–24 weeks GA
  - 6.5% for 25–26 weeks GA
  - 3.4% for 27 weeks GA

- Prevalence of ASD in genetic syndromes:
  - Angelman Syndrome (40%)
  - Phelan McDermid Syndrome (84%)
  - Cortical dysplasia-focal epilepsy syndrome (70%)
  - Fragile X (25% of males, 6% of females)
  - Tuberous sclerosis (20%)
  - Congenital Heart Disease (3%)
Sex differences in ASD

- Male to Female ratio: 3:1 \( (Loomes\ et\ al.,\ 2017,\ JAACAP)\)

- Phenotypic sex-dimorphism
  - No difference in severity of social impairment
  - Females: fewer repetitive/restrictive behaviors, higher internalizing problems (anxiety, depression)
  - Males: more externalizing problems (aggression, hyperactivity)

- Hypotheses:
  - Ascertainment bias toward “Male Phenotype”
  - Genetic heterogeneity
  - Multiple threshold hypothesis: Female Protective Factors/Male Risk factors (hormonal or X-chromosome linked)

\[ \text{Reich et al, 1975} \]
Sex differences in social selective attention in infants at risk for ASD

- Attentional “Female protective factor”:
  - Enhanced attention to faces, compared to both high-risk males and low-risk males and females
  - Greater attention to faces was associated with less severe social impairments at 2 years

Core Symptoms: Clinical implications

- Early diagnosis of ASD is stable: if autism symptoms are present, implement treatment & provide family support

- Not all children with ASD show ‘prototypical’ symptoms early on
  - Gender
  - Language and cognitive ability

- Monitor closely infants from high-risk populations for signs of social difficulties

- Initial severity of symptoms, levels of language, and rate of progress are good prognostic indicators
Comorbid conditions
Prevalence of DSM-IV Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>3-Mo Point Prevalence/100</th>
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<tbody>
<tr>
<td>Any disorder</td>
<td>70.8</td>
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<tr>
<td>Any main disorder</td>
<td>62.8</td>
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<tr>
<td>Any emotional disorder</td>
<td>44.4</td>
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<tr>
<td>Any anxiety or phobic disorders</td>
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<tr>
<td>Generalized anxiety disorder</td>
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<td>Separation anxiety disorder</td>
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<tr>
<td>Panic disorder</td>
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<td>Agoraphobia</td>
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<td>Social anxiety disorder</td>
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<td>Simple phobia</td>
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<td>Obsessive-compulsive disorder</td>
<td>8.2</td>
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<tr>
<td>Any depressive disorder</td>
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<tr>
<td>Major depressive disorder</td>
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<tr>
<td>Dysthymic disorder</td>
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<tr>
<td>Oppositional or conduct disorder</td>
<td>30.0</td>
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<tr>
<td>Oppositional defiant disorder</td>
<td>28.1</td>
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<tr>
<td>Conduct disorder</td>
<td>3.2</td>
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<tr>
<td>Attention-deficit/hyperactivity disorder</td>
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<tr>
<td>Other disorders</td>
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<tr>
<td>Enuresis</td>
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<td>Encopresis</td>
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<td>Tourette syndrome</td>
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<tr>
<td>Chronic tic disorder</td>
<td>9.0</td>
</tr>
<tr>
<td>Trichotillomania</td>
<td>3.9</td>
</tr>
</tbody>
</table>

Simonoff et al., JAACAP 2008
Comorbid disorders in ASD

• Affect family functioning, social and cognitive development, educational placement, hospitalizations, suicidality, etc.

• Unclear relationship between autism and comorbid disorders
  – Common cause
  – One is a consequence of the other
  – Initially independent but interact giving rise to complex clinical phenotypes

• Clinical considerations:
  – Diagnostic overshadowing
  – Limited precision of screening and diagnostic instruments
  – Few preventative and therapeutic interventions for young children with ASD
Emotional Reactivity and Regulation

- Temperament: individual differences in reactivity and regulation
  - Positive Affectivity: joy, reward seeking, high activity level
  - Negative Affectivity: anger/fear/distress in response to novelty
  - Effortful Control: self-regulatory capacity to promote adaptation

- Temperamental patterns are already apparent in infancy

- Largely stable over time, though subject to the influences of maturation and experience

Temperamental characteristics in toddlerhood are linked with later:
  - Positive Affectivity: risk for low social competence, poor peer relationships, and school adjustment
  - Negative Affectivity: risk for anxiety & depression
  - Effortful Control: risk for externalizing behaviors, aggression, attentional difficulties
Parent-report based temperamental markers in toddlers with ASD

- Sample: 326 16- to 36-month-old toddlers with ASD, DD, and TD, 80% of sample seen at 4 years

- ASD-specific atypical Effortful Control and Positive Affectivity (Surgency); shared with DD atypical Negative Affectivity

- Temperamental difficulties were independent of severity of autism symptoms (all $r < .12$)

- Highly stable over time
  - Effortful Control: $r = .56$
  - Negative Affect: $r = .61$
  - Positive Affectivity: $r = .54$

- Temperamental difficulties at 2 years contributed independently to severity of autism symptoms at 4

Macari et al. JCPP 2017
Comorbid Symptoms: Clinical Implications

- Predictors of later comorbid disorders may be present already in toddlers with ASD

- Early emotional difficulties contribute to later severity of autism symptoms

- Screening should be implemented early and continue throughout childhood as prevalence of various comorbidities increases with age

- Adequate detection and treatment of comorbid conditions may improve long term outcomes in children with ASD
Prodromal Signatures
Emergence of behavioral manifestations of autism
Core attentional features of autism

“Comings and goings, even of the mother, did not seem to register. Conversation going on in the room elicited no interest.”


Leo Kanner
Attentional markers in toddlers: Evidence from eye-tracking studies

Attentional markers of ASD in toddlers: Evidence from eye-tracking studies

Selective attention to faces in complex dynamic environments

Selective Attention Task 1.0

Chawarska, Macari, & Shic, (2012). JCPP

Selective Attention Task 2.0

Shic, Wang, & Chawarska, in press
Can limited attention to faces be detected earlier?

Infants at familial risk for ASD
Limited attention to dynamic faces in 6-month-old infants later diagnosed with ASD


Shic et al., (2014) Biological Psychiatry

Macari et al, under review
Emergence of behavioral manifestations of autism
Yale Autism Center of Excellence: Investigation into pre- and neonatal roots of ASD
Improving understanding of mechanisms that give raise to core autism symptoms in infancy

- Safe, non-invasive, non-demanding approach to evaluating brain function

- rs-fc patterns arise spontaneously, reflect activity of functional brain networks involved in e.g., visual and auditory processing, salience detection, or executive control

- Atypical hub topology and connectivity has been implicated in developmental and psychiatric disorders including autism and schizophrenia
Fetal and neonatal imaging studies

- Fetal rs-fc networks:
  - Hubs in primary and association sensory areas, motor areas, subcortical-limbic areas, cerebellum, and in regions analogous to FG and Wernicke’s area
  - Left hemisphere asymmetry

- Neonatal rs-fc networks: precursors of higher order networks like salience, default mode, and attention systems

- rs-fc characteristics in neonates linked with later language and cognitive performance and affective development

Scheinost et al., in prep
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Toddler Developmental Disabilities Clinic
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