Early Development in Autism

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SCSU Science of Autism

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Yale SCHOOL OF MEDICINE

Yale Child Study Center

Overview

Autism symptoms in toddlers: onset and diagnostic complexities

Prospective sibling studies

Early social-communication development

Early social attention

Early emotional development

Co-occurring conditions and potential risk markers

Autism Spectrum Disorder: DSM-5 (2013)

Diagnostic criteria:

A. Persistent deficits in social communication and social interaction across multiple contexts (in each of three areas)

B. Restricted, repetitive patterns of behavior, interests, or activities (in two of four areas)

C. Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life)

D. Symptoms cause clinically significant impairment in social, occupational, or other areas of functioning

E. Issues are not better explained by intellectual disability or global developmental delay

Phenotypic heterogeneity

Neurodevelopmental disorder: evolving constellation of features

Reciprocal Social Communication and Social Interaction

- Inconsistent eye contact
- Social overtures absent or limited
- Limited affective facial expressions directed to others
- Infrequent monitoring of others (e.g., responding to bids for joint attention)
- Limited attempts to share interests with others (e.g., initiating joint attention)
- Infrequent imitation
- Less gesture use
- Low frequency of communication
- Limited goals of communication; majority of bids protoimperative, fewer protodeclarative
- Reduced interest in peers
- Limited functional or pretend play, or present but repetitive with low creativity

Restricted, Repetitive Behavior, Interests, and Activities

- Repetitive actions with objects
- Hand and finger mannerisms – repetitive movements
- Hyperreactivity/hyporeactivity to sensory input or interest in specific sensory stimuli
- Fixated interests that are atypical in intensity or focus
- Rigidity, difficulties with changes in routine

Onset of ASD symptoms (retrospective accounts)

- Early onset (1st year):
  - early manifestations of lack of social reciprocity (*Kanner, 1943*)
- Later onset (2nd year):
  - Plateau: developmental slowdown after a period of typical development *(Landa et al., 2007; Siperstein & Volkmar, 2004; Gangi et al., 2018; Gangi et al., 2021)*
  - Delays plus loss: initial delays followed by loss of skills *(Ozonoff et al., 2008)*
  - Regression: social withdrawal and loss of words in 20-30% of cases *(Dawson et al., 2006; Eisenberg & Kanner, 1955; Landa et al., 2007; Volkmar & Cohen, 1989)*

Retrospective accounts may only detect the most dramatic losses; this method likely underreports subtle regression (Pearson et al., 2018)

When measured *prospectively* and dimensionally, regressive patterns of development seem to be the rule --- 69-88%; (Ozonoff et al., 2019 – see SI Neurosci & Biobeh Reviews 2019)

Complexities of onset and diagnosis

- Variable, protracted course of onset – all symptoms required may not yet be fully expressed in very young children (Kim et al., 2018; Ozonoff et al., 2018)
  - True for parent report screeners (Dai et al., 2020; Wieckowski et al., 2021)
  - True when evaluated over time by experts; not until age 3 or after age 5 (Bacon et al., 2018; Ozonoff et al., 2015, 2018)
- Specific autism symptoms in toddlers can vary with verbal and nonverbal ability (Bacon et al., 2018; Chawarska et al., 2014)
- Thus, prevalence rates of autism increase steadily into school age (Suren et al., 2019)

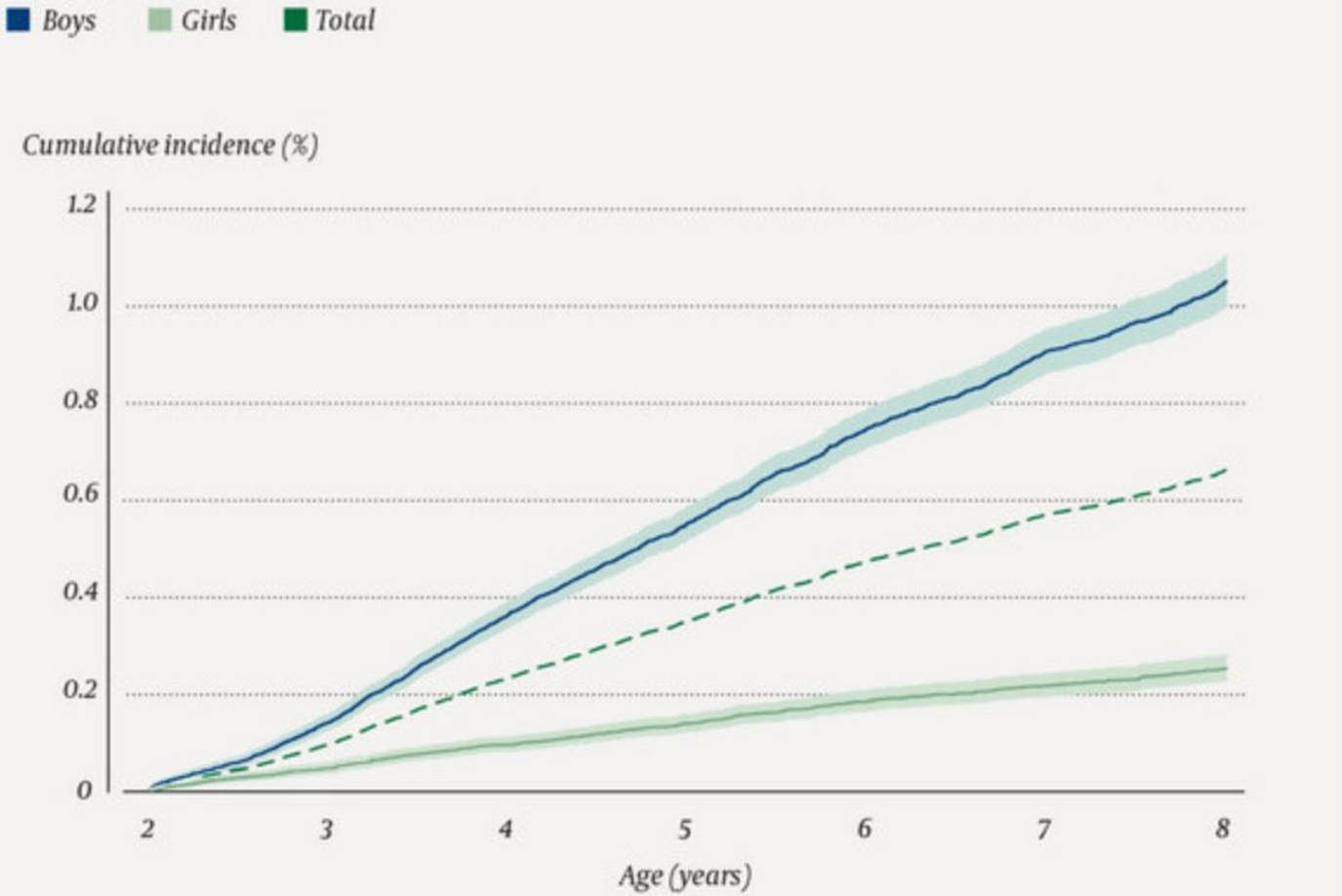


Figure 2 *Percentage share of children diagnosed with autism spectrum disorder, by age and gender. Data from the Norwegian Patient Registry and the National Registry 2008–16 that include children born 2006–14 (N = 538 815) registered with an autism diagnosis at between 2 and 8 years of age (cumulative percentages). Gender-specific curves are shown with 99.7 % confidence intervals.*

Surén, P., Havdahl, A., Øyen, A. S., Schjølberg, S., Reichborn-Kjennerud, T., Magnus, P., ... & Stoltenberg, C. (2019). Diagnosing autism spectrum disorder among children in Norway. *Tidsskrift for Den norske legeforening*.

More complexity for toddlers: DSM-5's impairment criterion

- "Symptoms cause clinically significant impairment in important areas functioning"

- Of consequence to the diagnosis of children under 3 *(Barton et al., 2013; Zander & Bölte, 2015)* since a proportion functions in the average range *(Hedvall et al., 2014; Kim et al., 2016)*
  → autism is only mildly impairing in some young children

Societal demands are lowest for infants and toddlers - surrounded by supportive caregivers *(Zander & Boelte, 2015)*

Once expectations increase, impairments become more apparent *(Ozonoff et al., 2015)*

Accommodating environments, compensatory abilities contribute to "late symptom onset" *(Livingston & Happe, 2017; Riglin et al., 2021).*

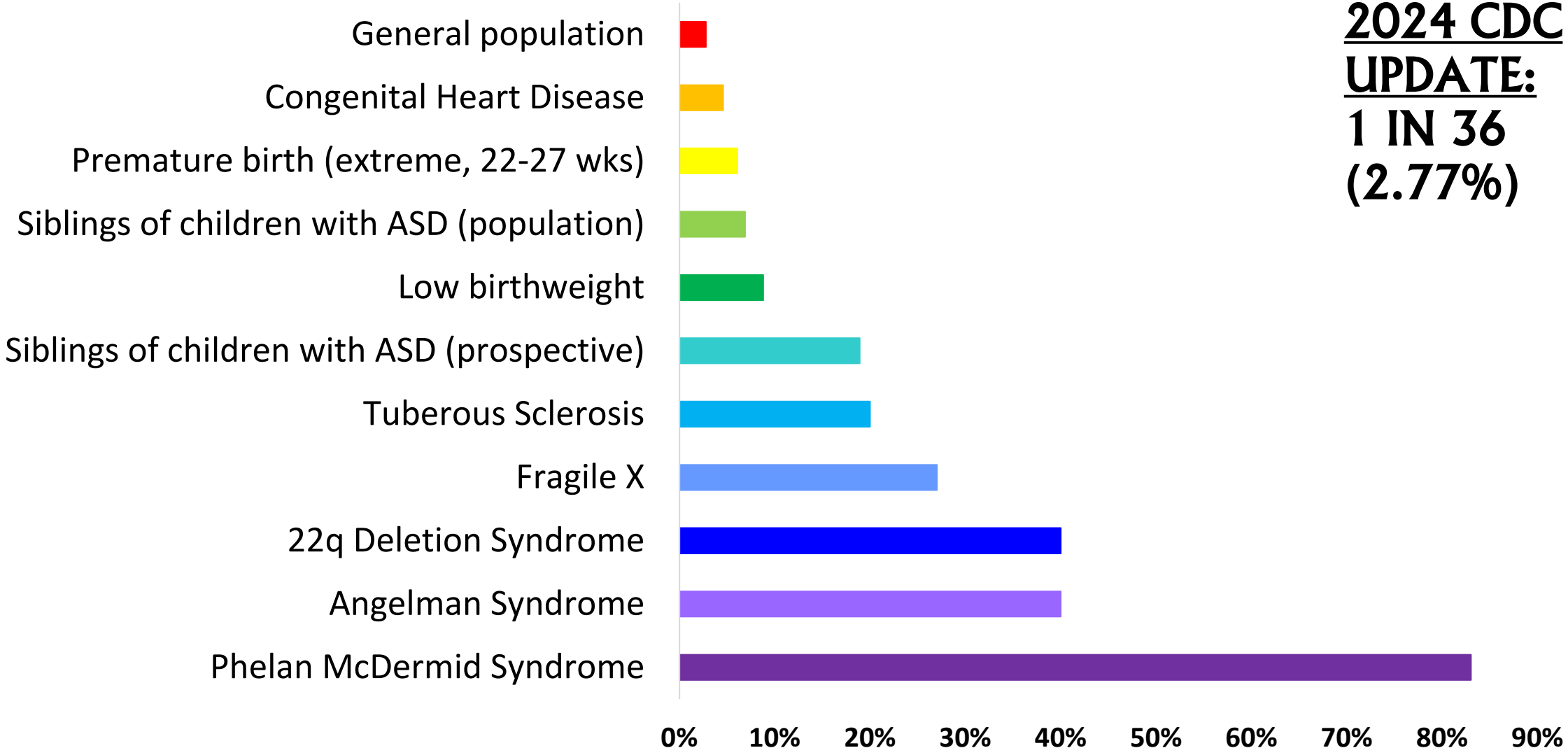
Prospective methodological approach

- Familial/genetic factors in family members of children with ASD increase their likelihood of developing the disorder (*Smalley, Asarnow, & Spence , 1988)*
- Recurrence rate in younger siblings of children with ASD:
  - Baby Sib prospective studies: 18.7% *(Ozonoff et al., 2011)*
  - Population-based cohort studies: 6.9% *(Grønborg et al., 2013);* 12.0% *(Miller et al., 2019)*
- Siblings also at increased likelihood of having other developmental problems (20-40%) *(Georgiades et al., 2013; Macari et al., 2012; Messinger et al., 2013; Ozonoff et al., 2014*)

Prospective studies of elevated-likelihood infant siblings

- identify early signs, patterns of onset
- examine early developmental trajectories of affected and unaffected siblings
- study ASD before effects of treatment, co-occurring conditions, and compensatory strategies change its manifestation
- eventually, understand MECHANISMS
- chance to study ASD as it unfolds

autism prevalence rates



2024 CDC UPDATE:
1 IN 36 (2.77%)

The prodrome of autism (birth-12 months)

Prodromal features of ASD in the first year of life

- Social communication at 12 months: significant differences reported in ASD group vs non-ASD
  - Less eye contact, affective responses, requesting, gestures, joint attention *(Macari et al., 2012; Mitchell et al., 2006; Ozonoff et al., 2010; Rozga et al., 2011; Zwaigenbaum et al., 2005)*
  - Fewer vocalizations *(Paul et al., 2011)*
- Social communication at 6 months: very few group differences
  - Intact eye contact and affective responses to mother *(Young et al., 2009; Rozga et al., 2011)* or examiner *(Bryson et al., 2006; Ozonoff et al., 2010)*
  - Intact social reciprocity and attention *(Bryson et al., 2006; Zwaigenbaum et al., 2005)*
  - Intact vocalizations *(Ozonoff et al., 2010; Paul et al., 2011)*

Limited evidence for pronounced behavioral signs <12m

Possible explanations:

- Natural course of autism
- Limited sensitivity of existing behavioral methods
- Overly narrow conceptualization of prodrome of ASD

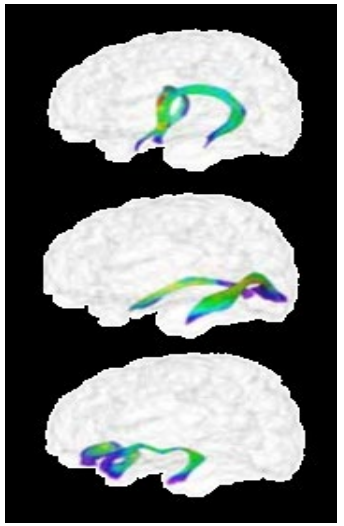
➢ ***Earliest signs may be outside the domain of social communication***

Positive findings in 6-month-olds with ASD

Jones, E. et al., 2016

Elsabbagh et al., 2012
Jones, E. et al., 2016
Lloyd-Fox et al., 2018
Gui et al., 2021

Chawarska et al., 2013
Jones, W. & Klin, 2013
Elison et al., 2013
Shic et al., 2014



Wolff et al., 2012
Hazlett et al., 2017
Shen et al., 2017

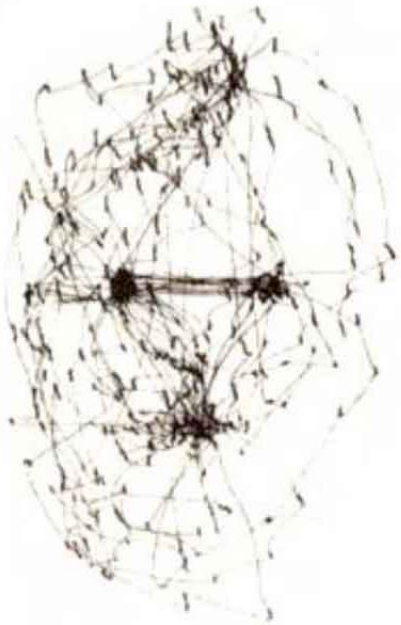
Chawarska et al., 2011;
Campbell et al., 2014

Limited endogenous regulation of attention to social stimuli

(Chawarska et al., 2013; Shic et al., 2014; Macari et al., 2021)

Eye-tracking: a window into attentional processes

"Eye movement reflects the human thought processes; so the observer's thought may be followed to some extent from records of eye movement…It is easy to determine from these records which elements attract the observer's eye…in what order, and how often." *(Yarbus, 1967)*



My experience is what I agree to attend to. Only those items which I notice shape my mind; without selective interest, experience is utter chaos. *(James, 1890)*

From: Annie Shic, 2010, WSJ

Spontaneous social monitoring in 6-month-old infants

- Participants: Age 6 months
- Four outcome groups based on familial likelihood status and clinical best estimate diagnoses (24/36 months)
  - ASD (*n*=12)
  - HR-ATYP (*n*=22)
  - HR-TYP (*n*=15)
  - LR-TYP (*n*=35)
- Data Acquisition:
  - SMI iView X™ RED
  - Five-point calibration
  - Sampling rate 60 Hz

ELSEVIER

Biological Psychiatry

Available online 11 January 2013

In Press, Corrected Proof — Note to users

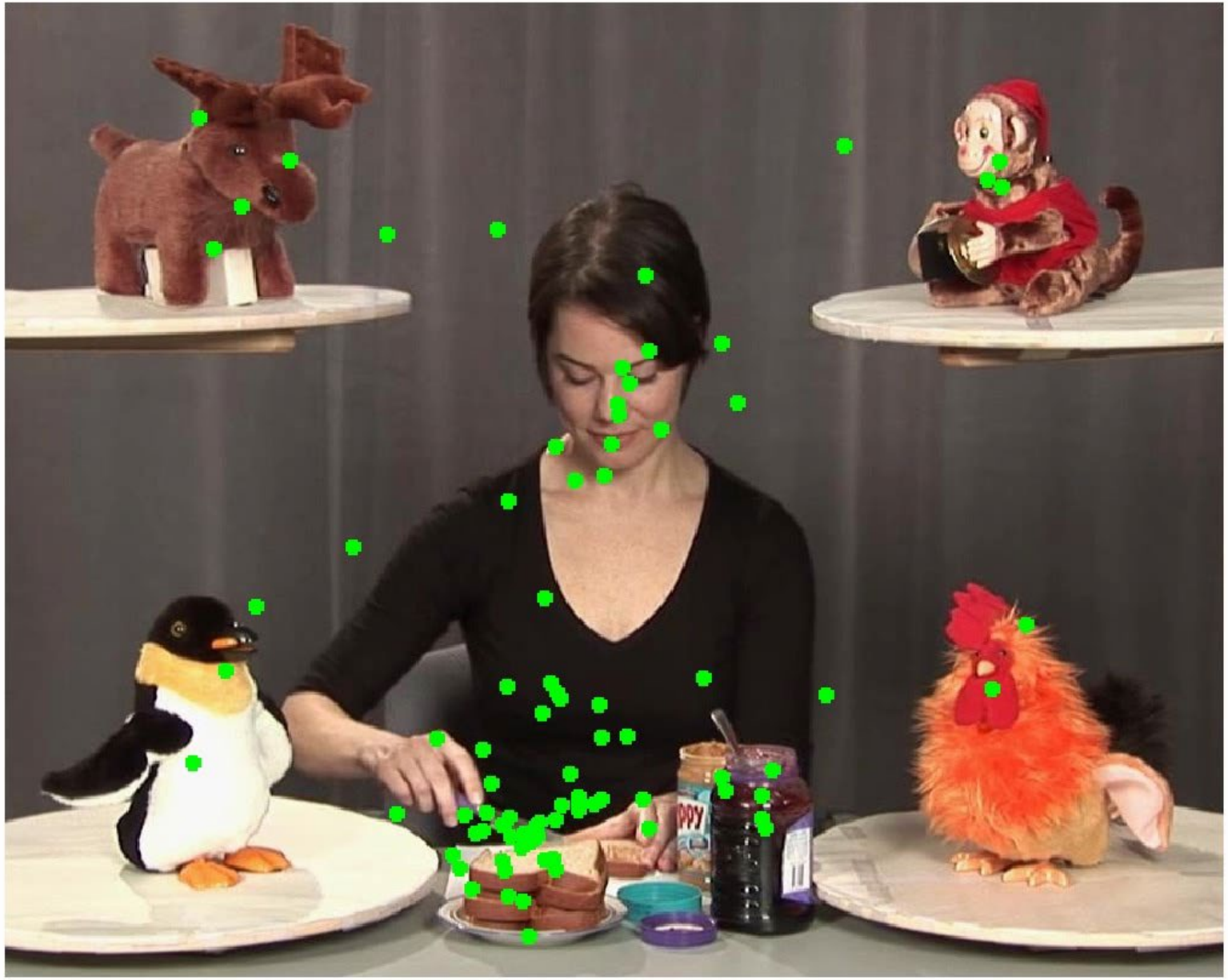
Archival Report

Decreased Spontaneous Attention to Social Scenes in 6-Month-Old Infants Later Diagnosed with Autism Spectrum Disorders

Katarzyna Chawarska, Suzanne Macari, Frederick Shic

Child Study Center, Yale University School of Medicine, New Haven, Connecticut.

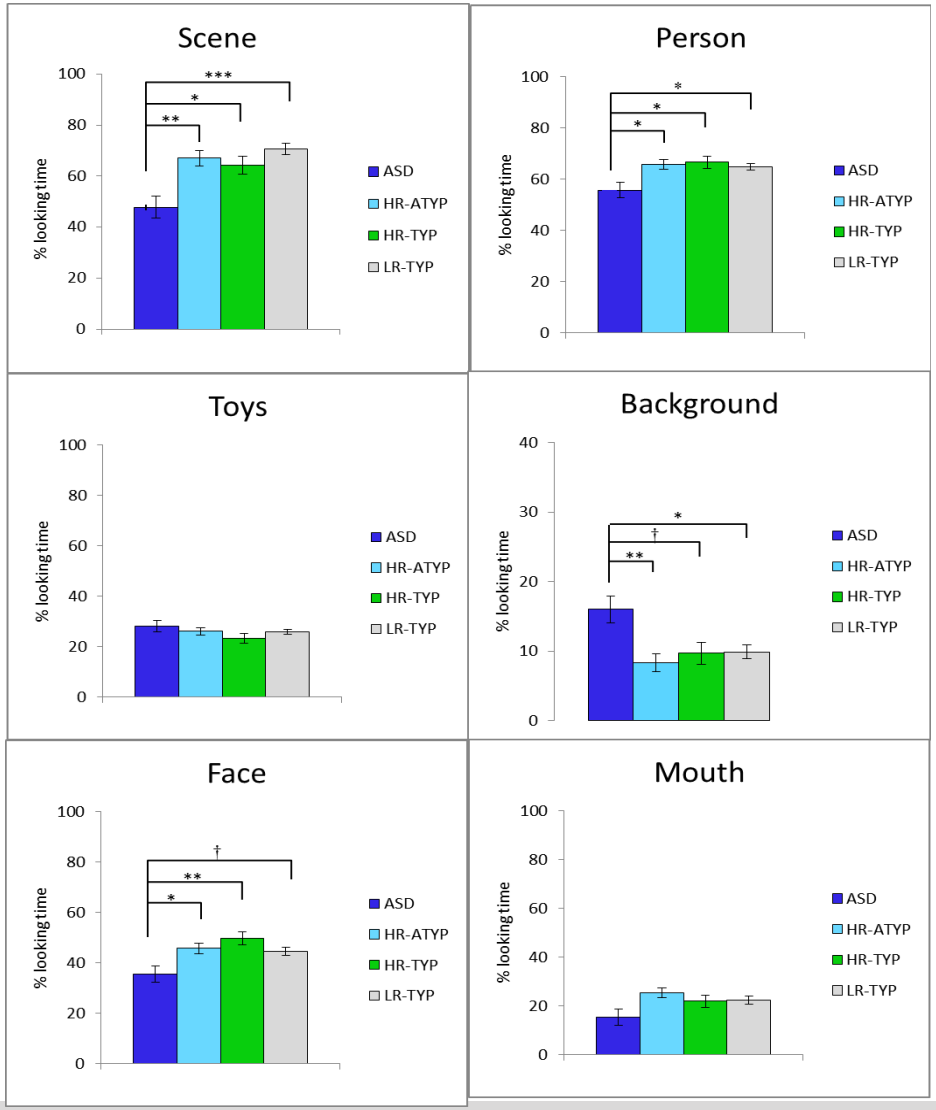
t = 2 m : 6 s : 100 ms; f = 3779



Distribution of attention across elements of the social scene

- Limited attention in ASD to complex social scenes, people, and faces

- Mechanisms?
  - Deficits in detecting and prioritizing social stimuli
  - Limited reinforcement value
  - Difficulties regulating attention to complex stimuli



Attentional markers of ASD in 6-, 9-, and 12-month-old infants: A study of live interaction

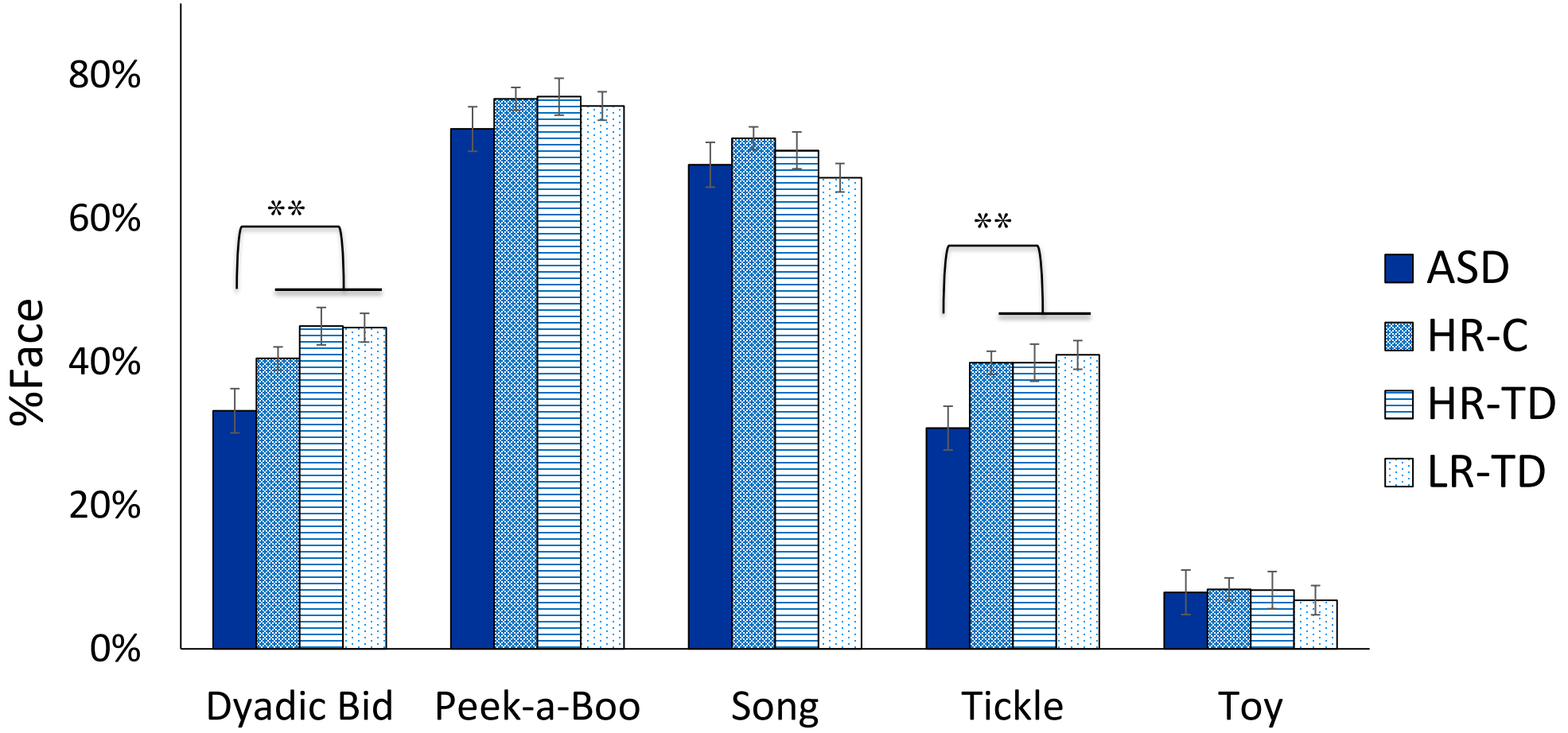
Social Orienting Probes

- Dyadic Bid (speech)
- Song
- Peek-a-Boo
- Toy Play
- Tickle

ASD (*n*=21); HR-C (*n*=72); HR-TD (*n*=32); LR-TD (*n*=49)

Macari et al., JAACAP 2021

Diminished attention to the examiner's face in 6-12-month-old infants with ASD – in 2/5 conditions



Macari et al., 2020

Reconciling discrepant findings across studies

- Granularity of measurement (vs. global clinician rating)
- Social measurement context (vs. object-based play)
- Unfamiliarity of social partner (vs. mother)
  - Familiarity of mother's face and long history of interaction helps maintain infants' otherwise fragile social attention *(Rozga et al., 2013; Young et al., 2010)*
  - Parents of EL infants (unknowingly) utilize strategies to enhance infants' attention and affect *(Wan et al., 2012)* and examiner/actress do not do this
- Aberrant functional connectivity during speech processing in autism; may impact attentiveness to speech (Leipold et al., 2023)

Attention to social information in infants and toddlers with ASD

- Limited attention to social cues is present in 6-12-month-old infants with ASD

impacts development of social cognition and communication, as well as specialization of the neural networks involved in processing social info

Early differences in social attention during interactions is likely to interfere with learning from social partners

Infants with ASD are already constructing a different social environment given selective deployment of attention

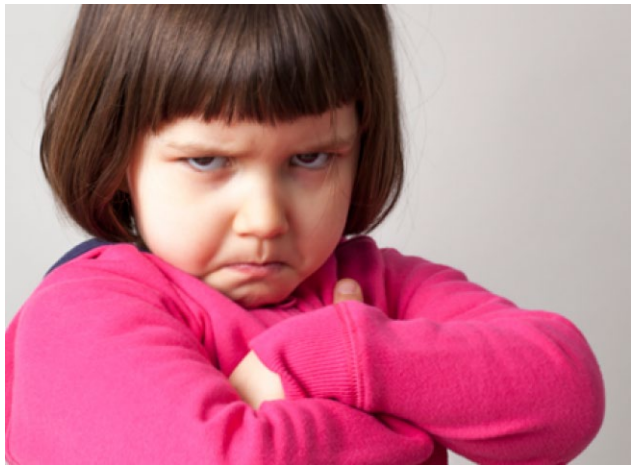
Emotions in autism





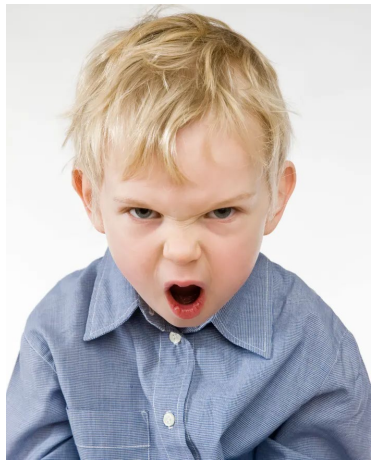




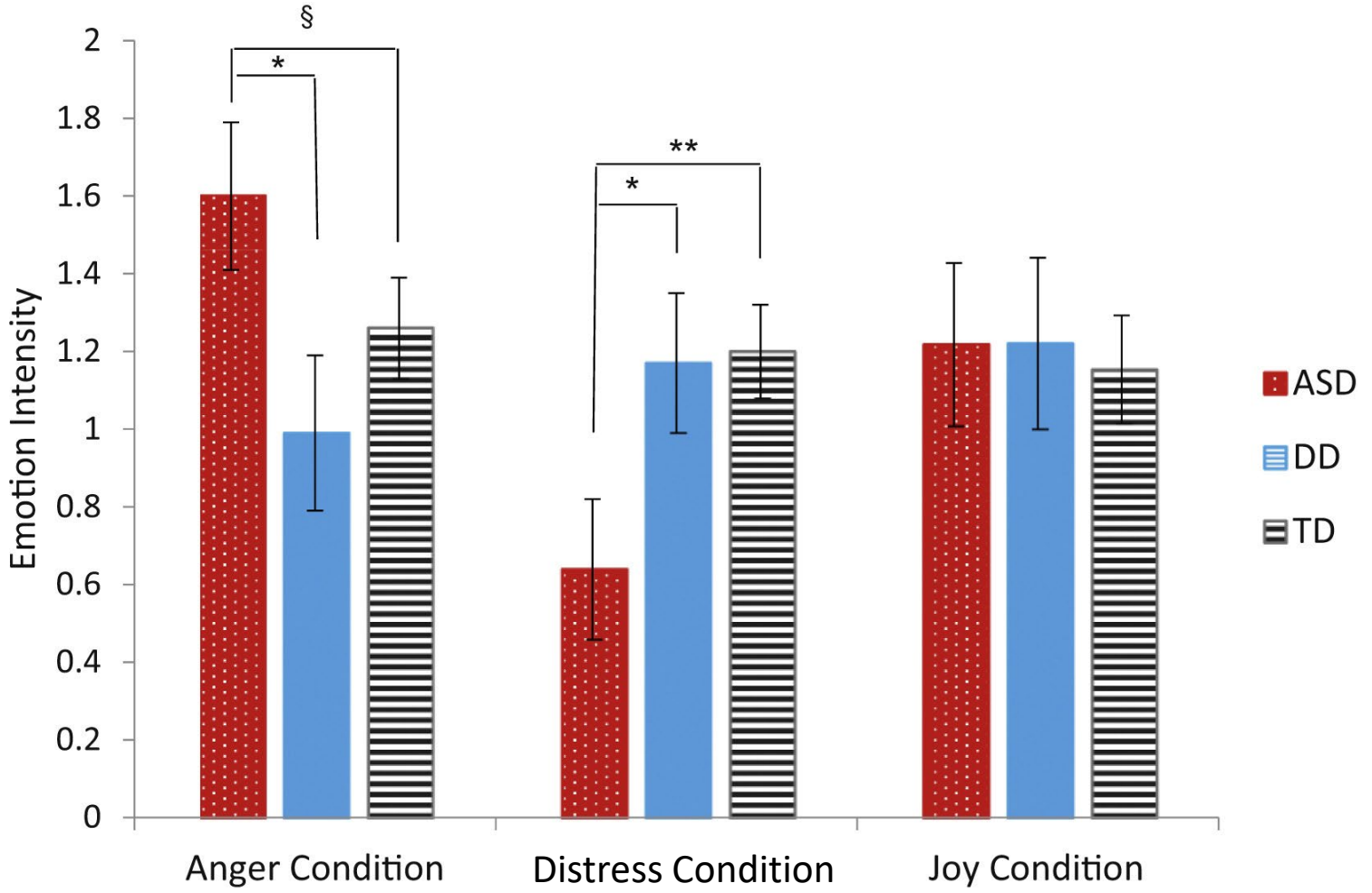








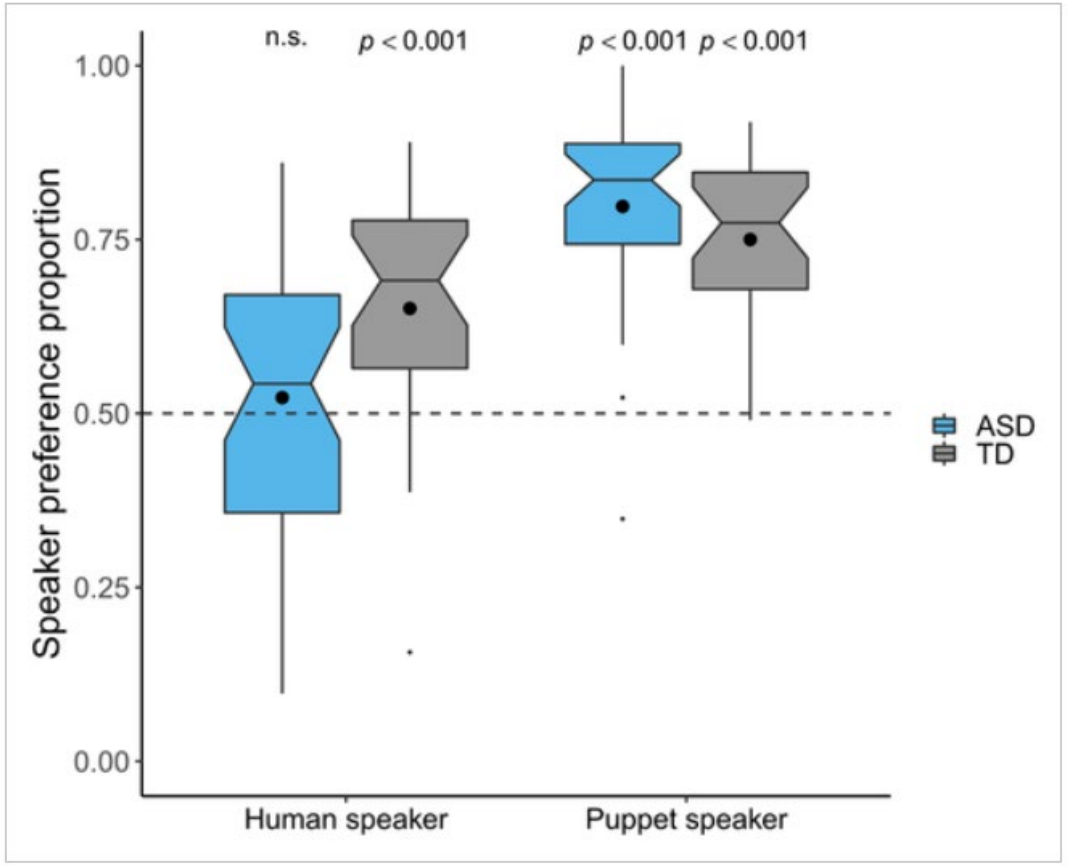
Toddlers with ASD show complex profiles of emotional reactivity to everyday situations



Shared positive affect (SPA) with parents during Puppet Show task – similar in ASD

Macari et al., JAACAP, 2018


SESAME STREET

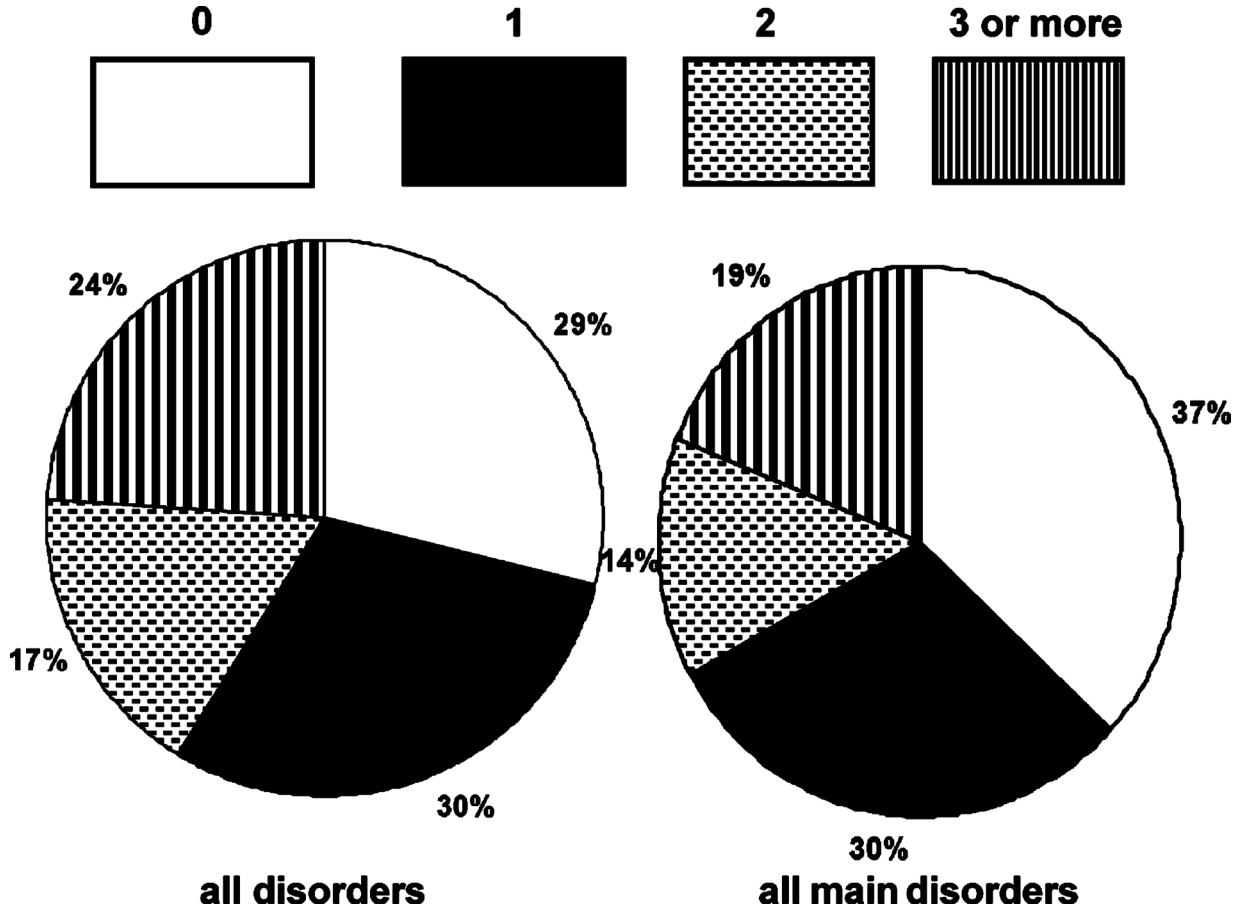


Macari, S., Chen, X., Brunissen, L., Yhang, E., Brennan-Wydra, E., Vernetti, A., Volkmar, F., Chang, J., & Chawarska, K. (2021). Puppets facilitate attention to social cues in children with ASD. *Autism Research: official journal of the International Society for Autism Research*, *14*(9), 1975.

Co-occurring conditions

Prevalence of co-occurring conditions in school-age children with ASD

Disorder	3-Mo Point Prevalence/100
Any disorder	70.8
Any main disorder[a]	62.8
Any emotional disorder[b]	44.4
Any anxiety or phobic disorders[c]	41.9
Generalized anxiety disorder	13.4
Separation anxiety disorder	0.5
Panic disorder	10.1
Agoraphobia	7.9
Social anxiety disorder	29.2
Simple phobia	8.5
Obsessive-compulsive disorder	8.2
Any depressive disorder	1.4
Major depressive disorder	0.9
Dysthymic disorder	0.5
Oppositional or conduct disorder	30.0
Oppositional defiant disorder	28.1
Conduct disorder	3.2
Attention-deficit/hyperactivity disorder	28.2
Other disorders[d]	24.7
Enuresis	11.0
Encopresis	6.6
Tourette syndrome	4.8
Chronic tic disorder	9.0
Trichotillomania	3.9



IQ was not related to prevalence of any co-occurring conditions (mean age 11 yrs)

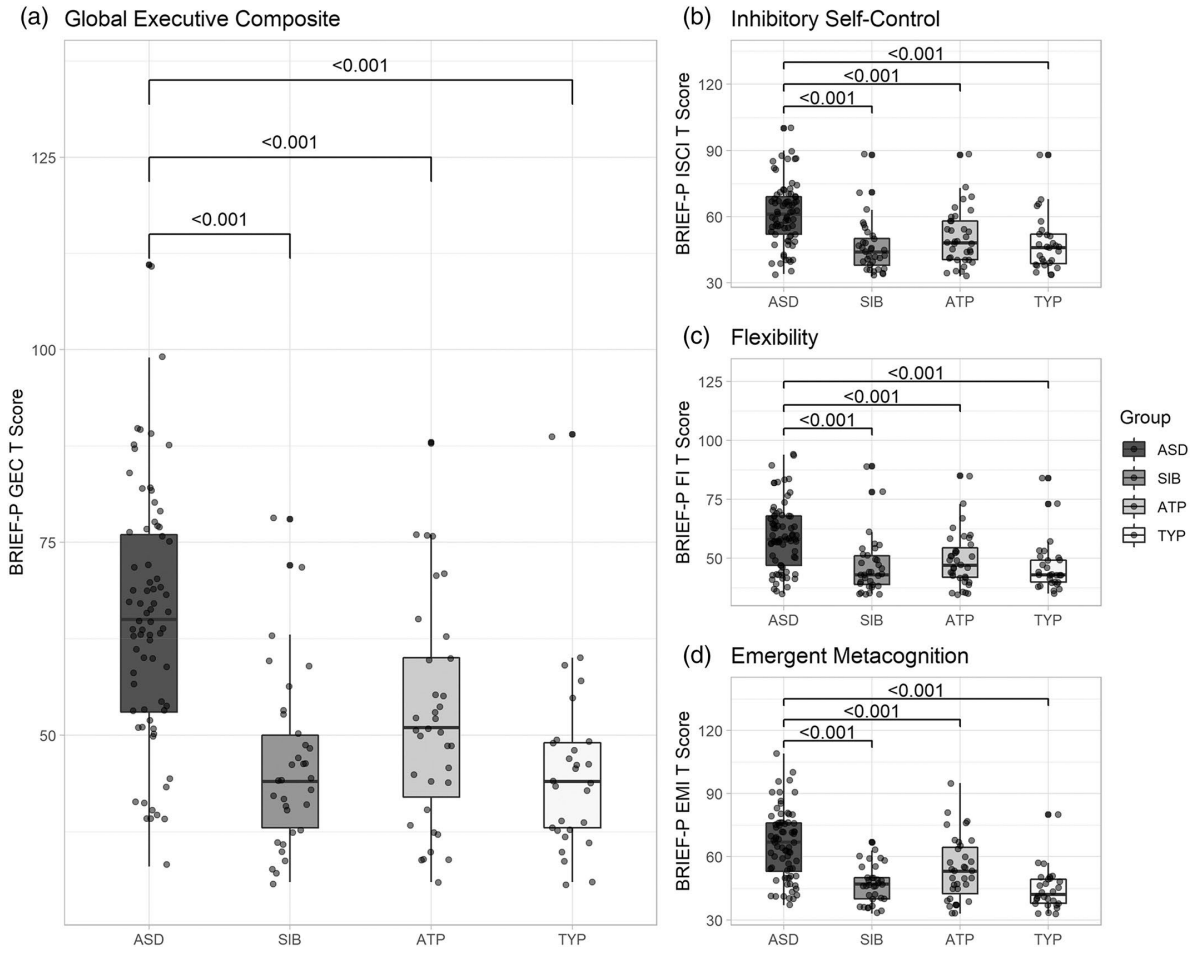
Simonoff et al., JAACAP 2008

Anxiety & ADHD in *young* children with ASD

- Anxiety symptoms are already more prevalent in preschoolers with ASD than in other children, across the range of IQ; most commonly specific fears and generalized anxiety *(Chawarska et al., in prep; Vasa et al., 2020)*
- 17-38% of children with ASD under the age of 7 years show significant ADHD-related symptoms *(Gadow et al., 2004; Hartley et al., 2008; Ronald et al., 2008; Snow & Lecavalier, 2011)*
- Children with co-occurring ASD and ADHD are at greater risk for poor cognitive performance, attention, memory, social adaptation, daily living skills and more behavioral problems than children w/o ADHD symptomatology *(Rosello et al., 2022)*
- 3-year-olds with ASD already are showing elevated clinical symptoms of ADHD compared to children with other neurodevelopmental disorders (it can be detected early!)

Executive functioning (EF) in *young* children with autism

- Regulating and controlling behavior (remembering and following directions, completing tasks independently, transitioning, inhibiting inappropriate behaviors)
- Impaired EF present already in preschoolers with ASD (43%-63%); prevalent in older children/adults.
- Low EF skills predict poor school readiness, impaired adaptive functioning, and higher social dysfunction, regardless of IQ
- Half of 3-year-olds with autism show clinically significant EF deficits *(Powell et al., 2022)*



Emotional/behavioral problems – risk markers in infancy?

- Magnitude of child and adolescent psychopathology (Polanczyk et al., 2015) in both internalizing (anxiety, depression) and externalizing (conduct/oppositional) domains motivates search for infant risk markers
- Documented early: by the second year, toddlers with ASD experience increased internalizing symptoms (Green et al., 2012; Raza et al., 2019); by preschool age they exhibit more internalizing and externalizing symptoms than peers (Li et al., 2019; Sacrey et al., 2022)
- Siblings of children with autism also experience more internalizing/externalizing problems *(Charman et al., 2016; Miller et al., 2016; Raza et al., 2019)*
- Identifying risk markers of emotional/behavioral problems could improve the precision of early intervention & prevention efforts (Sonuga-Barke & Halperin, 2010).

Emotional reactivity predicts later behavior difficulties

Precursors of emerging behavior problems can be identified in infancy: **atypical emotional reactivity** (distress, anger, and joy)

- Elevated distress associated with later shyness, social anxiety, internalizing behavior (Kagan et al., 1987; Colder et al., 2002; Putnam & Stifter, 2005; DeRosnay et al., 2006; Brooker et al., 2013)
- High levels of anger associated with externalizing behavior (Gartstein et al., 2012)
- High/low joy related to depression and externalizing problems (Putnam & Stifter, 2005; Dougherty et al., 2010; Degnan et al., 2011; Ghassabian et al., 2014)

Research on emotional reactivity predictors of internalizing, externalizing, or specific conditions in ASD and non-autistic siblings is limited…..

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All the children and families participating in our studies

Yale Study of Infant Emotional Development

WHO: infants 4 months of age or younger who have older sibling(s) or other family members with autism.

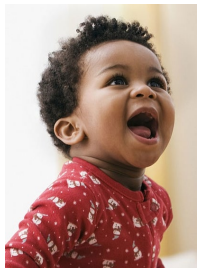
WHAT: Participation includes developmental monitoring through age 2 ½ by expert clinicians specializing in early diagnosis of autism and developmental difficulties.

Visits include assessment of social, adaptive, and cognitive/language development; studies of attention (watching videos); and play-based activities to assess infants' emotional development.

WHERE: 300 George St., Suite 900, New Haven, CT. Free and convenient parking. No cost to participate; participants receive up to $350.

Interested families can fill out our inquiry form or call **(203) 764-5933.**

https://bit.ly/SANABabyStudies





Comments, questions?

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