

# Autism Spectrum Disorder in Young Children: An Overview

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# Overview

- Core features of ASD
- Comorbid conditions
- Broader Autism Phenotype
- Prodromal signatures of ASD

# Autism Spectrum Disorder

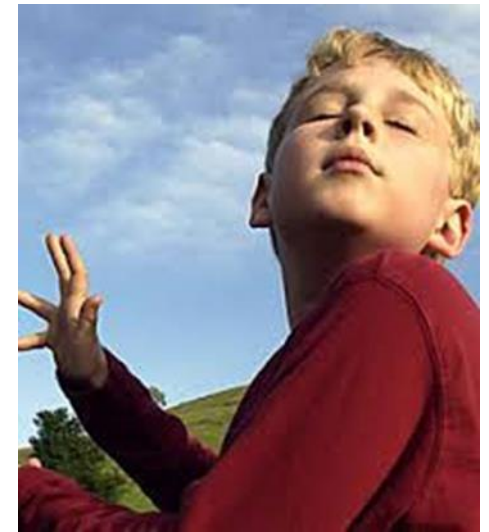
- Complex neurodevelopmental disorder
- Prevalence in 8 year olds: 1 in 68 cases (14.7 per 1,000)
- Lack of biological markers
- Marked heterogeneity
- Developmental disorder
- Early onset (< 3 years)



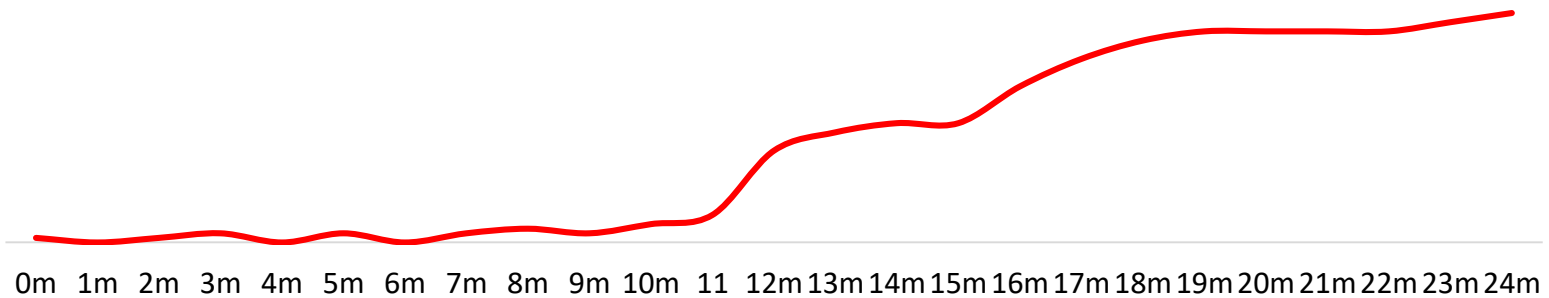
# Core characteristics

# 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

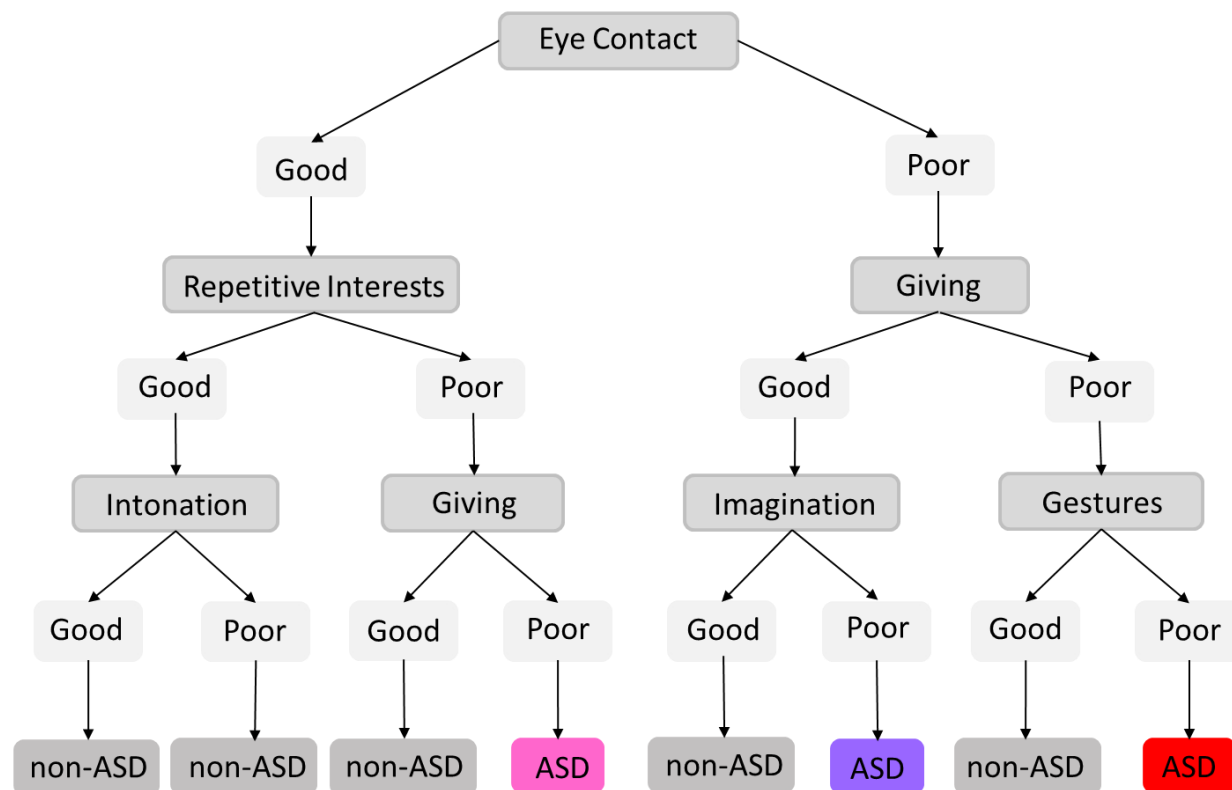


# Emergence of behavioral manifestations of autism



# What are the behavioral signatures of autism at 18 months?

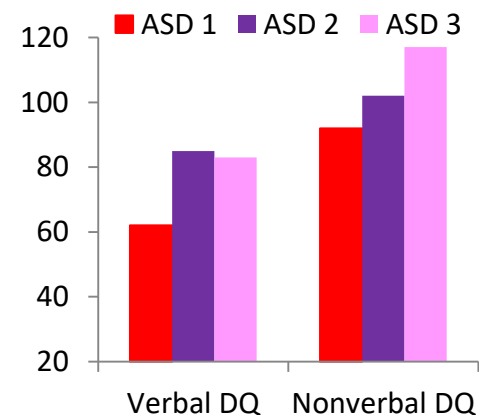
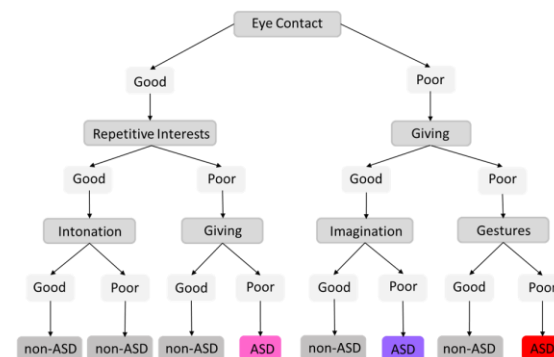
## Classification and regression tree analysis



*(Chawarska, Shic, Macari et al., BSRC (2014). 18-month predictors of later outcomes in younger siblings of children with ASD. Journal of American Academy of Child and Adolescent Psychiatry)*

# 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

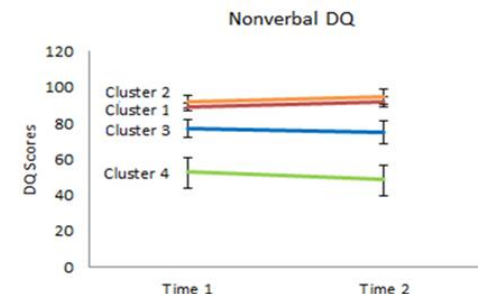
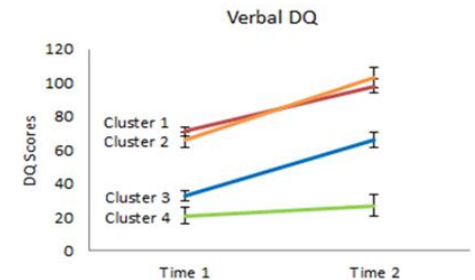


(Chawarska, Shic, Macari et al., BSRC (2014). 18-month predictors of later outcomes in younger siblings of children with ASD. *Journal of American Academy of Child and Adolescent Psychiatry*)



# Stability of early ASD diagnosis and predictors of outcome

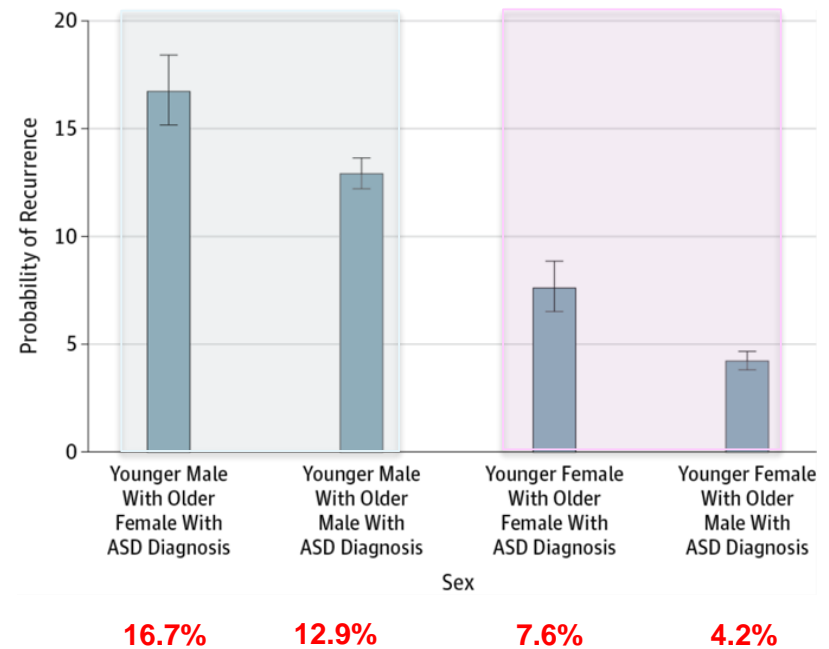
- Short term stability (2 to 4 years)
  - Very good for ASD diagnosis (80-90%) (*Chawarska et al. 2007; 2009; Kim et al. 2016; Guthrie et al, 2014*)
  - Changes expected within spectrum due to shifts in type and intensity of symptoms
- Long term stability (2 to 4 to 9 years) (*Lord et al., 2006*)
  - 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



*Kim, Macari, Koller, & Chawarska, 2016. JCPP*

# Risk for ASD: Familial factors

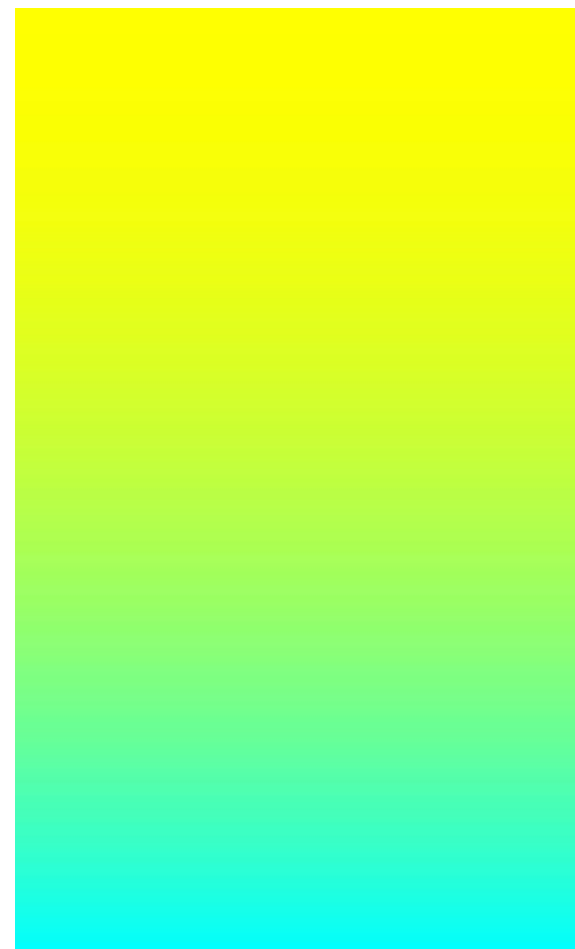
- Recurrence of ASD in younger siblings of children with ASD:
  - Prospective studies of younger siblings of children with ASD: 18-25% (*Ozonoff et al, 2011*)
  - Epidemiologic studies: 10.1% (*Risch et al., 2014*)
- Factor affecting recurrence rates:
  - Number of affected siblings in the family (*Ozonoff et al, 2011*)
  - Sex of the younger sibling (*Palmer et al., 2017*)
  - Sex of the affected sibling (*Palmer et al., 2017*)



*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



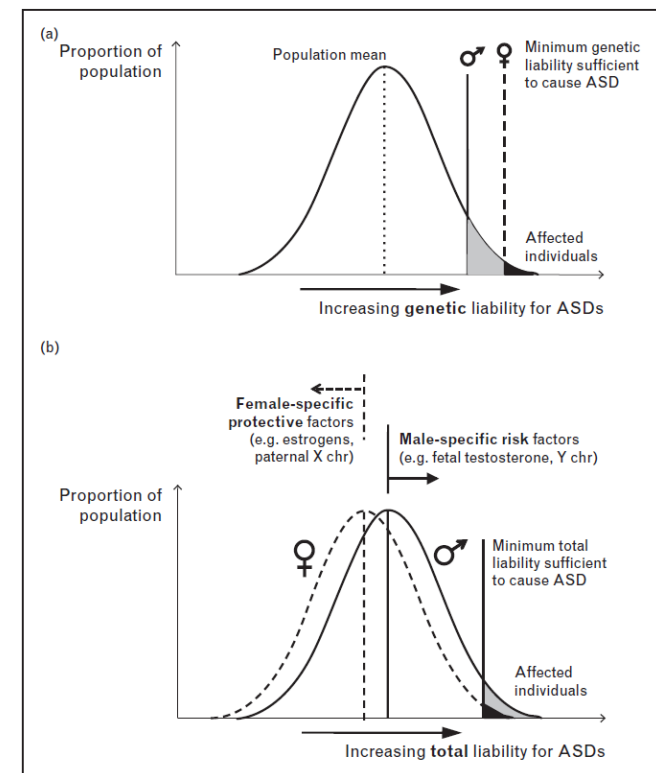
# Risk for ASD: Prematurity and Genetic Syndromes

- 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)



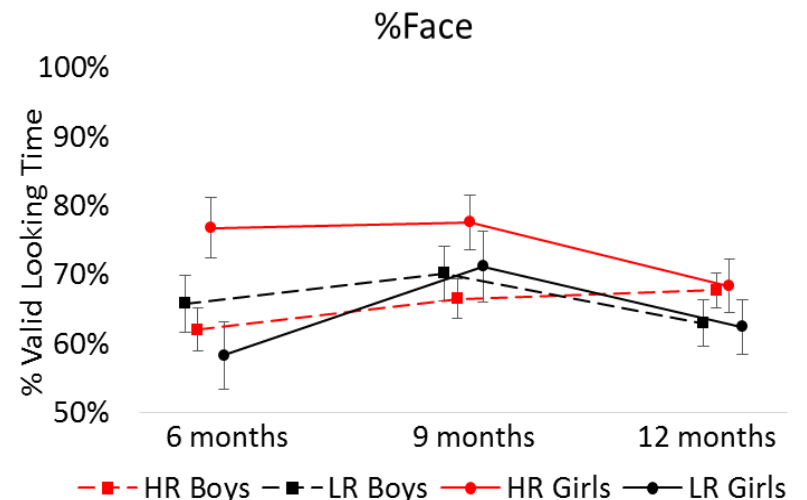
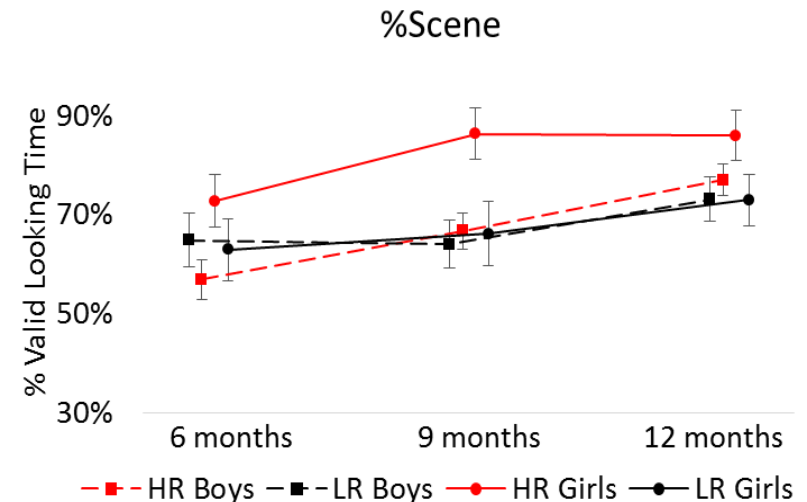
*Reich et al, 1975*

# 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

Chawarska, Macari, DiNicola, Powell, & Shic (2016). Enhanced social attention in female siblings of children with ASD. *Journal of American Academy of Child and Adolescent Psychiatry*



# 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

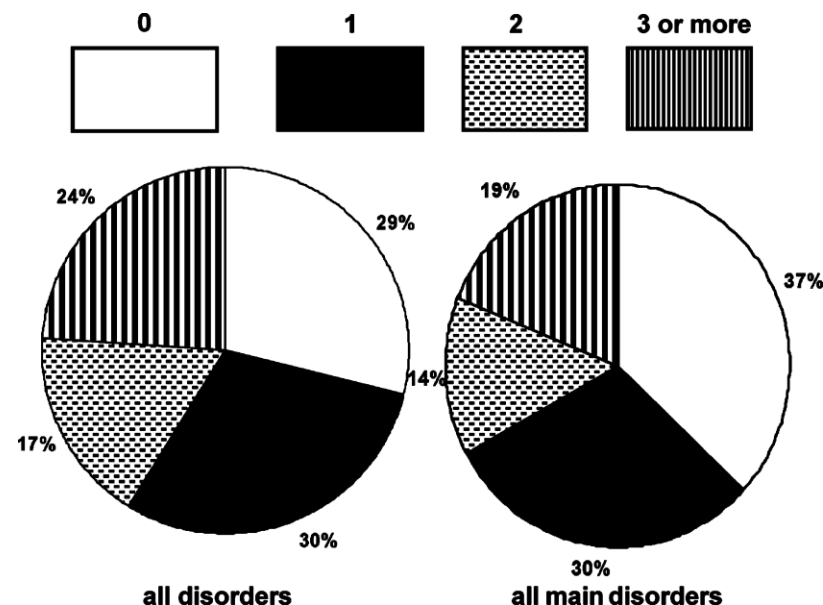


# Comorbid conditions



# Prevalence of comorbid conditions in ASD

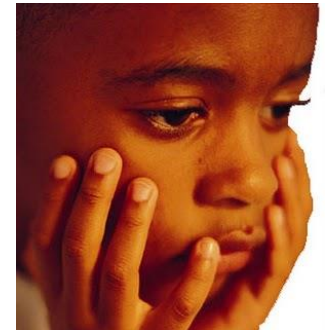
Prevalence of <i>DSM-IV</i> Disorders	
Disorder	3-Mo Point Prevalence/100
Any disorder	70.8
Any main disorder <sup>a</sup>	62.8
Any emotional disorder <sup>b</sup>	44.4
Any anxiety or phobic disorders <sup>c</sup>	41.9
Generalized anxiety disorder	13.4
Separation anxiety disorder	0.5
Panic disorder	10.1
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 <sup>d</sup>	24.7
Enuresis	11.0
Encopresis	6.6
Tourette syndrome	4.8
Chronic tic disorder	9.0
Trichotillomania	3.9



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

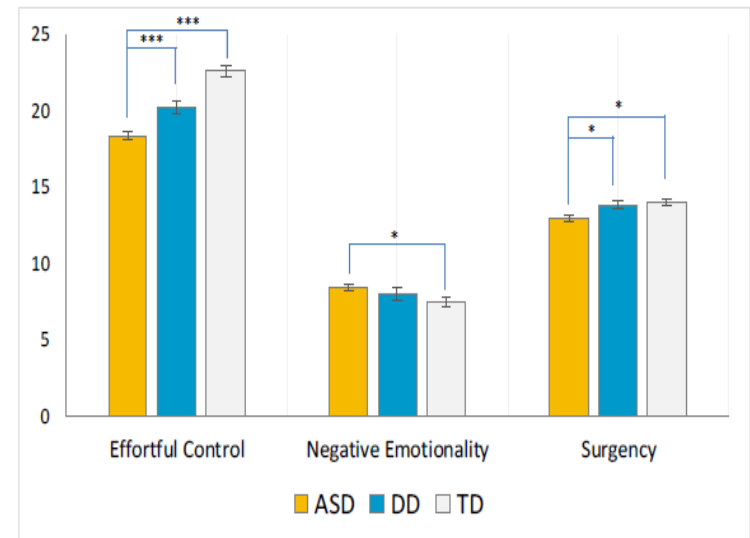


# Emotional Reactivity and Regulation

- 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

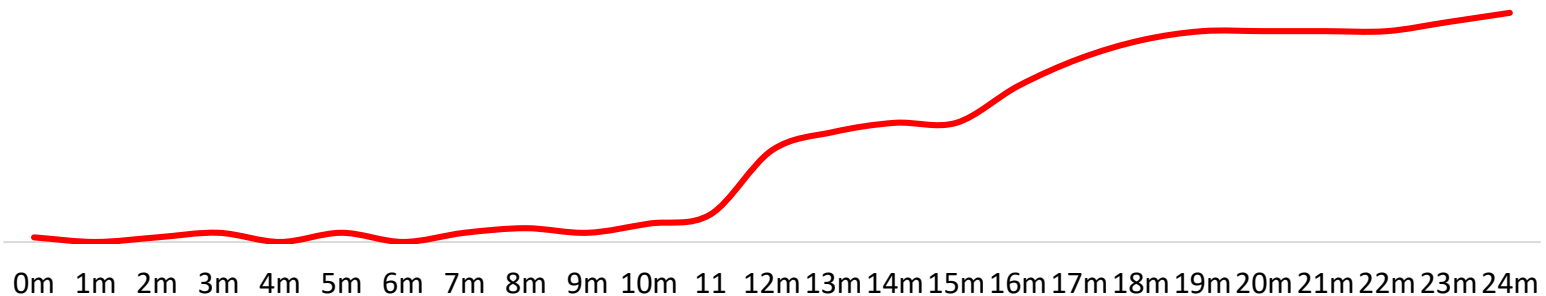
# Comorbid Symptoms: Clinical Implications

- 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.”

Kanner L. Autistic disturbances of affective contact. *Acta Paedopsychiatrica: International Journal of Child & Adolescent Psychiatry*. 1943/1968;35(4-8):98-136.(pp. 245-247).



*Leo Kanner*



# Attentional markers in toddlers: Evidence from eye-tracking studies



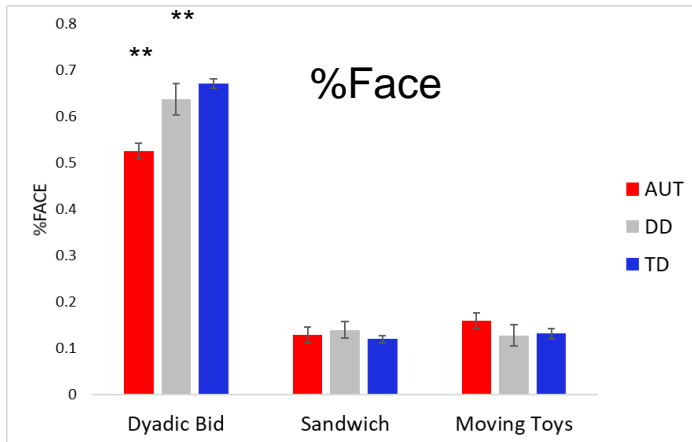
Chawarska, Macari, & Shic, (2012). *Journal of Child Psychology and Psychiatry*

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



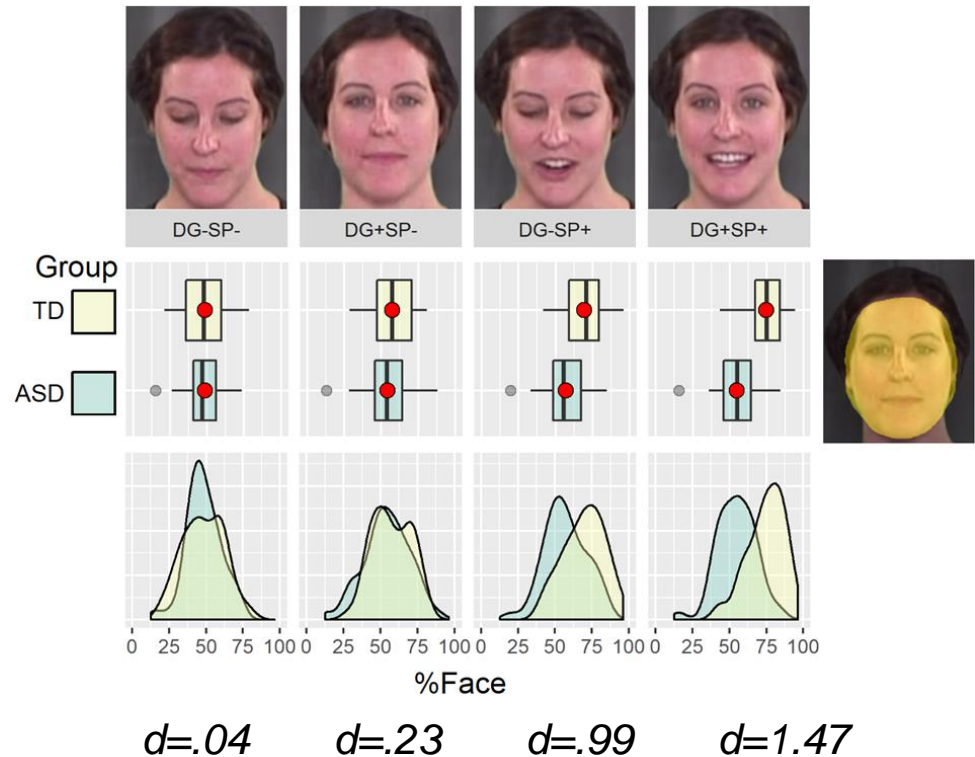
Chawarska, Macari, & Shic, (2012). *Journal of Child Psychology and Psychiatry*

# 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

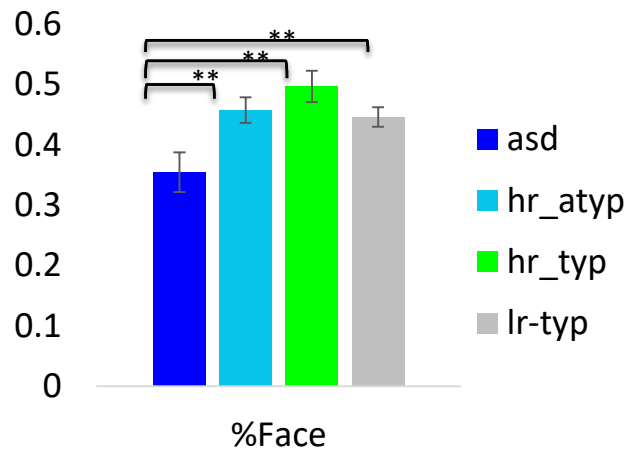
# Can limited attention to faces be detected earlier?



Infants at familial risk for ASD



# Limited attention to dynamic faces in 6-month-old infants later diagnosed with ASD



Chawarska et al., (2013) *Biological Psychiatry*.

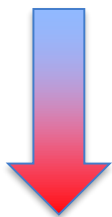


Shic et al., (2014) *Biological Psychiatry*



Macari et al, under review

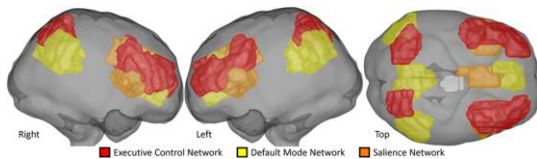
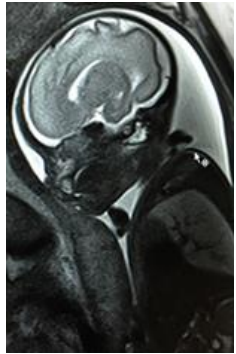
# Emergence of behavioral manifestations of autism



0m 1m 2m 3m 4m 5m 6m 7m 8m 9m 10m 11 12m 13m 14m 15m 16m 17m 18m 19m 20m 21m 22m 23m 24m



# Yale Autism Center of Excellence: Investigation into pre- and neonatal roots of ASD



# Improving understanding of mechanisms that give rise to core autism symptoms in infancy

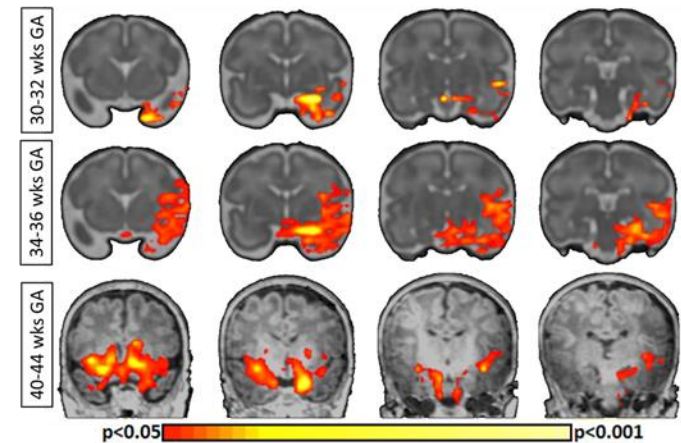
- Safe, non-invasive, non-demanding approach to evaluating brain function
- rs-fc patterns arise spontaneously, reflect activity of functional brain networks involved in e.g., visual and auditory processing, salience detection, or executive control
- Atypical hub topology and connectivity has been implicated in developmental and psychiatric disorders including autism and schizophrenia



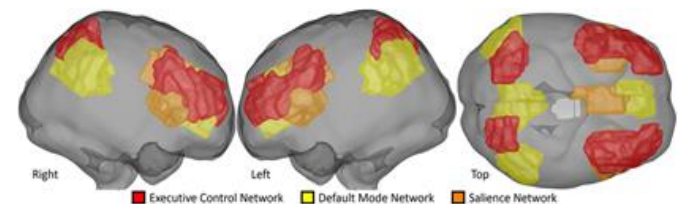


# Fetal and neonatal imaging studies

- 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 2017, Pediatric Research*



*Scheinost et al., in prep*



# Social and Affective Neuroscience of Autism Program Toddler Developmental Disabilities Clinic



# Acknowledgements

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