Developmental social neuroscience meets public health challenge: The next generations of children with autism spectrum disorder

11th Annual Autism Spectrum Disorder Update: Autism Through the Life Span
Palo Alto, California, March 17 2018

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Emory Center for Translational Social Neuroscience

EMORY UNIVERSITY SCHOOL OF MEDICINE

Children's Healthcare of Atlanta

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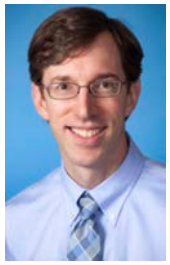
Thank You:

- The children and families for their participation in our research.
- Co-everything in eye-tracking research: Warren Jones.
- *Autism Navigator* research: Amy Wetherby & Jennifer Stapel-Wax
- My wonderful clinical science colleagues, Cheryl Klaiman, Kasia Chawarska, Celine Saulnier and others over the years
- My wonderful colleague investigators, Gordon Ramsay, Sarah Shultz, Longchuan Li, and our wonderful students and trainees over the years
- NIHMH, NICHD, The Marcus Foundation, JB Whitehead Foundation, The Simons Foundation, Georgia Research Alliance, Autism Science Foundation, Children's Healthcare of Atlanta Foundation, Cox Foundation



Warren Jones, PhD

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Marcus Autism Center: Addressing the needs of children and families today; building a better future for the next generations

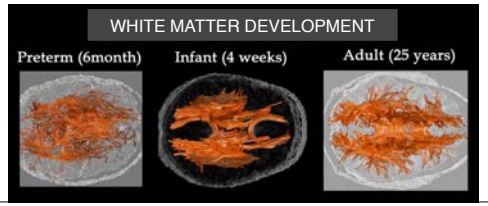
Reciprocal Social Interaction & Early Brain Development

Universal Principle: the Platform for Development of Social Brain

Born to Socially Orient

Reciprocal Social Interaction

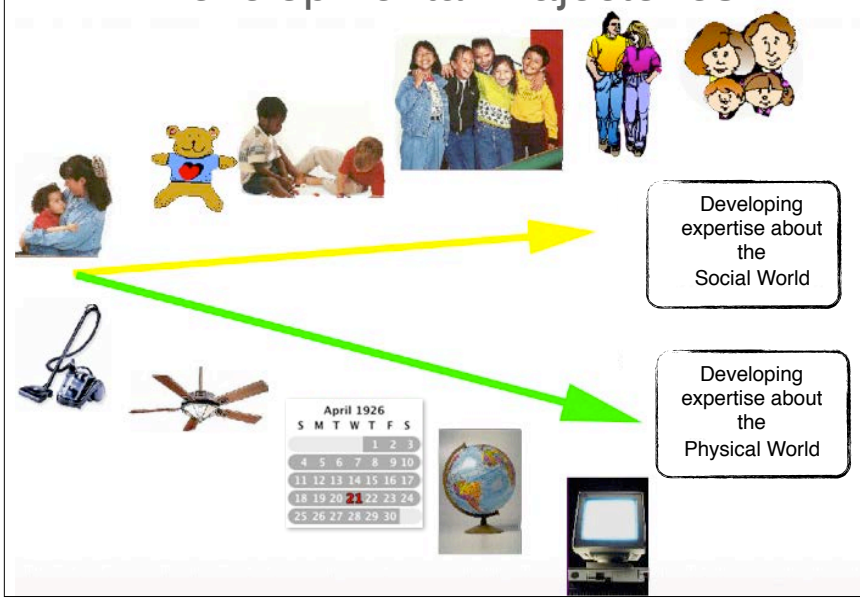
Neuroplasticity



Autism:

Unlike in normative development, predispositions to orient to, and engage with people are significantly reduced.

Developmental Trajectories



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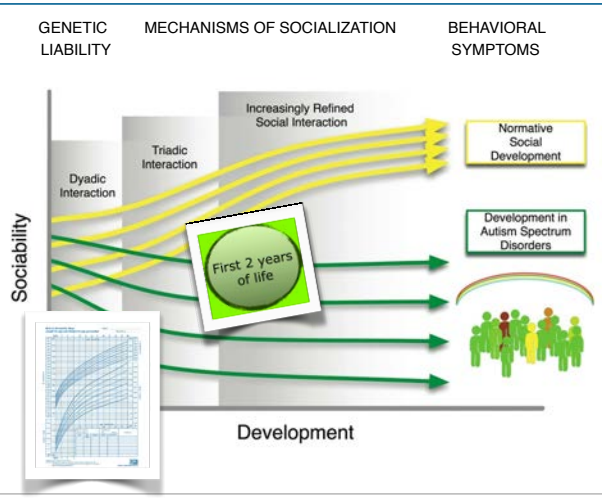
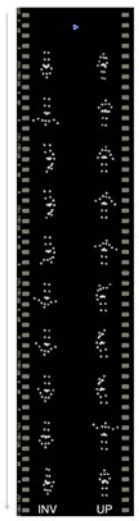
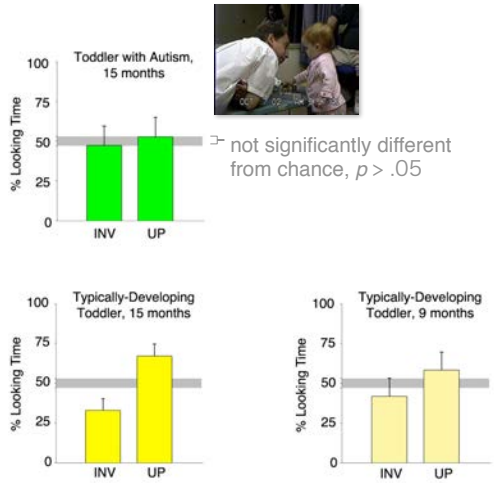
ASD symptoms RESULT from deviations from normative socialization



Jones et al. (2008). *Arch Gen Psy*, 65(8), 946-54; Klin et al. (2009). *Nature*, 459, 257-61; Jones & Klin (2009). *J Am Acad of Child Psy, 48(5): 471-3; Jones & Klin (2013). Nature*, 504, 427-431; *Klin et al. (2015). Neurosci Biobehav Rev, 50, 189-203; Constantino et al. (2017). Nature, 547, 340-344.*

Attention to Biological Motion





not significantly different from chance, $p > .05$

Klin A & Jones W. (2008). *Dev Science*, 1: 40-46.

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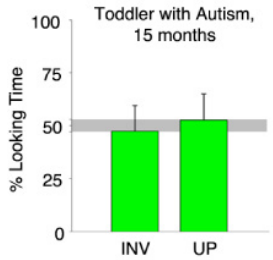
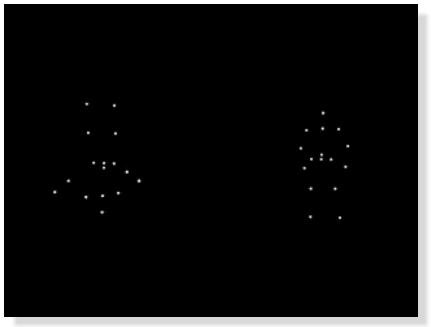
Attention to Biological Motion





Klin A & Jones W. (2008). *Dev Science*, 1: 40-46.

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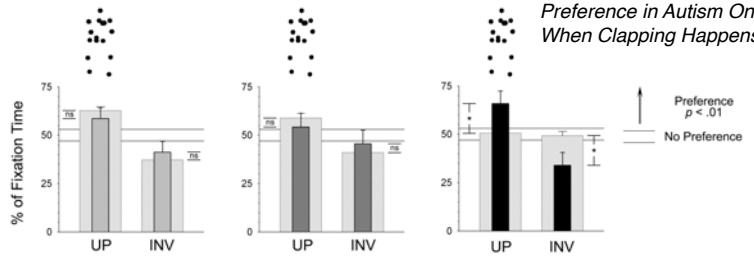
Two-year-olds with autism orient to non-social contingencies rather than biological motion

Ami Klin[1], David J. Lin[1]†, Phillip Gorrindo[1]†, Gordon Ramsay[1,2] & Warren Jones[1,3]

Preference in Autism Only When Clapping Happens



Typically-Developing Children | Developmentally-Delayed Children | Children with Autism

Klin, Lin, Gorrindo, Ramsay, & Jones, *Nature*, 2009.

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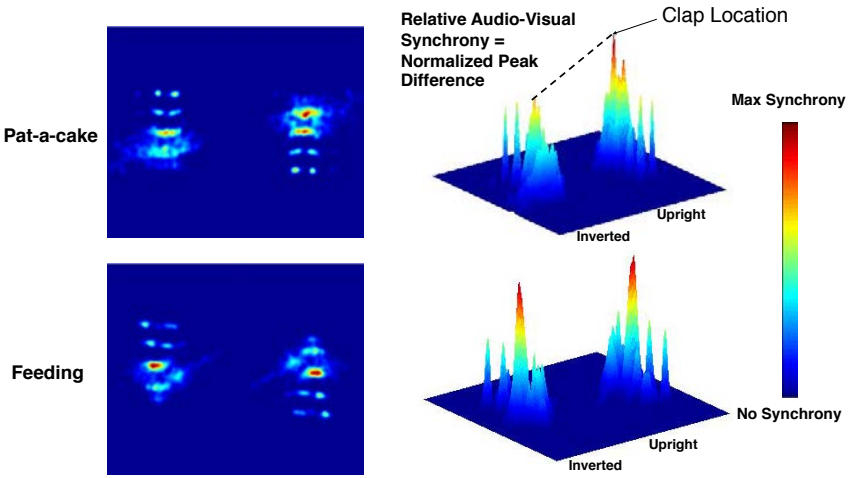
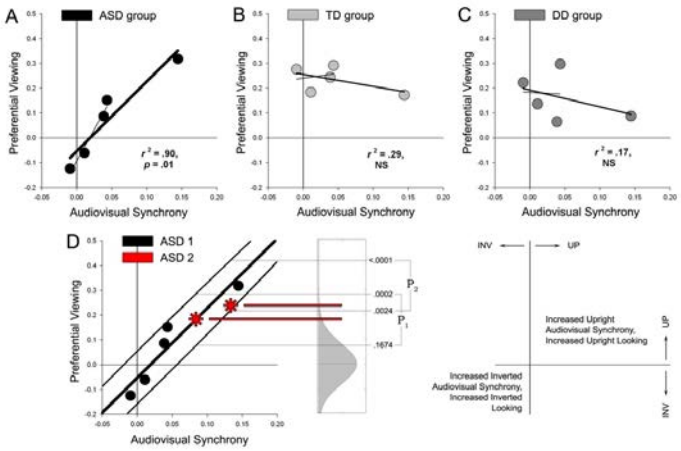
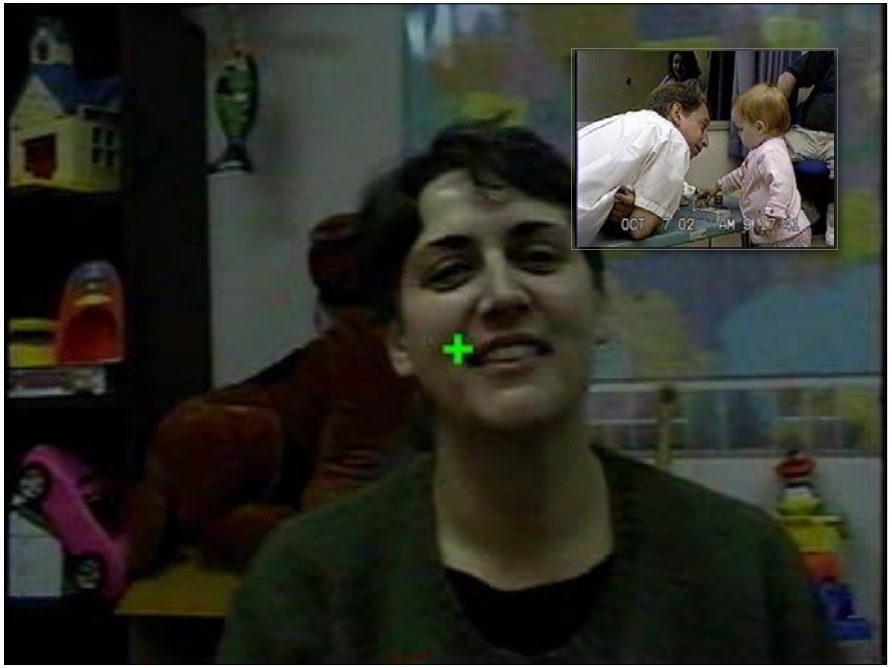
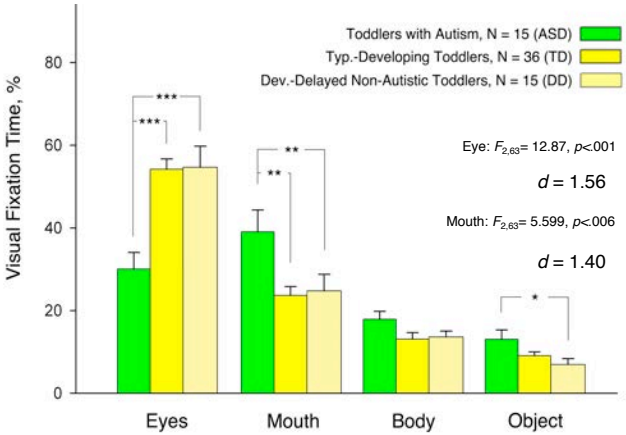
Cumulative Audiovisual Synchrony





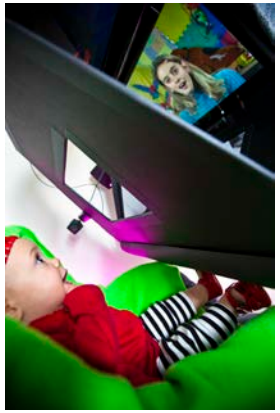


How do 2-year-olds with autism watch the face of a caregiver?



Jones, Carr, Klin (2008). *Arch Gen Psychiatry*. 65(8):946-54.

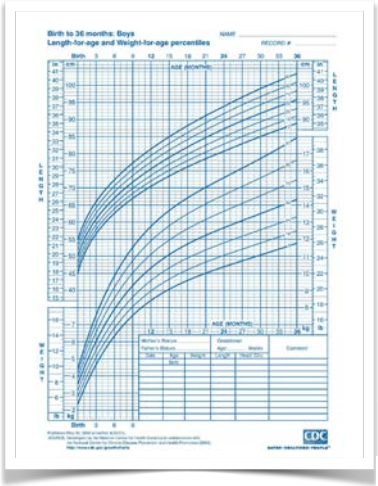
Eye-tracking measures of Social Visual Engagement



Jones & Klin (2013). *Nature.*

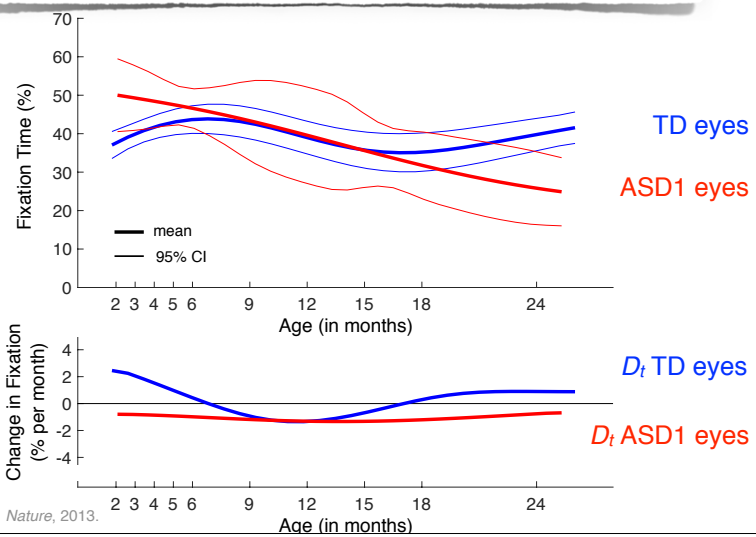
Typically-Developing 5-Month-Old

Growth Charts: of Social Visual Engagement



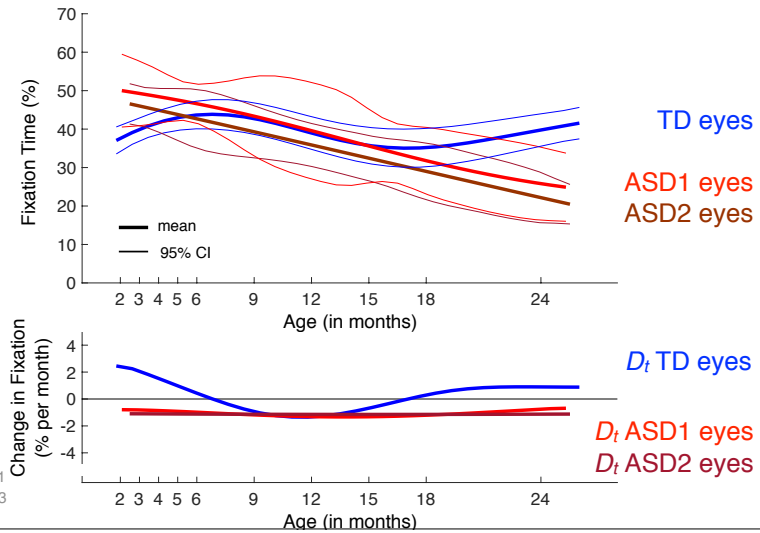
Attention to eyes is present but in decline in 2–6-month-old infants later diagnosed with autism

Warren Jones[1,2,3] & Ami Klin[1,2,3]

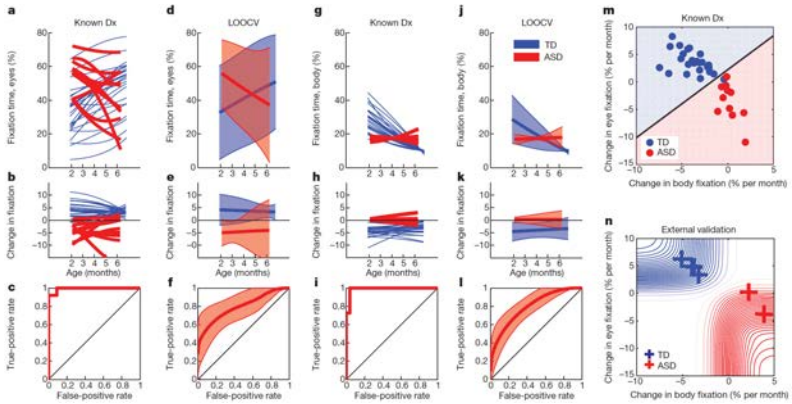


Jones & Klin, *Nature*, 2013.

First Replication Cohort

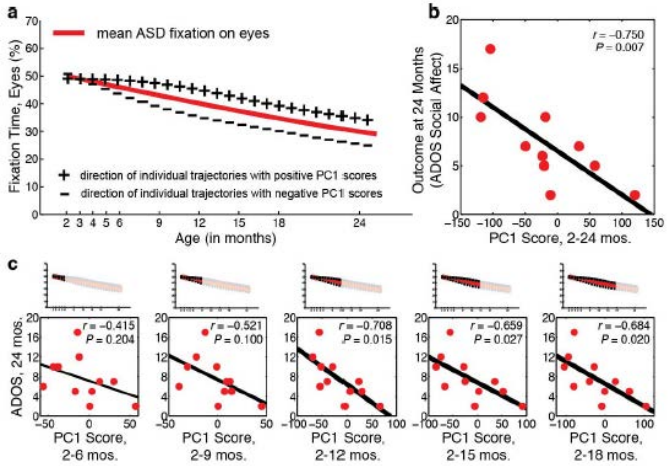


Eye Fixation in the first 6 months of life



- Markers of ASD in the first 6 months of life
- Predictive of individual child's diagnostic classification at outcome (24-36 months)
- Internal and external validation of results

Predicts level of disability at outcome



- Decline in eye fixation (2-12 through 2-24 months) predictive of outcome levels of ASD severity at 36 months

How to link these quantifications of behavior to the genetic bases of autism?

Measuring the genetic structure of social visual engagement

John Constantino, MD

250 toddlers:

- **82 monozygotic** twins (41 MZ pairs)
- **84 dizygotic** twins (42 DZ pairs)
- **84** non-sibling comparison children (42 non-sib control pairs)
- age **21.3**(4.3) months
- non-sibs matched <1 day

Constantino et al. Nature, 2017; 547(7663):340-344

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The genetic basis of Social Visual Engagement

Nature, 2017; 547(7663):340-344

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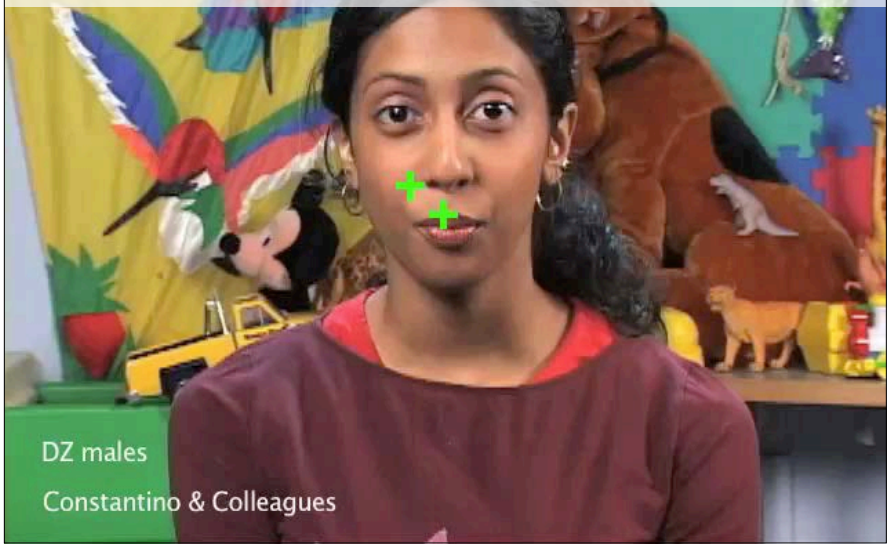
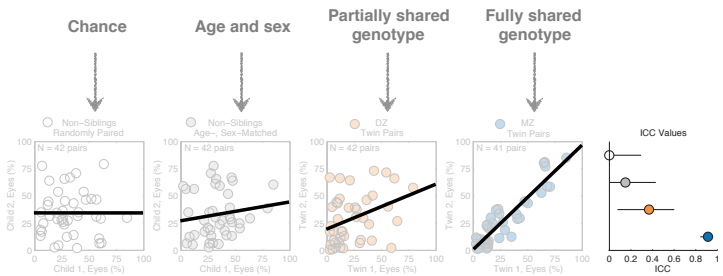
Concordance in social visual engagement as a function of zygosity.



Individual variation in eye-looking is strongly influenced by genetics.



Nature, 2017; 547(7663):340-344

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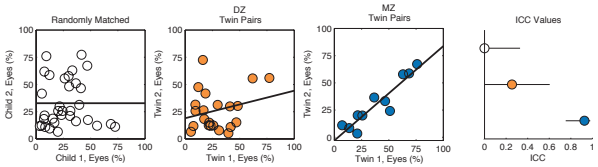
Strong genetic influence persists across development.



Twins tested again 15 months later, at 36 months.
(N=22 MZ, N=44DZ)

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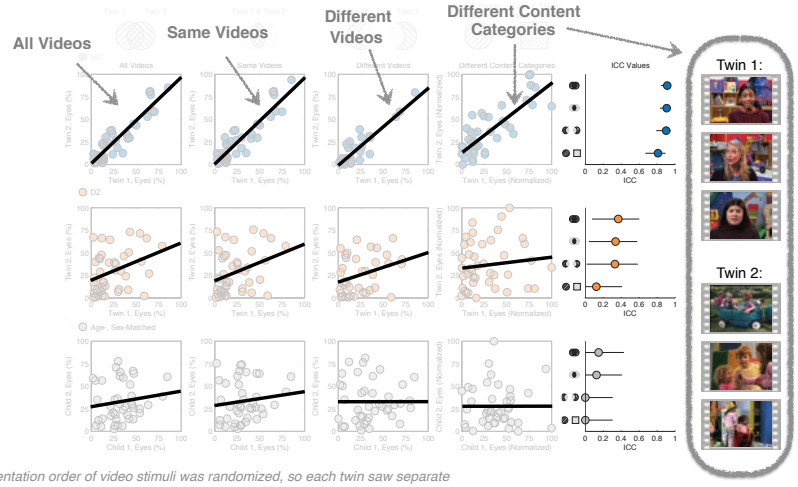
Genetic influence persists whether twins watch the same or different videos.



Presentation order of video stimuli was randomized, so each twin saw separate videos, the majority of which were the same (M(SD)=86.4(19.3)%) but some of which were different (13.6(19.3)%), seen by only one among the pair.

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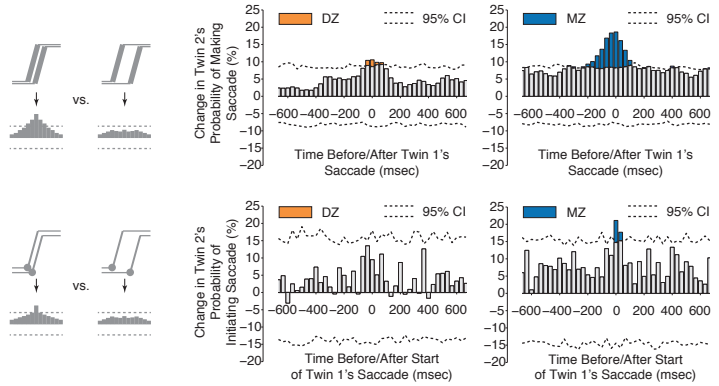
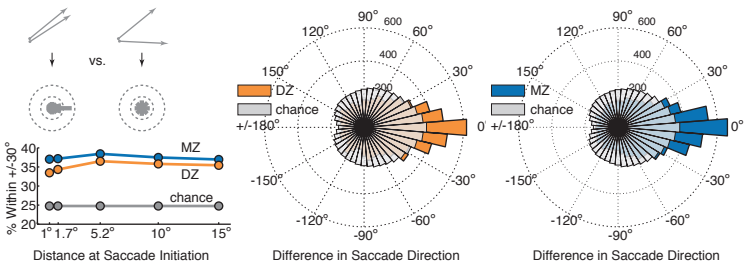
Genetic influence exerts effects on a moment-by-moment basis.

MZ twins are more likely to…



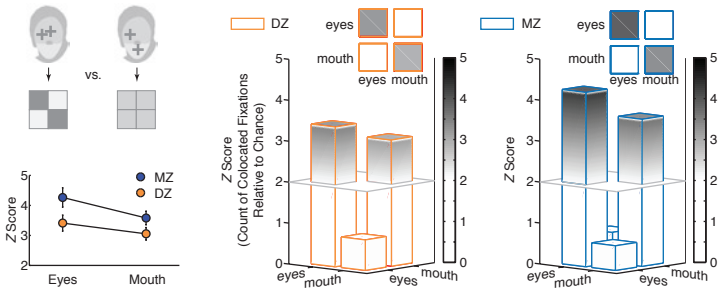
…move their eyes **at the same moments** in time.

MZ twins are more likely to…



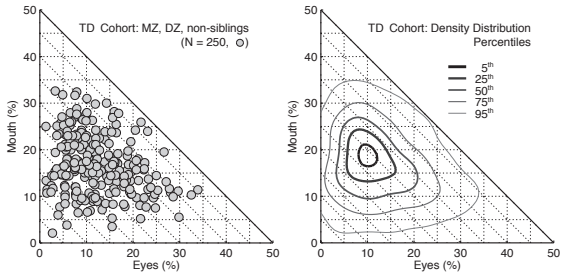
…move their eyes **in the same directions**.

MZ twins are more likely to…



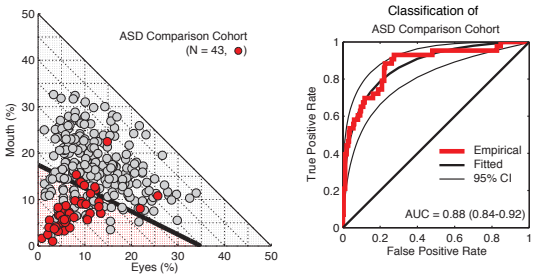
…fixate on the **same semantic content** at the **same moments in time**.

The markers of social visual engagement that are most highly heritable…



…are also those that most clearly distinguish typically-developing children from those with autism.

The markers of social visual engagement that are most highly heritable…



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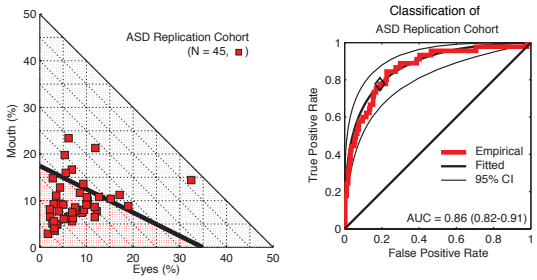


…are also those that most clearly distinguish typically-developing children from those with autism.

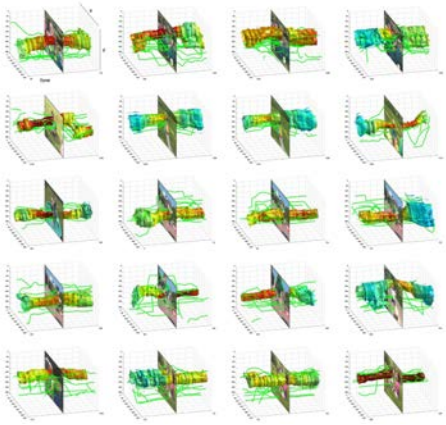
high ***Heritability*** (eye- & mouth-looking)

+ high ***Probability*** (shifting eyes at same moments, in same directions, towards same content)

= profound influence on
human biological niche construction

Scarr & McCartney, 1983.

Hundreds of natural experiments within a 5-minute free viewing video experiment



- In ASD: ~570 divergences in 5 minutes of video
- ~13,680 divergences in a 2-hour period of real-life social experience
- 6 hour social exposure/day results in ~15,000,000 divergences over the course of one year of real-life exposure to social environments

TD normative funnels =

ASD comparison scanpaths =

Translational Opportunities

- High-throughput, low-cost, deployment of universal screening in the community
- Early detection, early intervention, optimal outcome
- Prevention or attenuation of intellectual disability in ASD

Public Health Opportunities

- Support a system that does not have sufficient expert clinicians
- A new, promising view of autism, with universal design implications
- Genetic influence informs modality of early treatment
- Reduce the child, family, health, education, and societal costs of autism

Massive Challenge - Massive Opportunity

- 60,000 children born every year will have autism (1:68); societal cost of autism is $126B/year in US alone; early detection and intervention is a game changer (NIH)
- A cohort of children with autism followed from birth reaching 3 years of age without developmental delays: diversity, not disability
- 700,000 children with autism in schools; annual cost $37B/year; median age of diagnosis of autism in the US: 4.5 - 5.5 years
- 6,600,00 special education children (13% of all students); 9% with autism; 20% language impairment; 12% with developmental delays or intellectual disability
- These are all conditions originating in disrupted early brain development due to genetic, medical or environmental vulnerabilities
- Maybe ~10% are "inevitable"; in ~90%, burdens can be significantly attenuated if not prevented altogether
- Neurodevelopmental Medicine of the 21st century: optimizing outcomes

Developmental Social Neuroscience meets Public Health Opportunities

- We are genetically programmed to be social beings
- This programming is altered in autism
- But social experiences are co-created by environment
- We can engineer these experiences via parent-delivered treatment

Augmenting Access to Early Treatment

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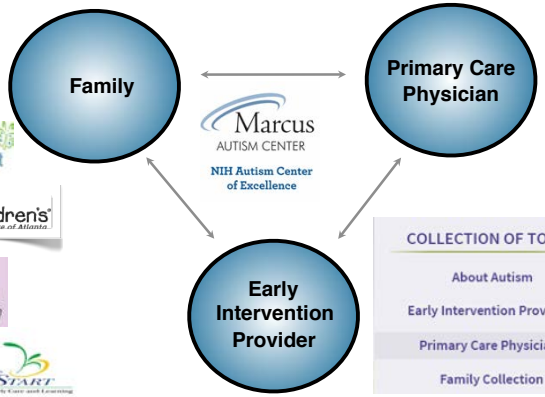

Amy Wetherby, PhD

Jennifer Stapel-Wax, PsyD

Kids Health First
Children's Healthcare of Atlanta
Babies Can't Wait
Bright Start

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the Community: Families, Pediatricians, Early Intervention Providers

Parent-Delivered Early Social Interaction

Wetherby et al., 2014

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Treating deviations from normative social engagement: Parent-Delivered Social Interaction

Amy Wetherby, PhD

PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Parent-Implemented Social Intervention for Toddlers With Autism: An RCT

WHAT'S KNOWN ON THIS SUBJECT: Randomized controlled trials (RCTs) of intensive clinician-implemented interventions have demonstrated significant improvements in outcomes of toddlers and preschool children with autism spectrum disorder. RCTs of parent-implemented interventions have demonstrated improvements in parent skills, but generally they have not demonstrated effects on children's outcomes.

WHAT THIS STUDY ADDS: This RCT found significantly greater improvements with individual home coaching on child outcome measures of social communication, adaptive behavior, and developmental level. These findings support the efficacy of a parent-implemented intervention using little professional time, which increases potential community viability.

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Departments of [a]Clinical Sciences, [b]Autism Institute, [c]School of Communication Science and Disorders, and [d]Psychology, Florida State University, Tallahassee, Florida; and [e]Department of Psychiatry, Weill Cornell Medical College, New York, New York

KEY WORDS
autism, early intervention, toddlers, parent-implemented, outcomes

ABBREVIATIONS
ADOS—Autism Diagnostic Observation Schedule
ASD—autism spectrum disorder
CSBS—Communication and Symbolic Behavior Scales
EI—early intervention
ESI—Early Social Interaction

Universal design because there is only one platform for early brain development

- For children with complex genetic burden: Autism, Williams syndrome
- For children with compromising medical conditions: Extremely Preterm, Congenital Heat Disease
- For children from disadvantaged backgrounds

Pediatric Medicine of the 21st century: The criticality of Public Health considerations

- Not necessarily curing "diseases"
- BUT OPTIMIZING OUTCOMES
- Universal screening, accessing identification, increasing access to early intervention
- Cost-effective, community-viable
- Value Proposition!

5 Steps for Brain-Building
Serve and Return

Dr. Jack Shonkoff

Center on the Developing Child
HARVARD UNIVERSITY

Dr. David Willis

An Early Brain and
Child Development Focus
HRSA

LANGUAGE NUTRITION

TALK WITH ME BABY

Dr. Brenda Fitzgerald

DPH
Georgia Department of Public Health

CDC

Brain Trust 4 Babies

Take Away Messages - 1

- Autism is a massive public health challenge and an enormous public health opportunity
- Children's lifetime outcomes can be optimized with
  - ✦ *Early Detection, Access to Diagnostic Services, Access to Early Intervention*
- The greatest burdens of autism are not inevitable and be significantly ameliorated
  - ✦ *Intellectual Disability, Language Disability, Severe Behavior Challenges*
- What moves early brain development is reciprocal social engagement, and early experiences shape the trajectories of social and communication skills and social-communicative brain
- Infants & toddlers create their own social environment: these behaviors are under stringent genetic control and disrupted (and diagnostic) in the case of young children with autism

Take Away Messages - 2

- But we can engineer social learning experiences via manipulation of children's environment - via parent-delivered treatments
- We need cost-effective and community-viable solutions for
  - ✦ *Universal Screening, Diagnosis, and Early Treatment*
- Solutions for screening and diagnosis are not far off
- Solutions for early treatment are being studied at a grand scale right now
- Solutions for optimizing the development of children with autism are relevant to a much broader group of children
- The future of neurodevelopmental medicine is likely to be focused on optimizing the outcome of children born with genetic, medical or environmental challenges rather than on the "cure" of these complex conditions

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Our ultimate goal:
To change the narrative of autism

To make autism
an issue of diversity,
not of disability