Bringing science to the community: A new system of healthcare delivery for infants & toddlers with autism spectrum disorders

National Autism Conference, State College, PA
August 3, 2015

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Emory Center for Translational Social Neuroscience

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Children's Healthcare of Atlanta
Marcus AUTISM CENTER
NIH Autism Center of Excellence

Thank You

- The children and families who support our clinical and research activities
- Warren Jones and many wonderful colleagues and students
- The Marcus Foundation
- The JB Whitehead and Woodruff Foundations
- The Children's Healthcare of Atlanta Foundation
- The Georgia Research Alliance

as well as

- The National Institute of Mental Health
- The National Institute of Child Health and Human Development
- The National Science Foundation
- The Simons Foundation
- The Autism Science Foundation
- Autism Speaks
- United Way
- Cox Foundation

Conflicts of Interest

No conflicts of interest associated with this presentation

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Marcus Autism Center

Marcus Autism Center at a glance

Children's Healthcare of Atlanta

- Translation
- Impact
- Clinical Resources

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Excellence

EMORY UNIVERSITY SCHOOL OF MEDICINE

- Science
- Faculty Advancement
- Research Resources

CLINICAL OPERATIONS

- >5,700 unique patients/yr
- Tx: set protocols (x visits)
- > 65% on Medicaid
- ~ 40% minorities/under-served

- Clinical Assessment/Diagnosis
- Treatment Programs
  - Center/Home/School/Community
- Care Coordination Program
- Educational Outreach Program

RESEARCH INITIATIVES

- CAUSES
- TREATMENT
- COMMUNITY-VIABLE SOLUTIONS
- IMPLEMENTATION SCIENCE

COMMUNITY-VIABLE OUTREACH MODEL

The Science of Clinical Care

Research Enterprise

- CAUSES
- TREATMENT
- COMMUNITY-VIABLE SOLUTIONS
- "VALUE PROPOSITION"

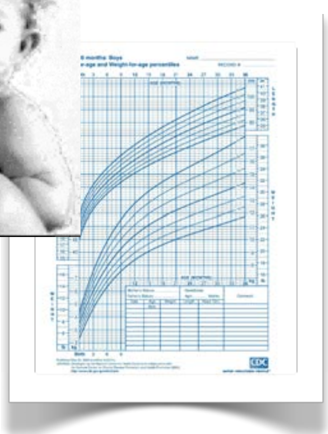
RESEARCH INITIATIVES

RESEARCH INFRASTRUCTURE

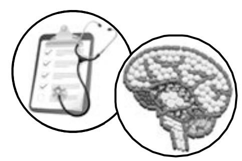
- 13 RESEARCH CORES
- 9 INTERNAL, 4 COLLABORATIVE
- RESEARCH ADMINISTRATION
- INFORMATICS
- DATA MANAGEMENT & ANALYSIS

Strategy for Reseach Enterprise

Concept



Diagnosis & Treatment



Clinical Trials

Social Neuroscience

Animal Models

Neurobiology

Genetics

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Autism as a Public Health Challenge

- Prevalence: 1 : 68   [1:42 in boys]
- Community Disparities (dx; access)
- Societal Cost/Year in the US: $ 136 billion
- Lifetime Cost of Care Per Child: $ 2.4 million
- Despite strong genetic bases, diagnosis is behavioral, reference standards excellent (ADI-R/ADOS/expert clinician)
- Majority of autism diagnoses in US outside academic medical centers
    - ✳ usage of ADI-R and ADOS in fewer than 0.1% and 2.1%, respectively
    - ✳ questionnaires/checklists in 30%

CDC, 2014; Peacock et al., 2012; Cidav et al., 2012; Mandell et al., 2013; 2014; Wang et al., 2013; Buescher et al., 2014; Wiggins et al., 2006

Challenges and Opportunities:
Reducing Age of Diagnosis & Improving Access to Care

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- Brain disorder of genetic origins
- Adverse outcomes can be attenuated
- Importance of early diagnosis and intervention for lifelong outcome and cost of care
- American Academy of Pediatrics
  - Screening (18 and 24 months), but still low uptake
- 8% of primary care providers routinely screen for ASD
- Median age of diagnosis in US: 4-6 to 5.7 years
- Later still in disadvantaged communities
- No Community-viable system of care
- Reimbursement systems NOT in place

Johnson & Myers, 2007; Dosreis et al., 2006; Heidgerken et al., 2005; Honigfeld et al., 2012; Shattuck et al., 2009; Mandell et al., 2005; 2009

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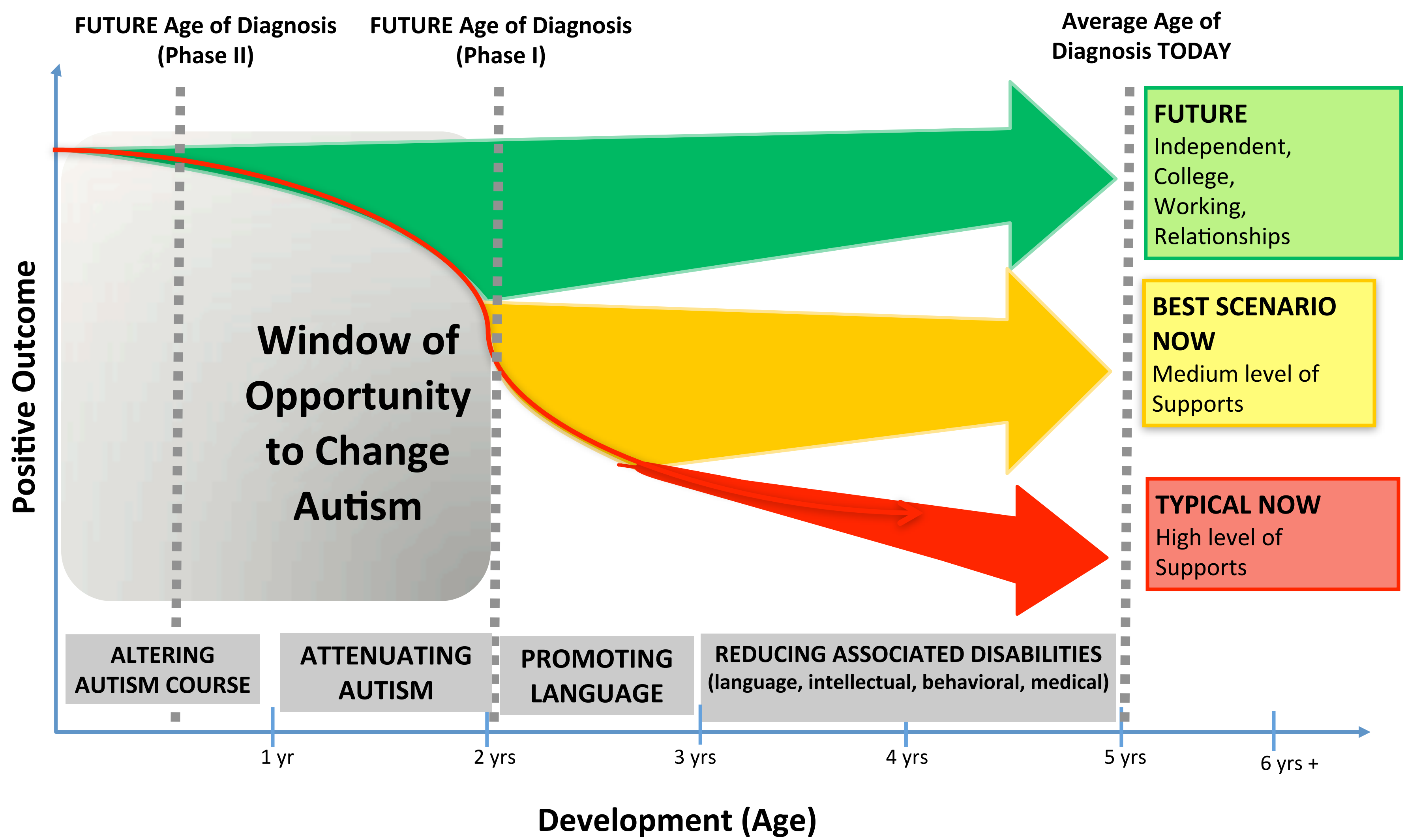
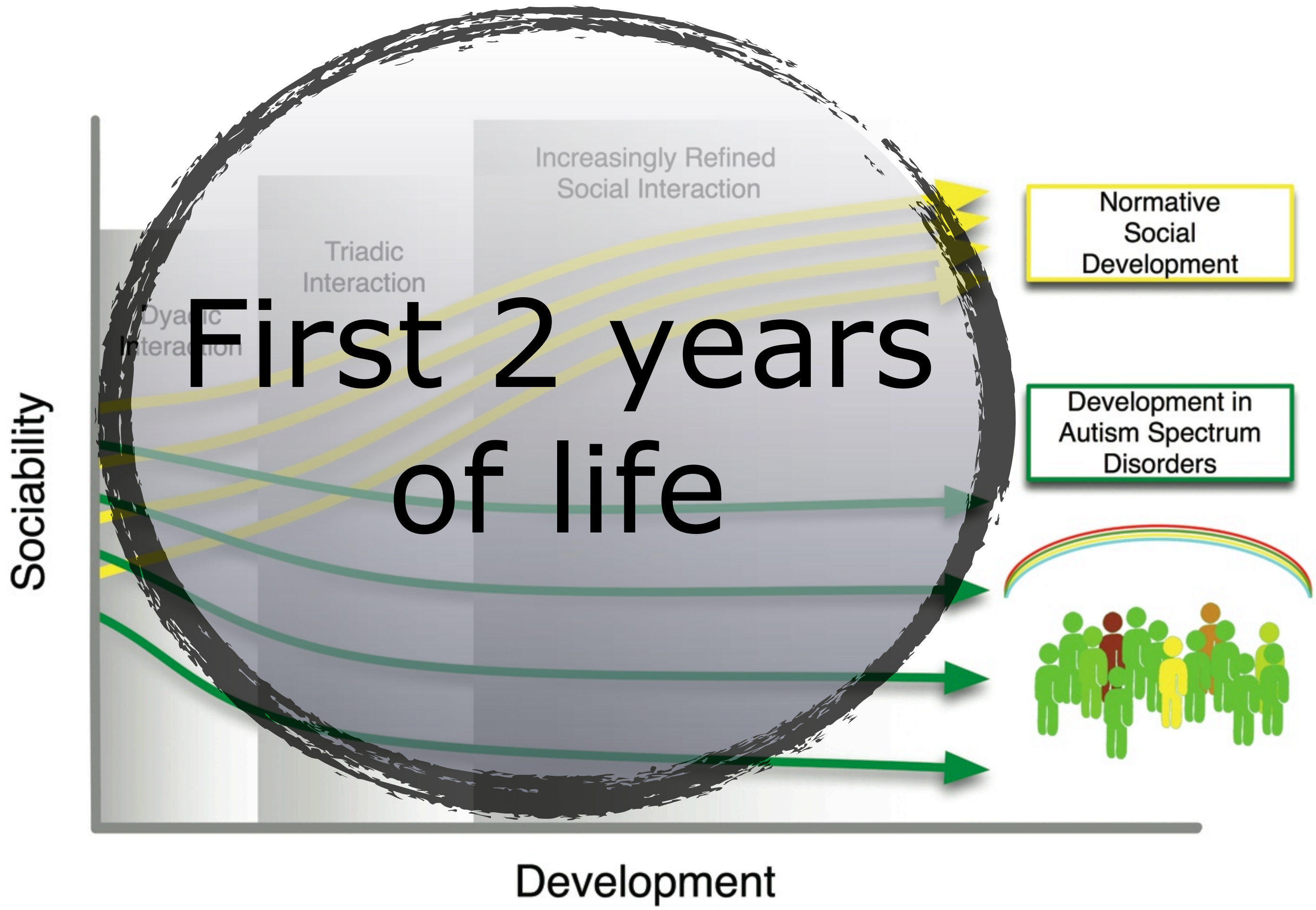
The importance of early identification & treatment: altering the life course of children



GENETIC LIABILITY

MECHANISMS OF SOCIALIZATION

BEHAVIORAL SYMPTOMS



No Genetic Determinism

No Brain Determinism

JE LeDoux PhD

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. (2014). Neurosci Biobehav Rev.*

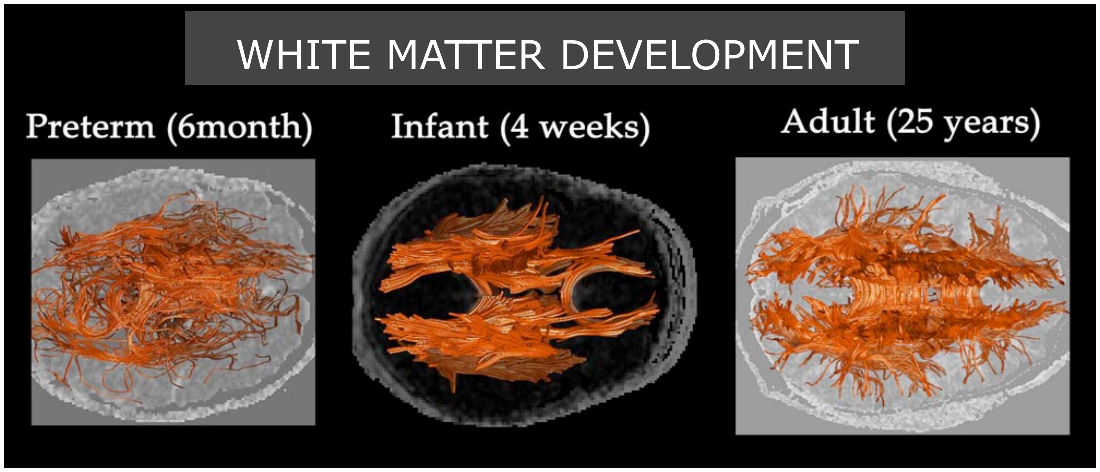
Autism Disrupts the Platform for Brain Development

Born to Socially Orient

MH Johnson PhD

Reciprocal Social Interaction

Neuroplasticity

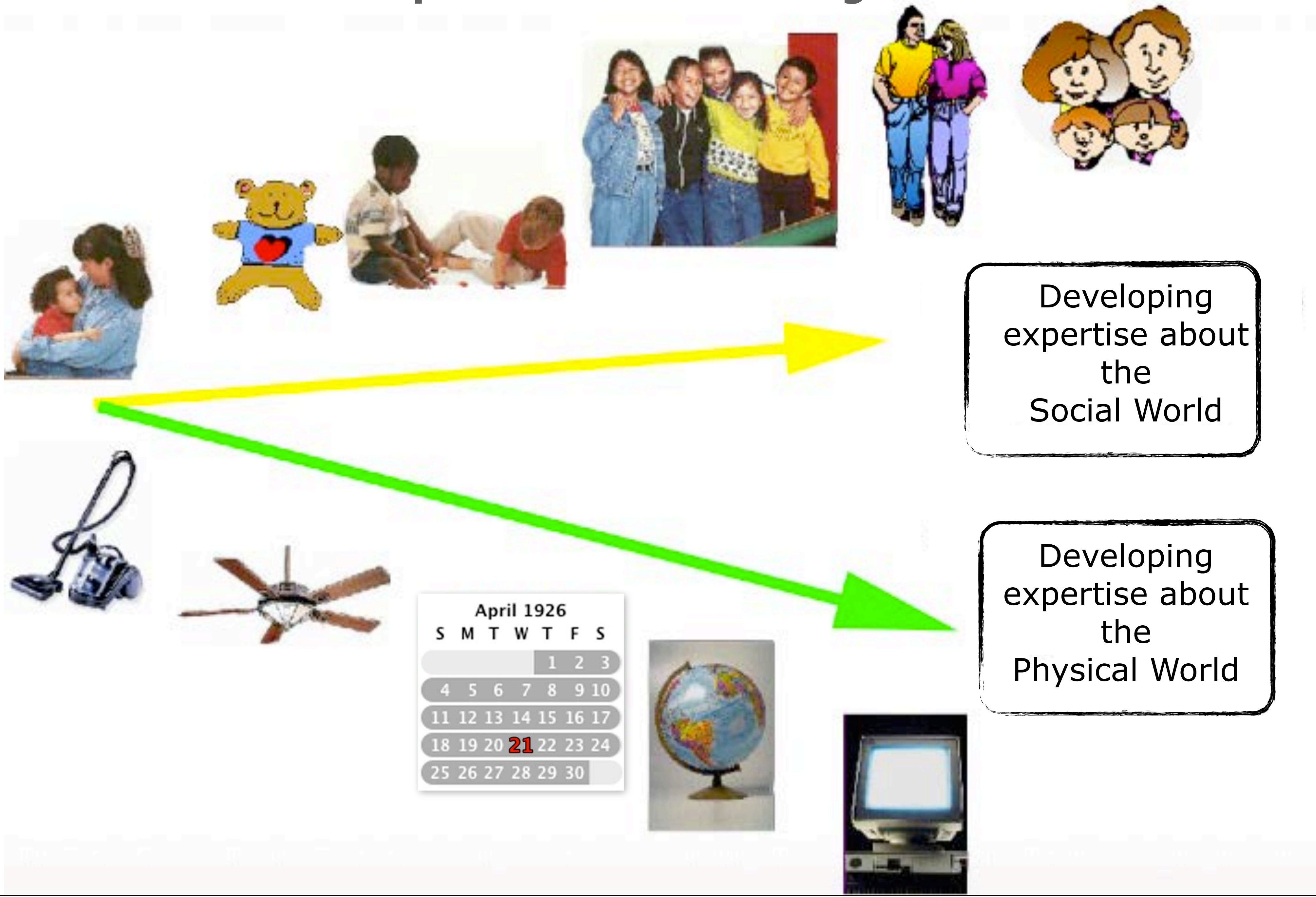


H-J Park PhD

Autism:

Unlike in typical development, predispositions to orient to, and engage with people are absent or significantly reduced.

Developmental Trajectories



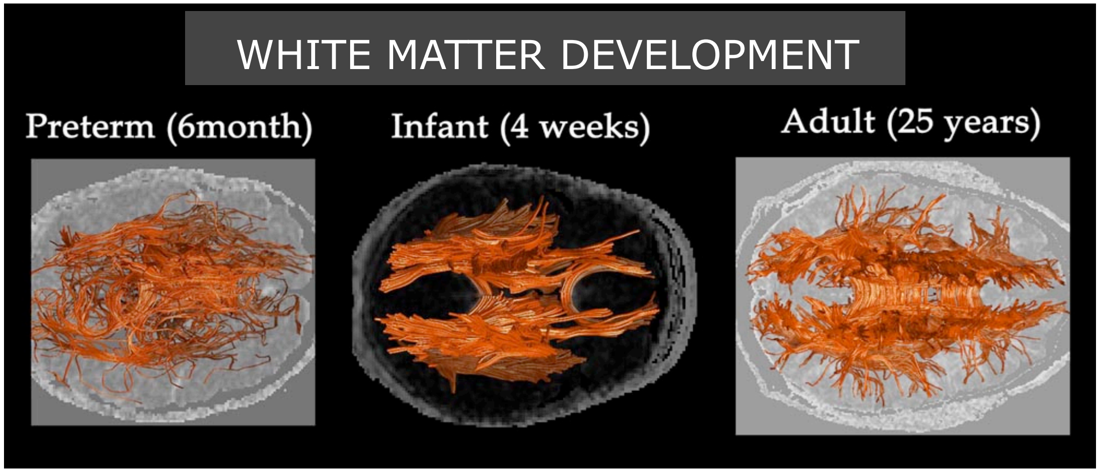
Autism Disrupts the Platform for Brain Development

Born to Socially Orient

MH Johnson PhD

Reciprocal Social Interaction

Neuroplasticity



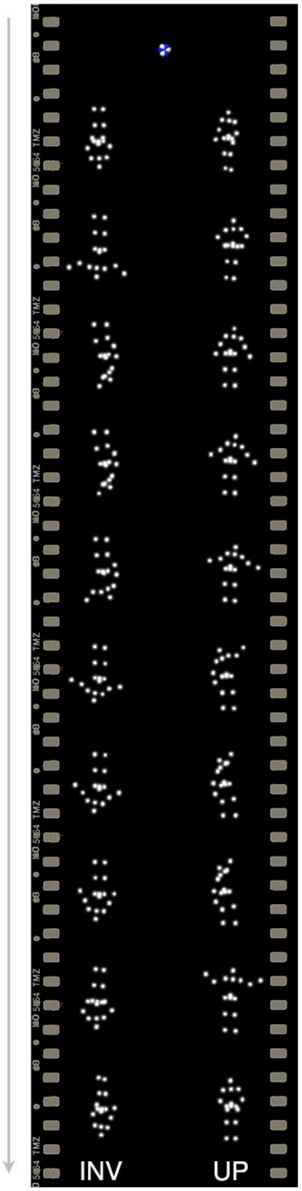
H-J Park PhD

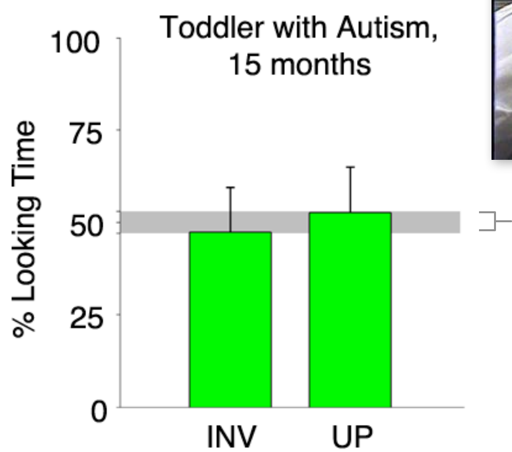
Toddlers

Klin et al. (2003). *Philos Trans R Soc Lond B Biol Sci*. 358(1430):345-60.

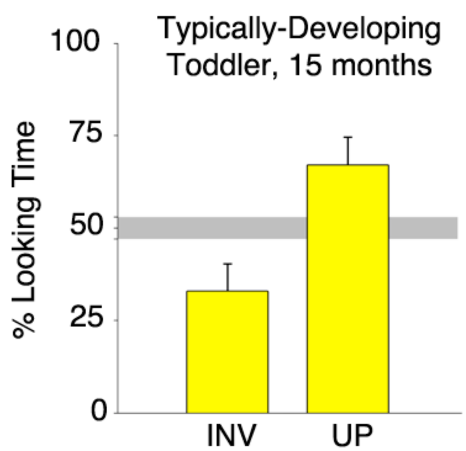
Attention to Biological Motion

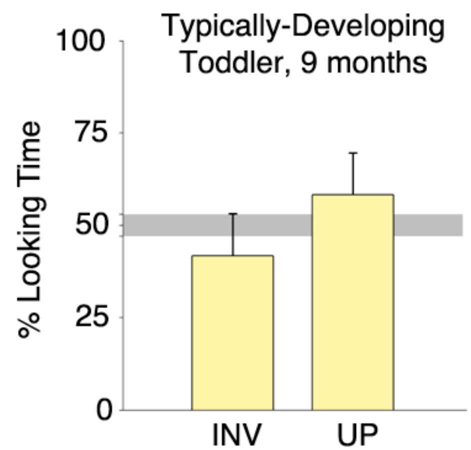
Attention to Biological Motion



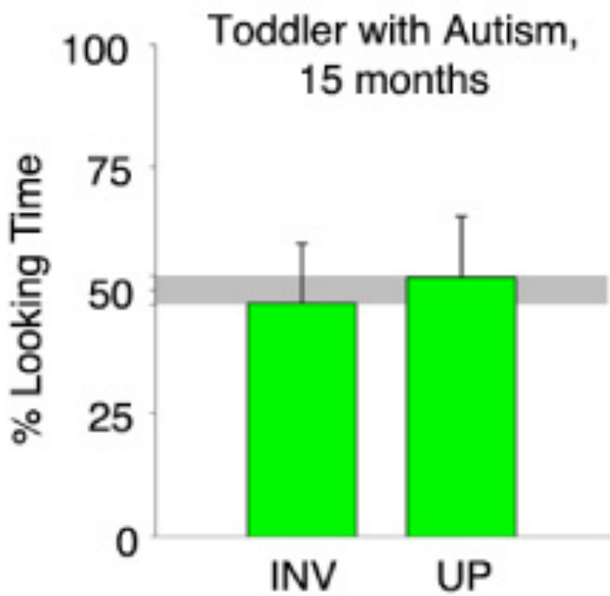


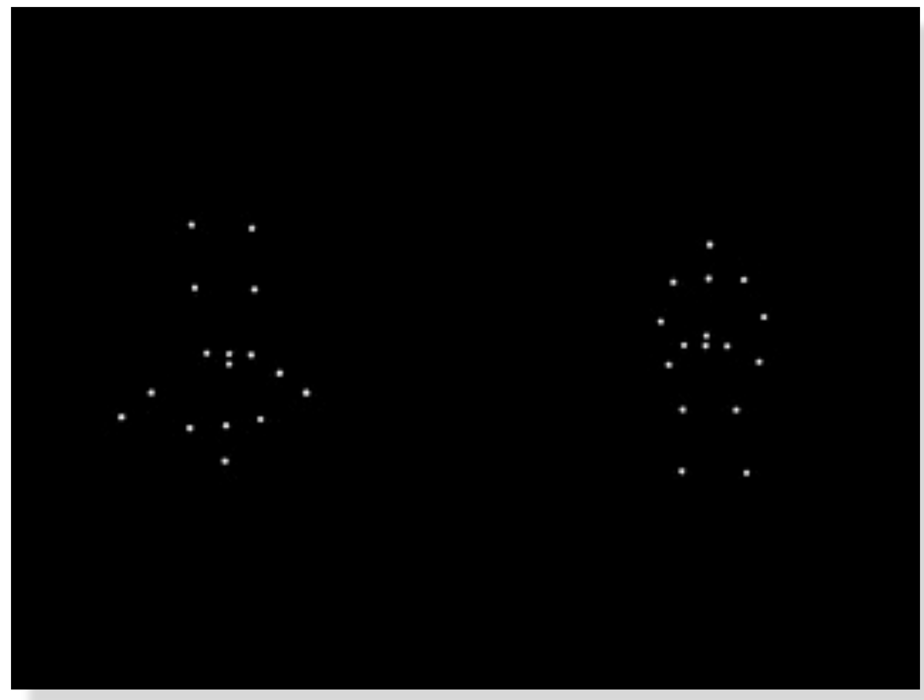
not significantly different from chance, $p > .05$





Klin & Jones (2008). *Developmental Science* 11(1),40-6.


Toddler with Autism,
15 months
100
75
50
25
0
% Looking Time
INV
UP




clapping
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nature International weekly journal of science

Vol 459 | 14 May 2009 | doi:10.1038/nature07868

nature

LETTERS

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

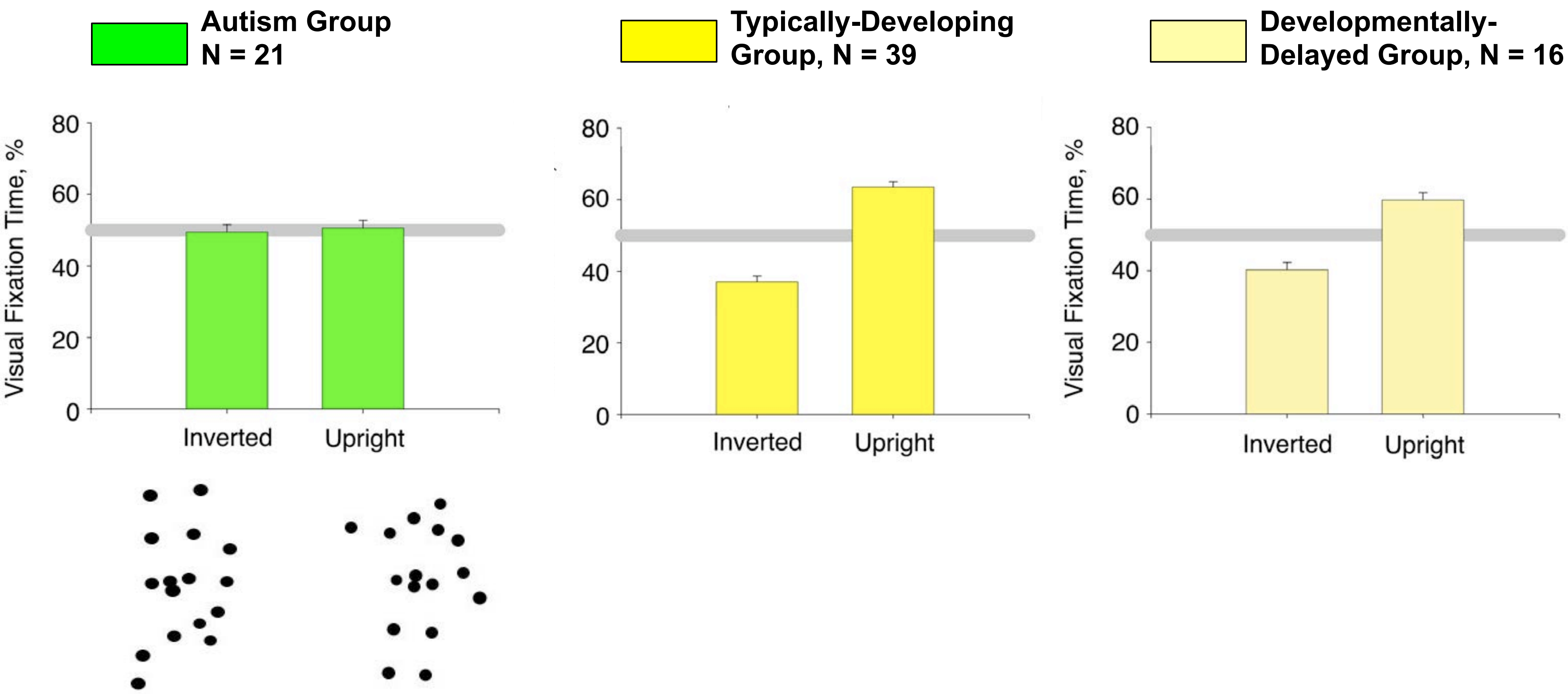
Ami Klin[1], David J. Lin[1]†, Phillip Gorrindo[1]†, Gordon Ramsay[1,2] & Warren Jones[1,3]

Typically developing human infants preferentially attend to biological motion within the first days of life[1]. This ability is highly conserved across species[2,3] and is believed to be critical for filial attachment and for detection of predators[4]. The neural underpinnings of biological motion perception are overlapping with brain regions involved in perception of basic social signals such as facial expression and gaze direction[5], and preferential attention to biological motion is seen as a precursor to the capacity for attributing intentions to others[6]. However, in a serendipitous observation[7], we recently found that an infant with autism failed to recognize point-light displays of biological motion, but was instead highly sensitive to the presence of a non-social, physical

conspecific, looking at others to entreat or avoid interaction, learning by imitation, or directing preferential attention to cues that build on biological motion (such as facial expression and gaze direction[5]).

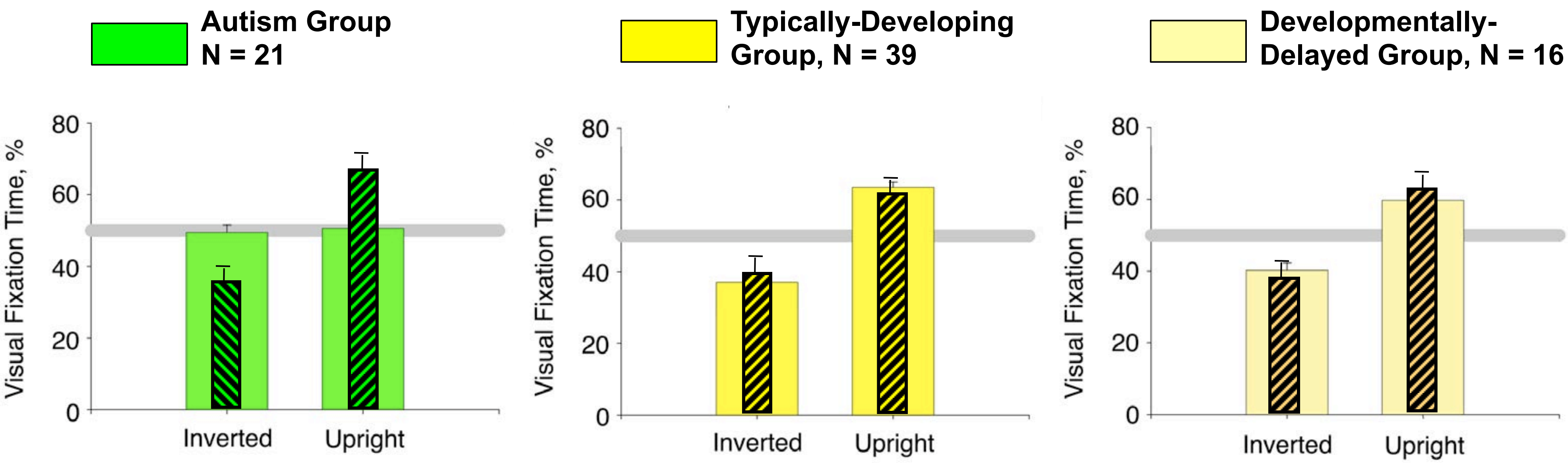
Notably, many of the same behaviours have also been shown as deficits in children with autism: deficits in social interaction, diminished eye contact and reduced looking at others, problems with imitation, deficits in recognizing facial expressions, and difficulties following another's gaze[20]. Autism is a lifelong, highly prevalent, and strongly genetic disorder defined by impairments in social and communicative functioning and by pronounced behavioural rigidities[21]. Although the preponderance of evidence points to prenatal factors instantiated in infancy, knowledge of the first two years of life in

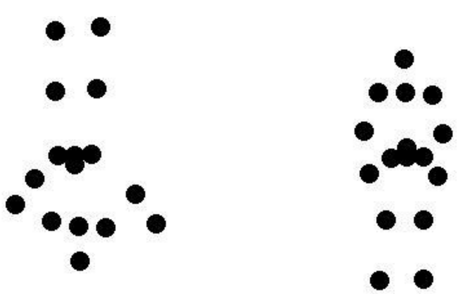
Two-year-olds with autism do not exhibit preferential attention to biological motion



Klin, Lin, Gorrindo, Ramsay, & Jones (2009). ***Nature, 459, 257-261.***

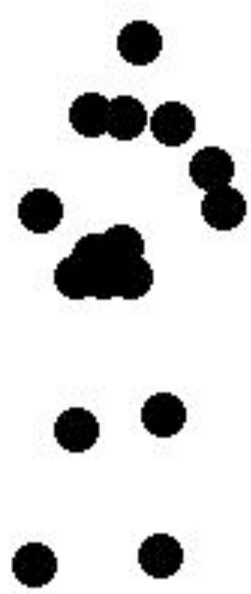
But during 'Pat-a-Cake'...

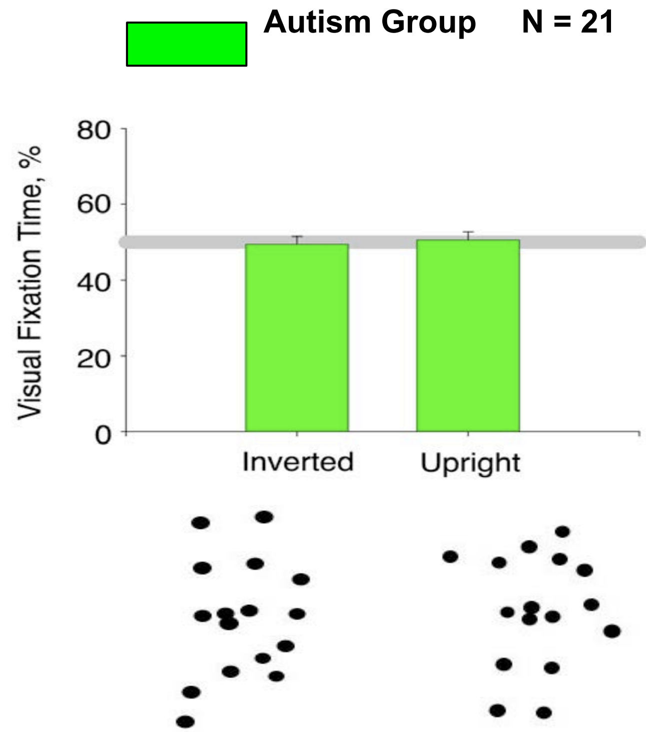




Klin, Lin, Gorrindo, Ramsay, & Jones (2009). *Nature, 459, 257-261.*

Exploring Audiovisual Synchrony

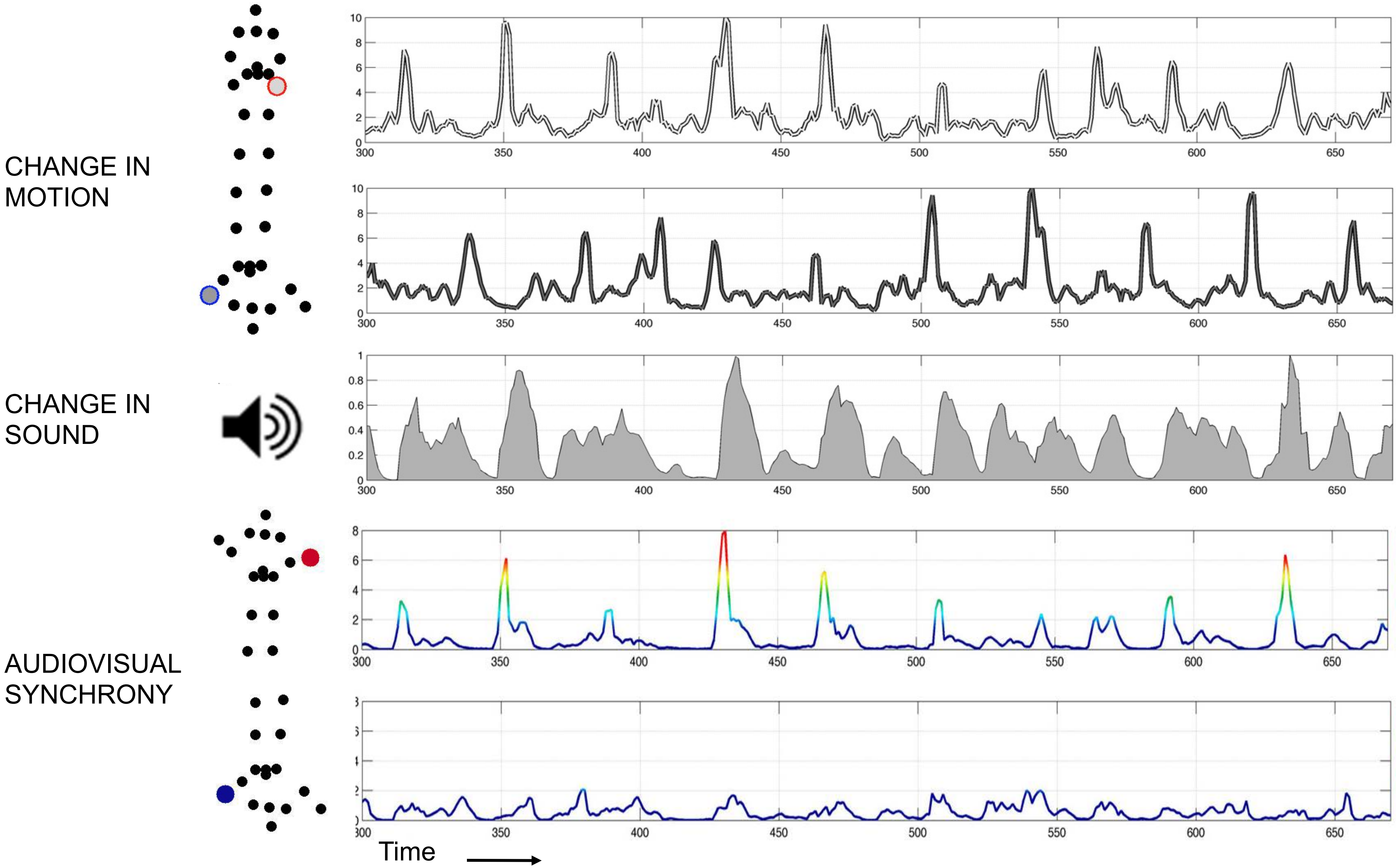


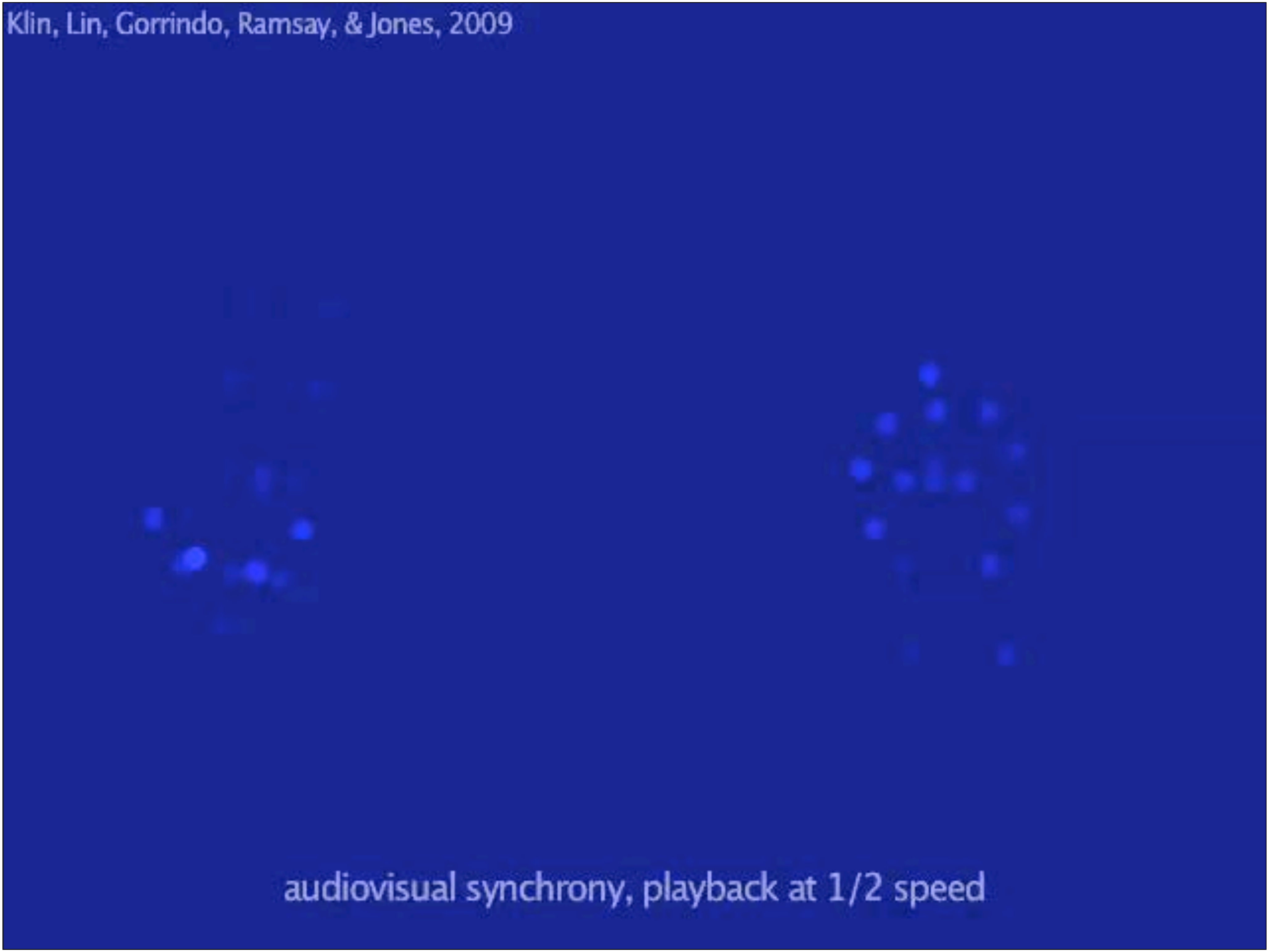


- A “pat-a-cake” finding led to the hypothesis that children’s visual behavior was being guided by physical, not social contingencies.

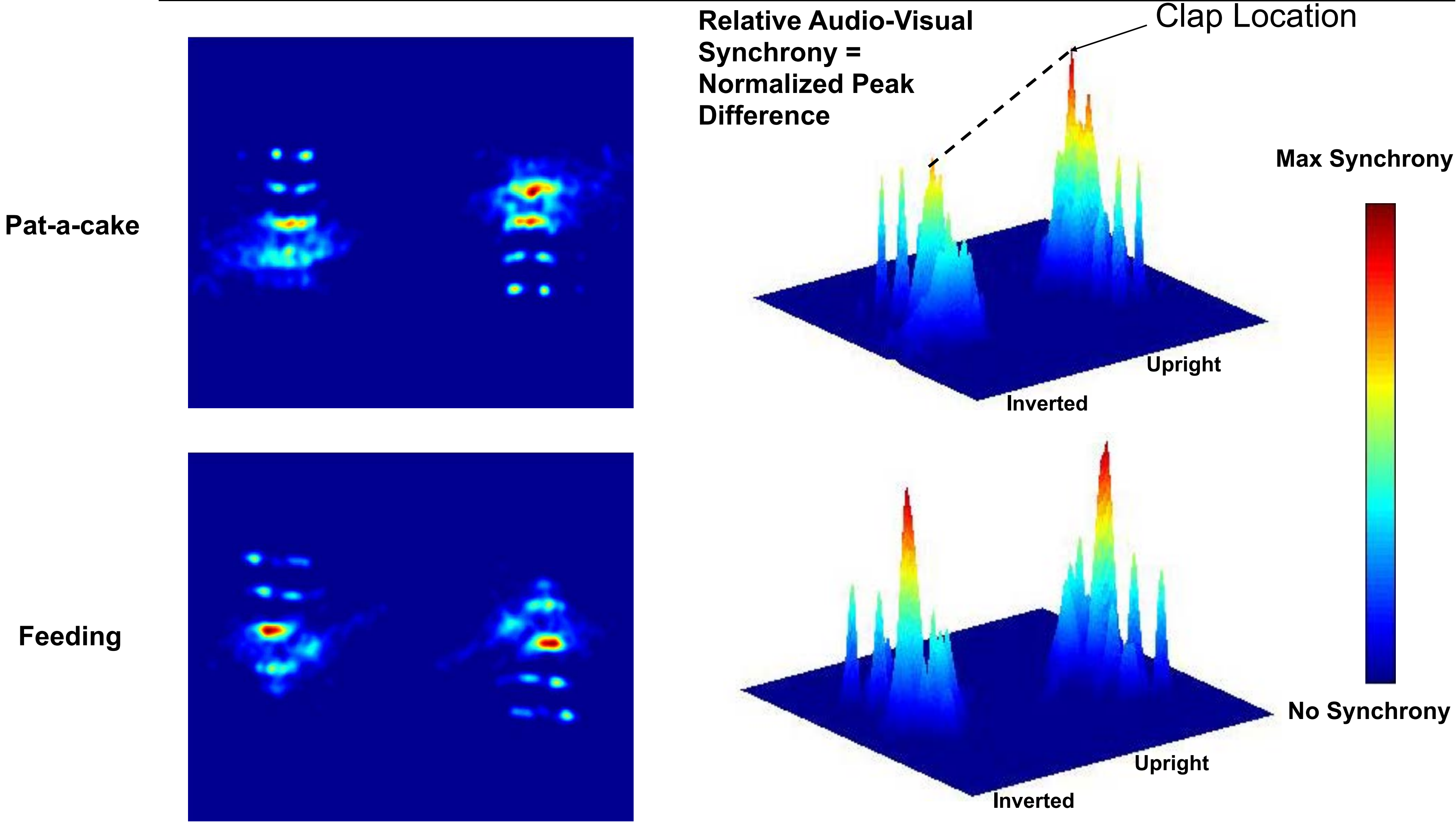
Audiovisual Synchrony Quantification

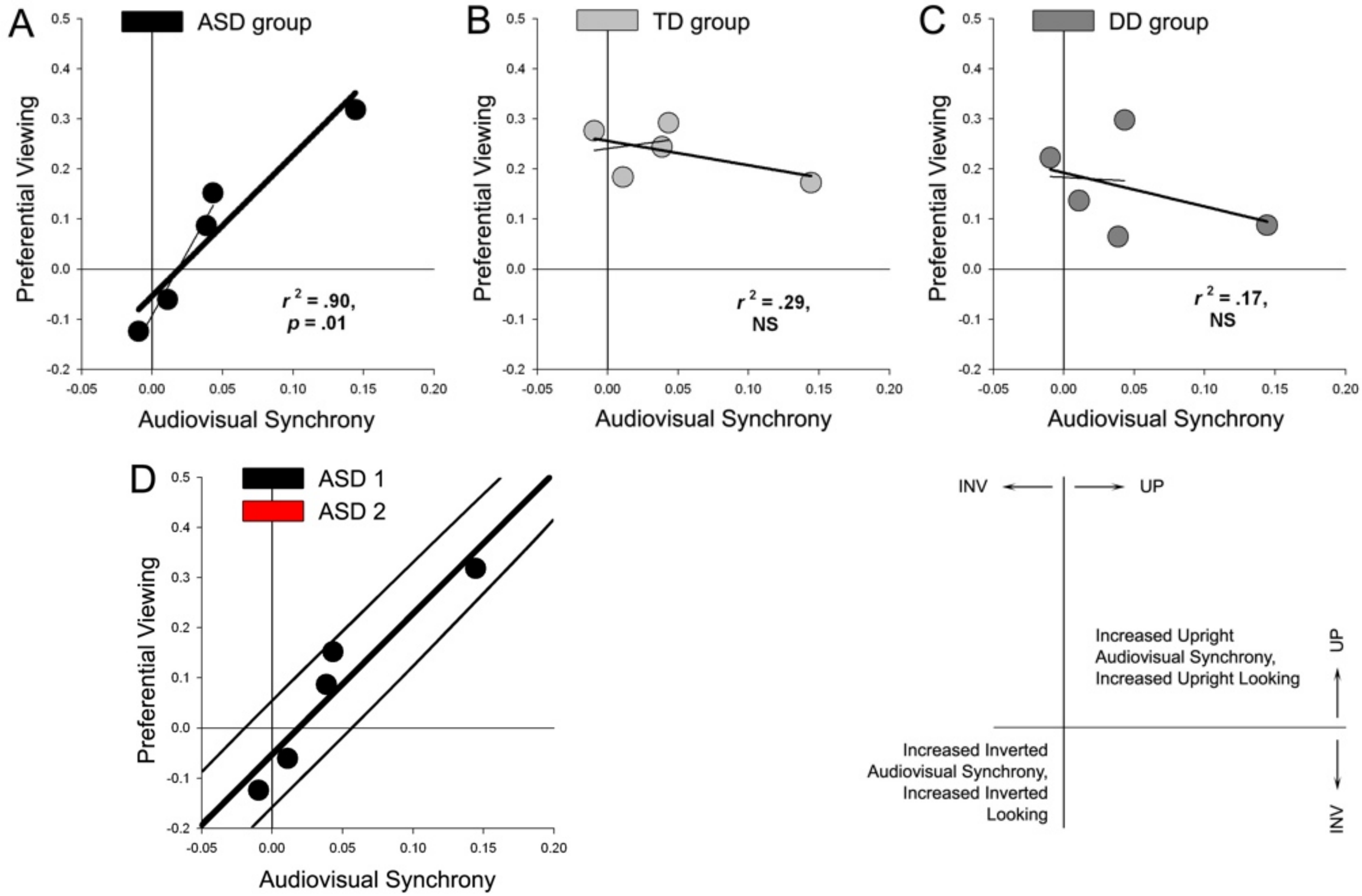
Change in Motion * Change in Sound = Audiovisual Synchrony




Klin, Lin, Gorrindo, Ramsay, & Jones, 2009
audiovisual synchrony, playback at 1/2 speed

Cumulative Audiovisual Synchrony in Point-Light Animations



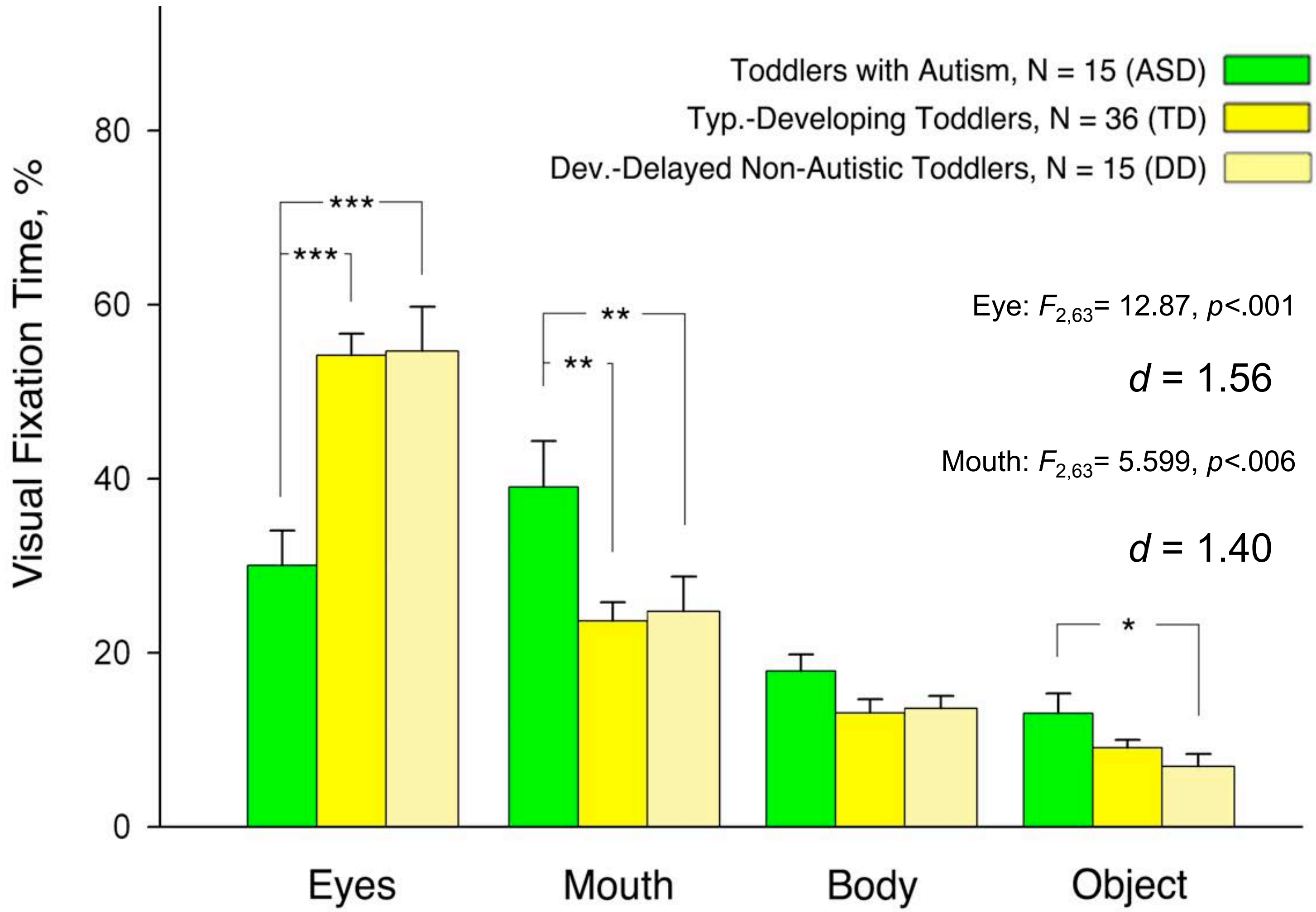


Klin, Lin, Gorrindo, Ramsay, & Jones (2009). *Nature, 459, 257-261.*

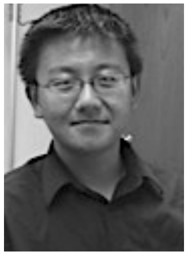
Patterns of visual fixation to approaching caregiver

Jones, Carr, Klin (2008). ***Archives of General Psychiatry*****. 65(8):946-54.**

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

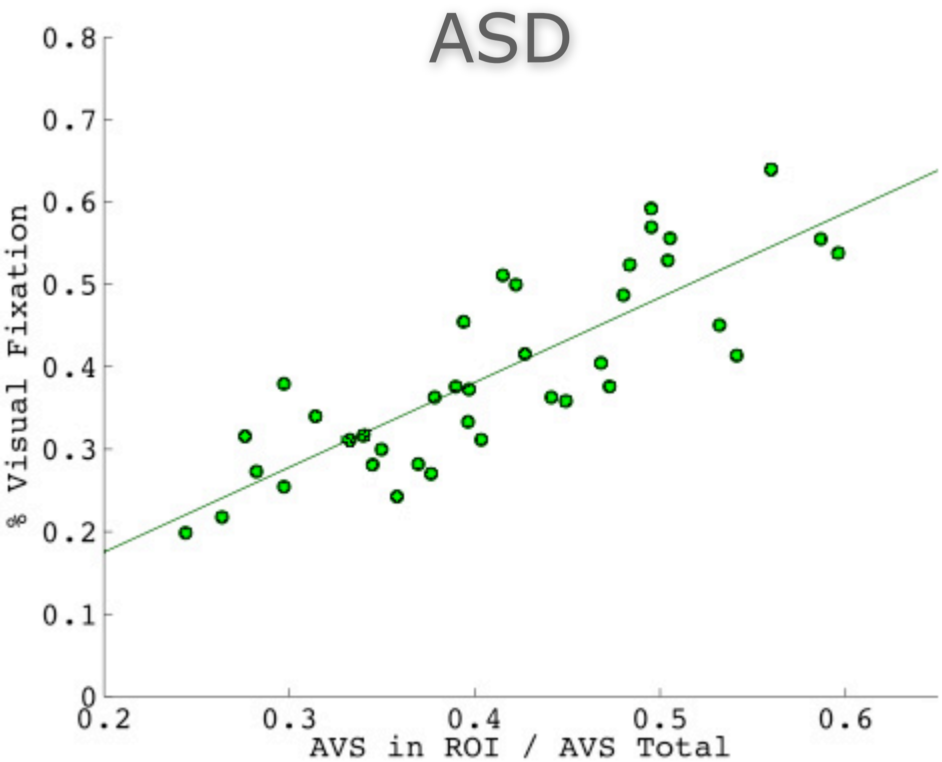


Jones, Carr, Klin (2008). *Arch Gen Psychiatry*. 65(8):946-54.

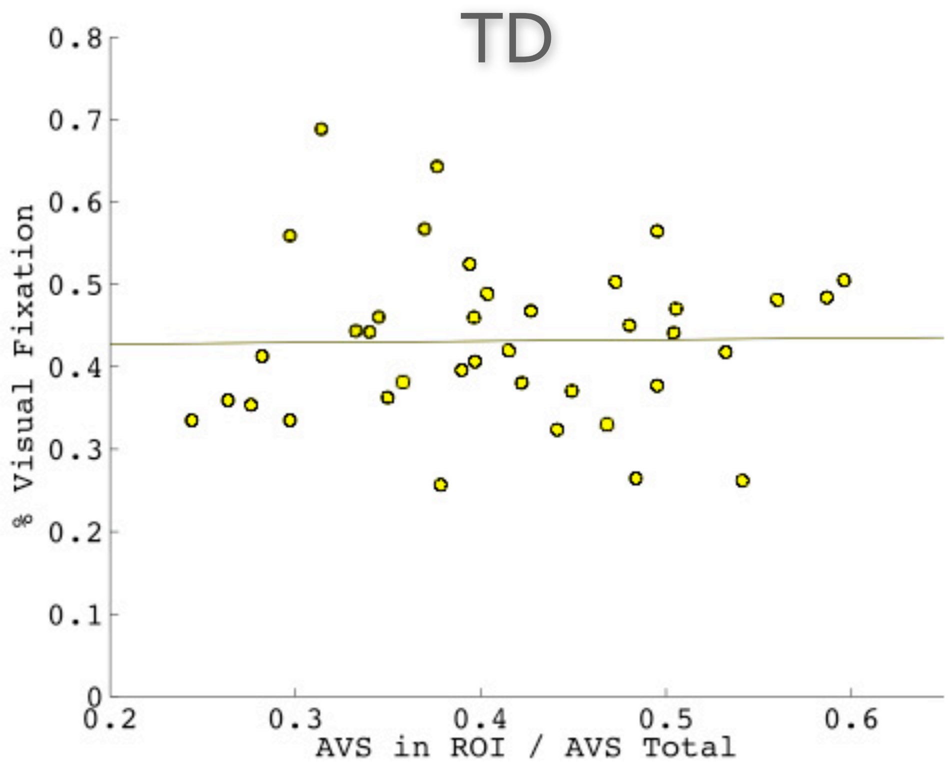


Jennings Xu

Fixation on Mouth and Eyes as a Function of Audiovisual Synchrony

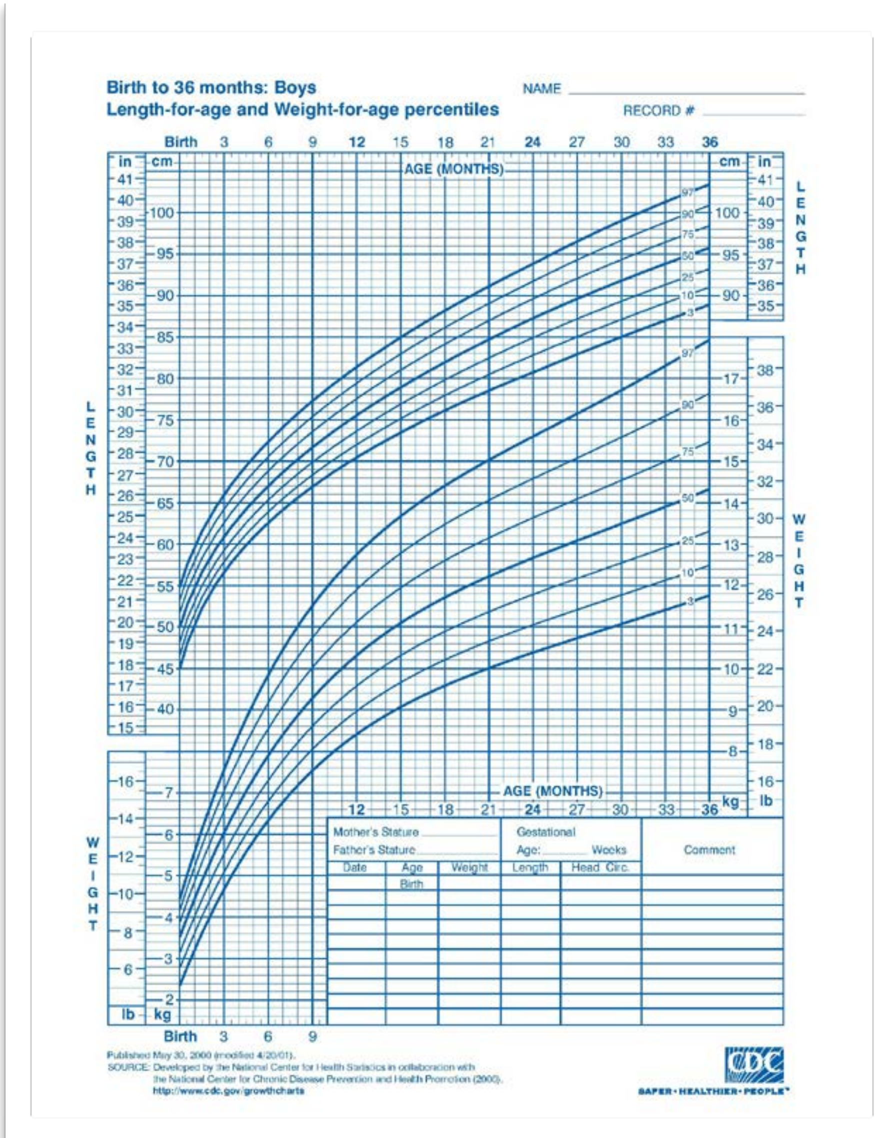


	R^2	p
Eye	0.296	0.016
Mouth	0.302	0.015
Both	0.685	<1.5e-10



	R^2	p
Eye	0.111	0.164
Mouth	0.161	0.089
Both	0.0003	0.919

Growth Charts of Social Engagement



Marcus Autism Center, An NIH Autism Center of Excellence

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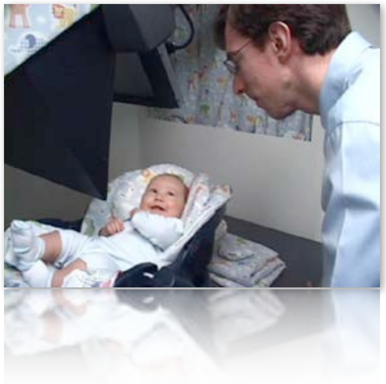
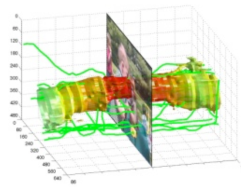
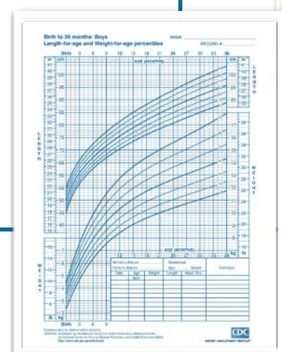
Social Visual Engagement in Infants(0 to 36 months)



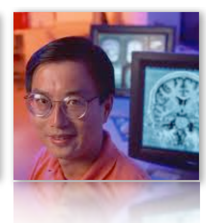




Social Vocal Engagement in Infants (0 to 36 months)

Treatment in Infants & Toddlers (beginning at 12 months)

Social Visual Engagement & Brain Development in a Model System



Georgia Tech

EMORY

YERKES NATIONAL PRIMATE RESEARCH CENTER

[redacted]

nature International weekly journal of science

LETTER

doi:10.1038/nature12715

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]

Deficits in eye contact have been a hallmark of autism[1,2] since the condition's initial description[3]. They are cited widely as a diagnostic feature[4] and figure prominently in clinical instruments[5]; however, the early onset of these deficits has not been known. Here we show in a prospective longitudinal study that infants later diagnosed with autism spectrum disorders (ASDs) exhibit mean decline in eye fixation from 2 to 6 months of age, a pattern not observed in infants who do not develop ASD. These observations mark the earliest known indicators of social disability in infancy, but also falsify a prior hypothesis: in the first months of life, this basic mechanism of social adaptive action—eye looking—is not immediately diminished in infants later diagnosed with ASD; instead, eye looking appears to begin at normative levels prior to decline. The timing of decline highlights a narrow developmental window and reveals the early derailment of processes that would otherwise have a key role in canalizing typical social development. Finally, the observation of this decline in eye fixation—rather than outright absence—offers a promising opportunity for early intervention that could build on the apparent preservation of mechanisms subserving reflexive initial orientation towards the eyes.

Autism Spectrum Disorders (ASDs) affect approximately 1 in every 88 individuals[6]. These disorders are lifelong, believed to be congenital, and are among the most highly heritable of psychiatric conditions[7]. However, the genetic heterogeneity of ASD—with estimates suggesting

Data were collected at 10 time points: at months 2, 3, 4, 5, 6, 9, 12, 15, 18 and 24. We studied 110 infants, enrolled as risk-based cohorts: $n = 59$ at high-risk for ASD (full siblings of a child with ASD[19]) and $n = 51$ at low-risk (without first-, second- or third-degree relatives with ASD). Diagnostic status was ascertained at 36 months. For details on study design, clinical characterization of participants, and experimental procedures, see Methods and Supplementary Information.

Of the high-risk infants, 12 met criteria for ASD[20] (10 males, 2 females), indicating a conversion rate of 20.3%[19]. One child from the low-risk cohort was also diagnosed with ASD. Given the small number of girls in the ASD group, we constrained current analyses to males only, 11 ASD (10 from the high-risk cohort and 1 from the low-risk), and 25 typically developing (all from the low-risk cohort).

At each testing session, infants viewed scenes of naturalistic caregiver interaction (Fig. 1a, b) while their visual scanning was measured with eye-tracking equipment. The 36 typically developing and ASD children viewed 2,384 trials of video scenes.

Control comparisons tested for between-group differences in attention to task and completion of procedures. There were no between-group differences in duration of data collected per child (typically developing = 71.25 (27.66) min, ASD = 64.16 (30.77) min, data given as mean (standard deviation), with $t_{34} = 0.685, P = 0.498$; two-sample t-test with 34 degrees of freedom, equal variances); or in the distribution of ages at which successful data collection occurred ($k = 0.0759$, The New York Times

MIND | NOVEMBER 6, 2013, 1:05 PM | 241 Comments

Baby's Gaze May Signal Autism, a Study Finds

By PAM BELLUCK

Kay Hinton/Emory University

In the eye-tracking lab at Marcus Autism Center, researchers are tracking a baby's eye movements on a video.

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E-MAIL

Updated, 1:11 a.m. | When and how long a baby looks at other people's eyes offers the earliest behavioral sign to date of whether a child is likely to develop autism, scientists are reporting.

In a study published Wednesday, researchers using eye-tracking technology found that children who were found to have autism at age 3 looked less at people's eyes when they were babies than children who did not develop autism. But contrary to what the researchers expected, the

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Los Angeles Times

abc NEWS

Autism signs 'present in first months' of life

By Helen Briggs
BBC News

BBC

CNN

SCIENTIFIC AMERICAN™

Infants


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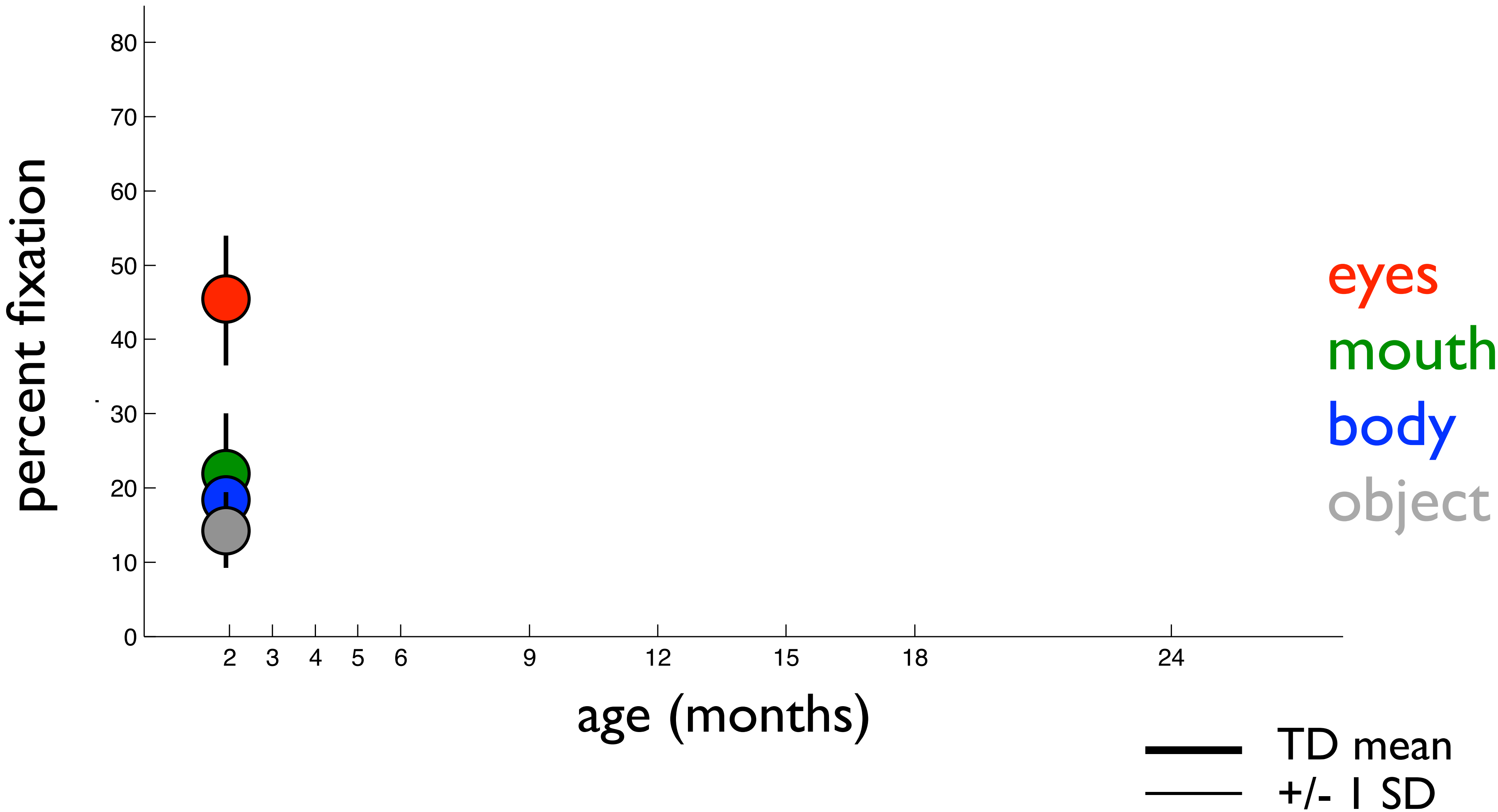
Growth Charts of Social Visual Engagement

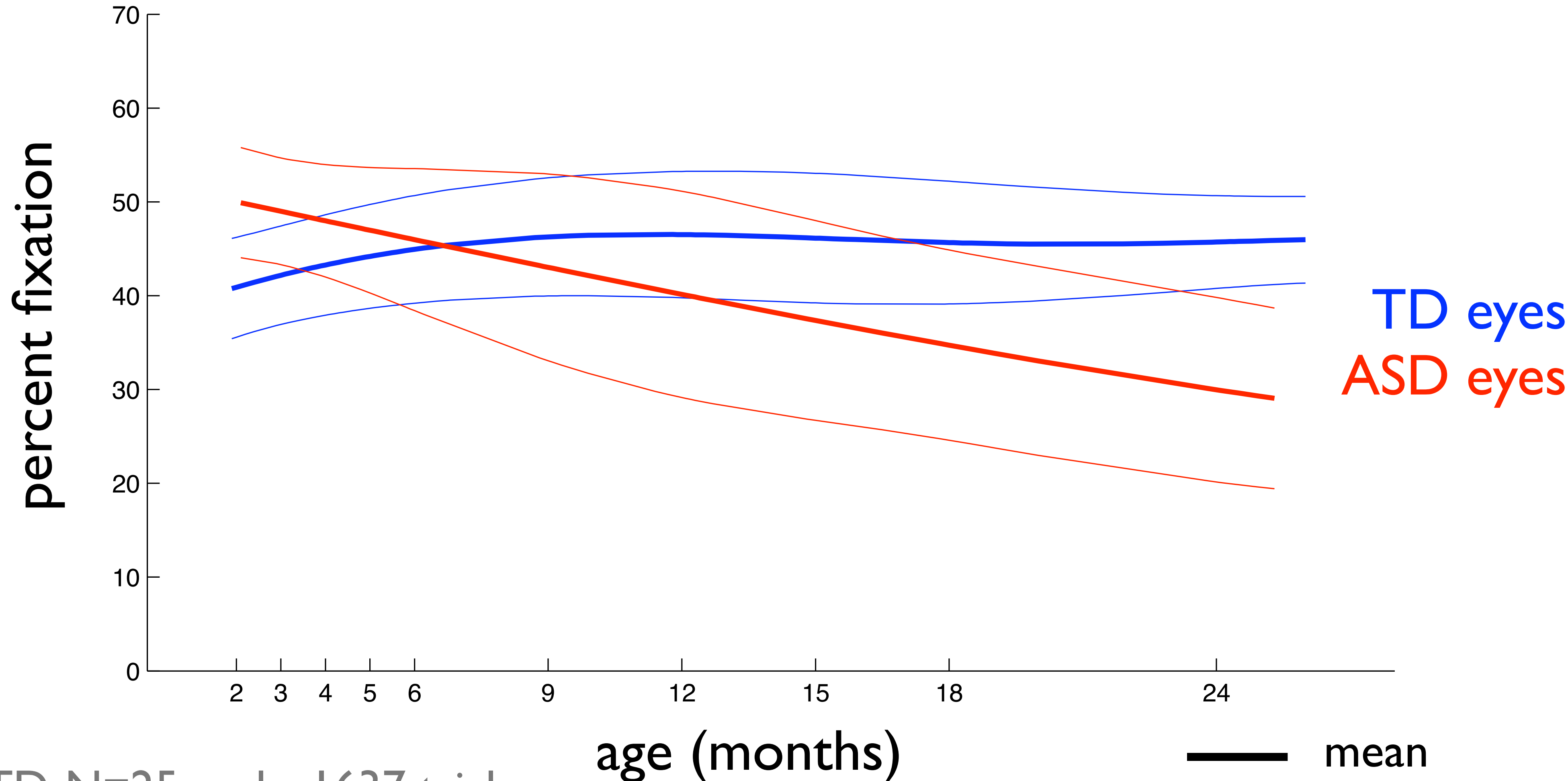
(Typically-Developing Children)



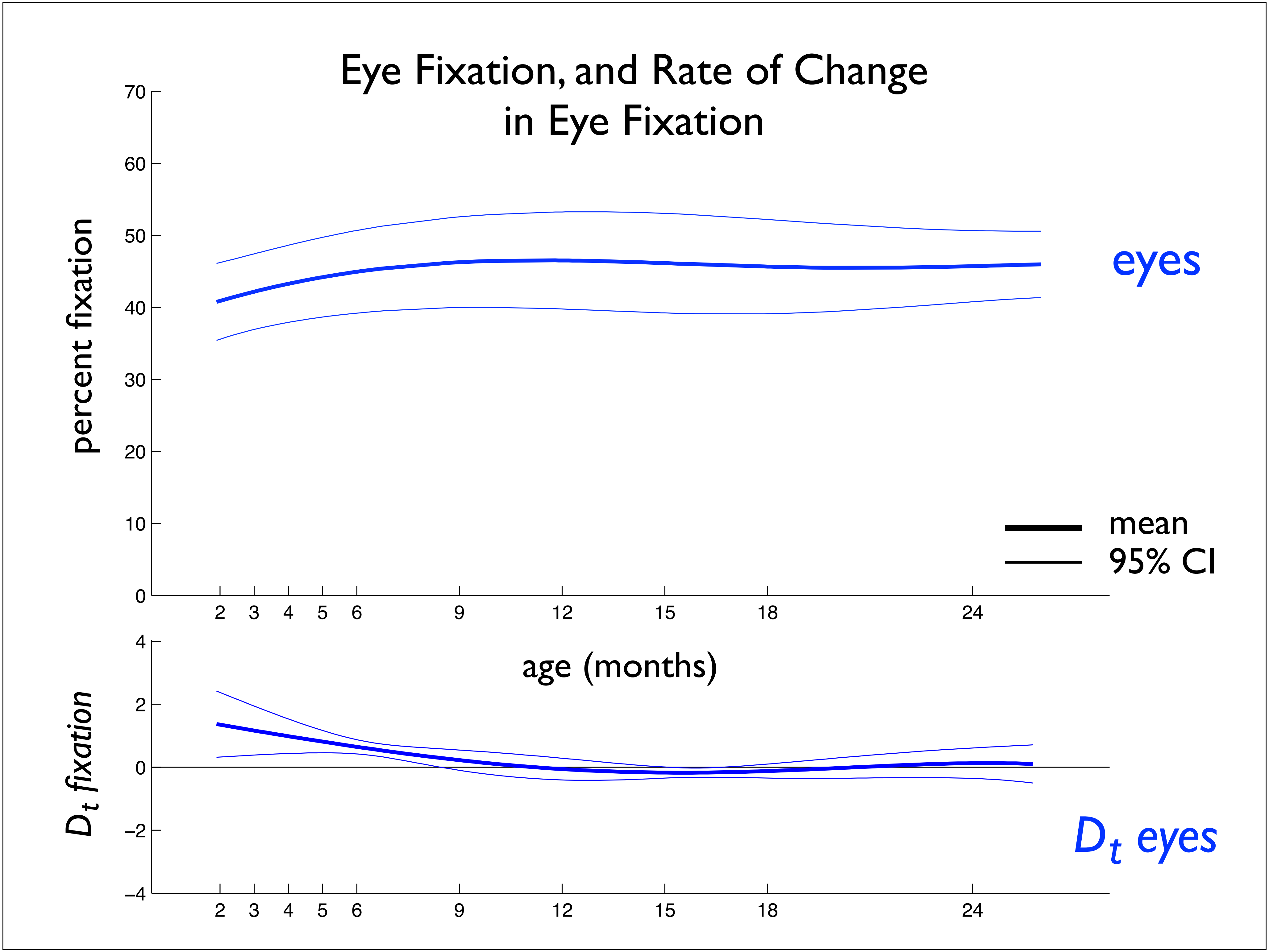
Jones & Klin (2013). *Nature, 504, 427-431.*

Eye Fixation

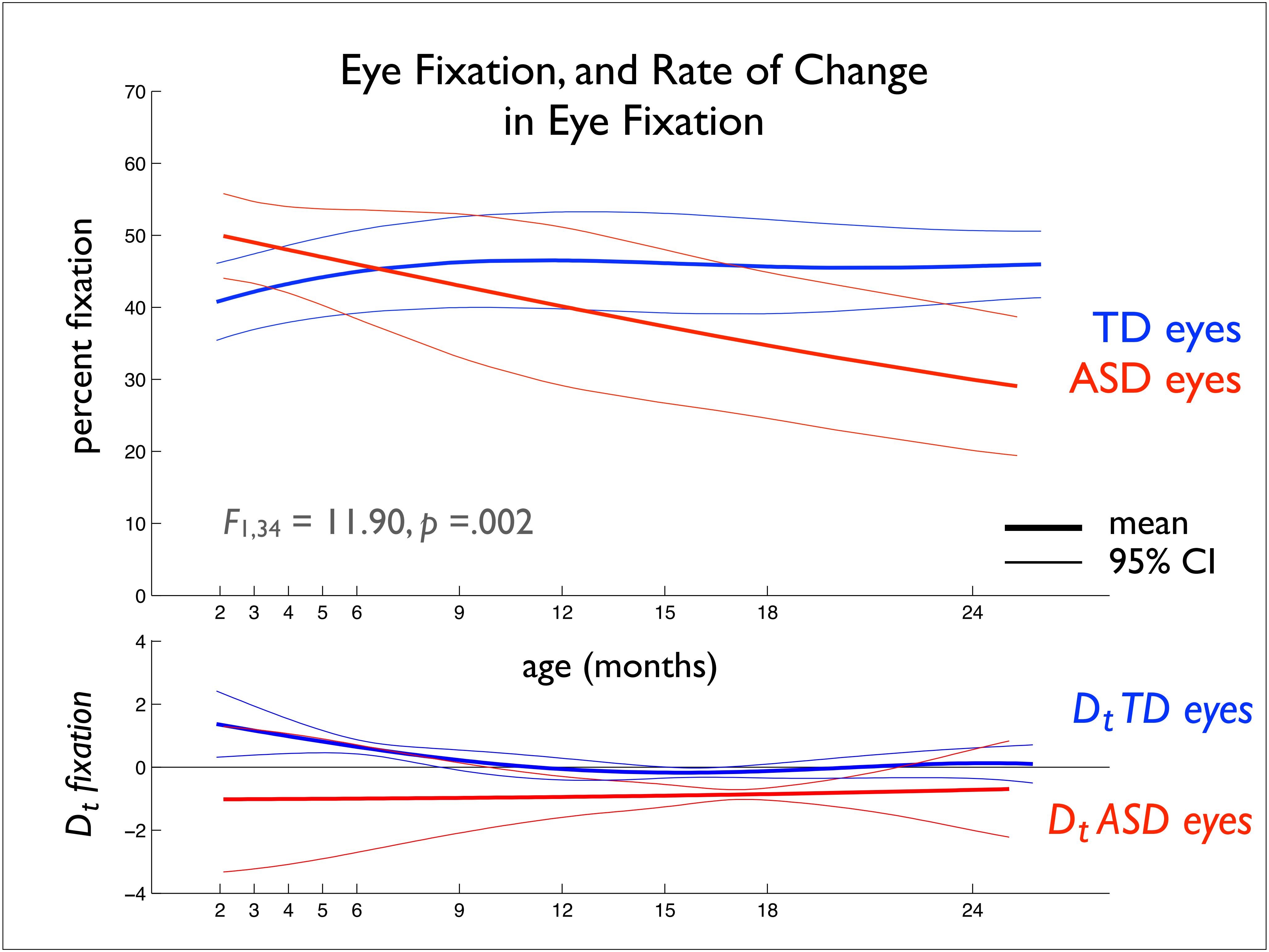
Children with ASD relative to Typically-Developing Norms



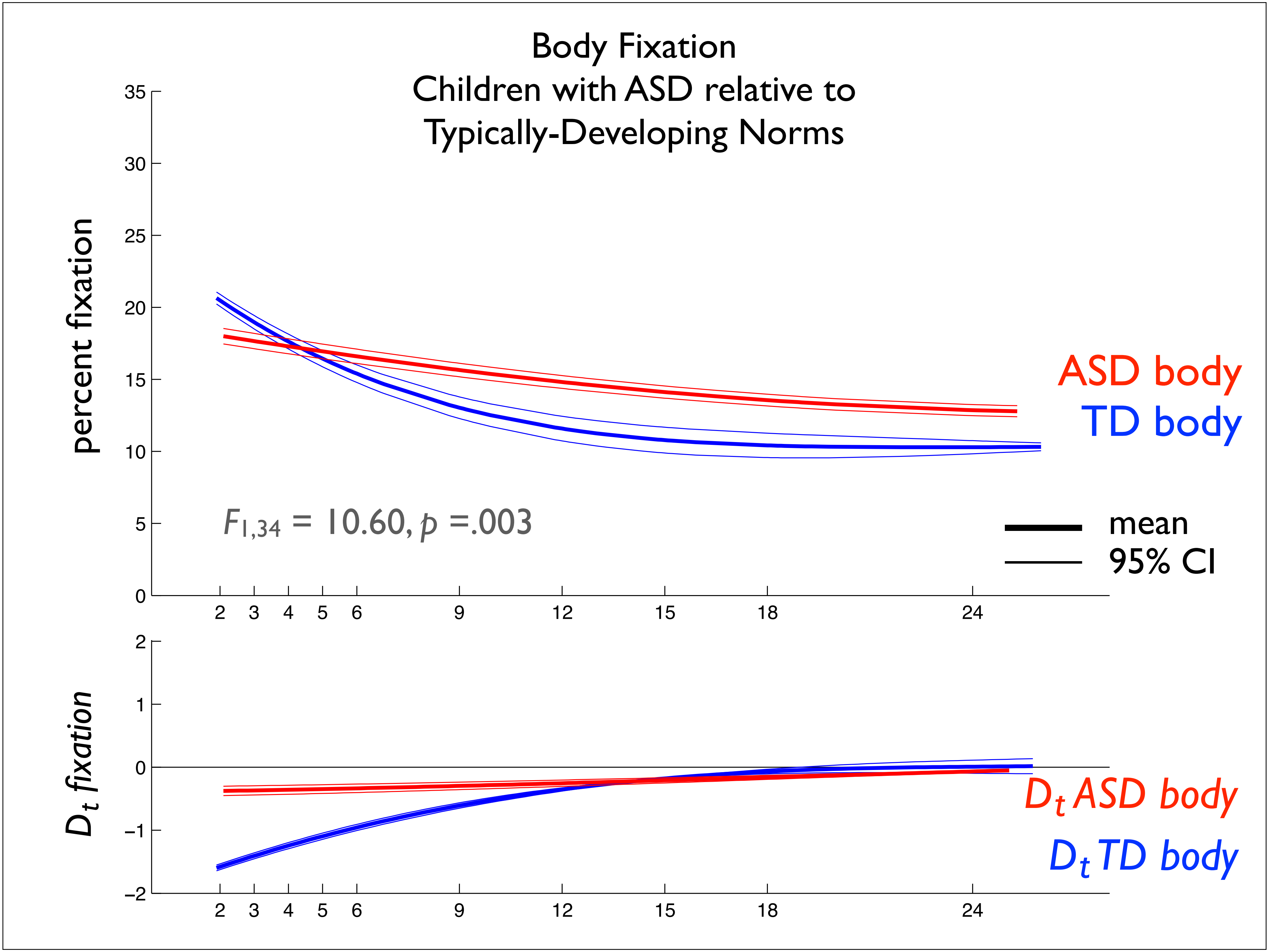
TD, N=25, male, 1637 trials
ASD, N=11, male, 747 trials



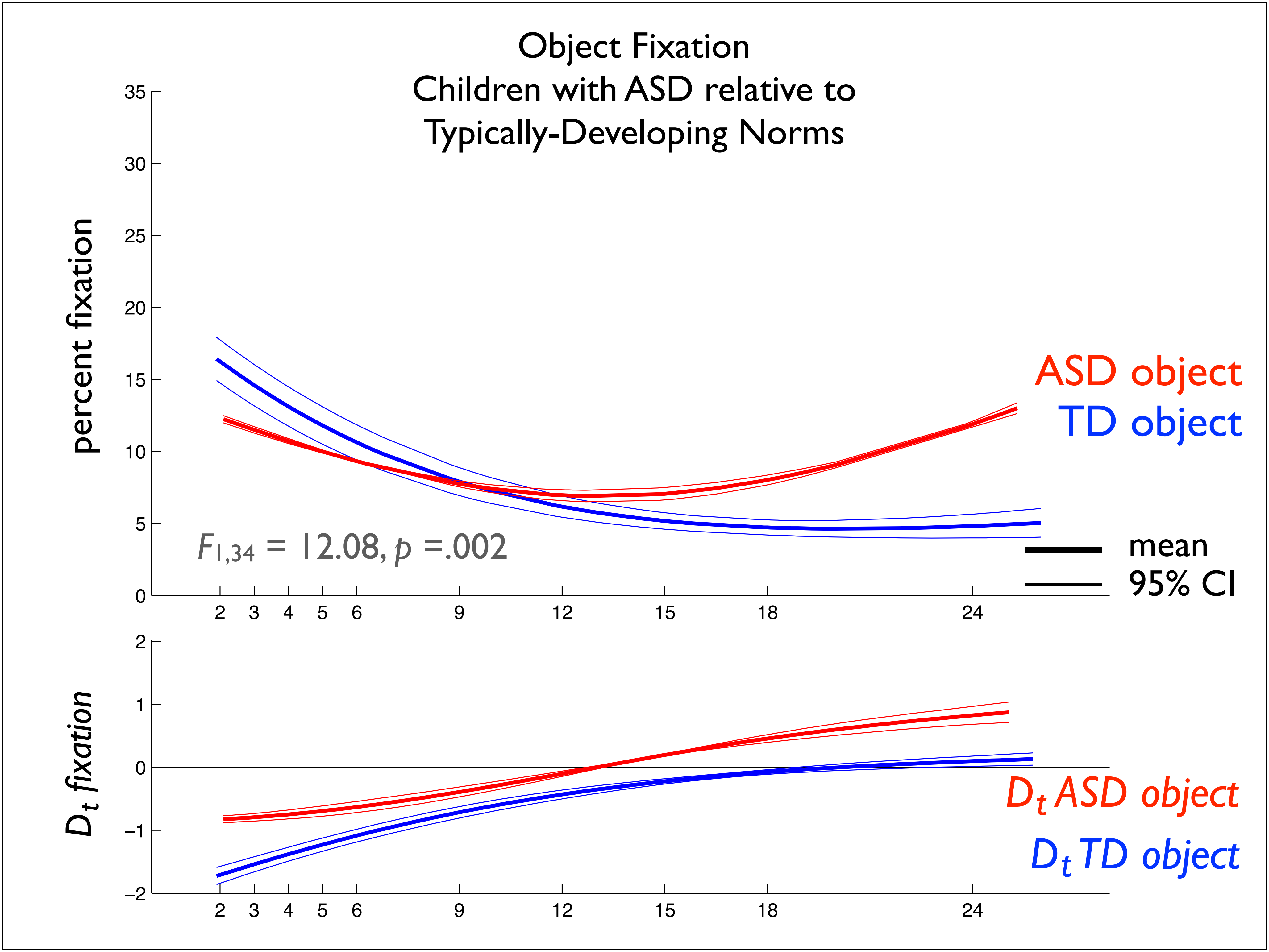
Eye Fixation, and Rate of Change
in Eye Fixation
percent fixation
70
60
50
40
30
20
10
0
2
3
4
5
6
9
12
15
18
24
eyes
mean
95% CI
age (months)
D_t fixation
4
2
0
−2
−4
D_t eyes



Eye Fixation, and Rate of Change
in Eye Fixation
percent fixation
70
60
50
40
30
20
10
0
2
3
4
5
6
9
12
15
18
24
TD eyes
ASD eyes
$F_{1,34}$ = 11.90, p =.002
mean
95% CI
age (months)
D_t fixation
4
2
0
−2
−4
D_t TD eyes
D_t ASD eyes

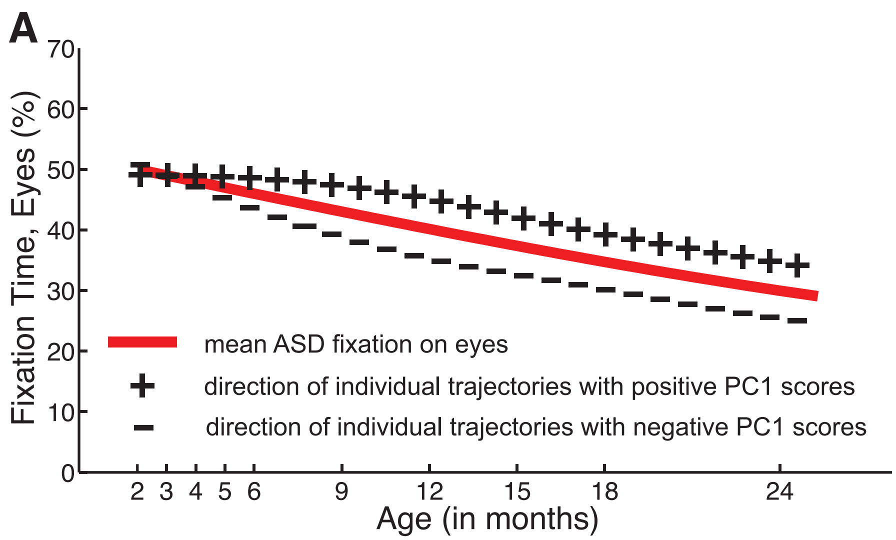


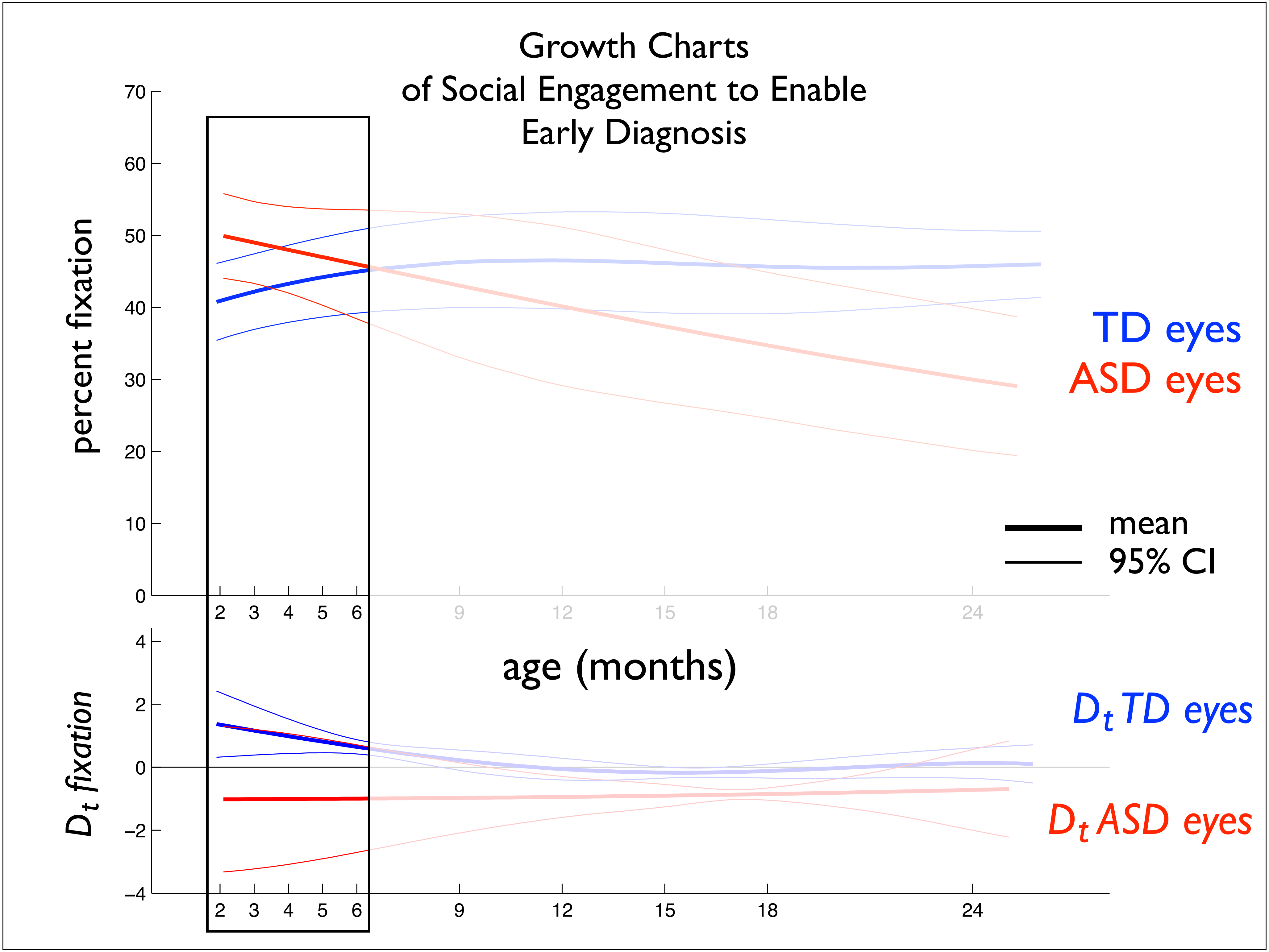
Body Fixation
Children with ASD relative to
Typically-Developing Norms
percent fixation
35
30
25
20
15
10
5
0
2
3
4
5
6
9
12
15
18
24
ASD body
TD body
$F_{1,34}$ = 10.60, p =.003
mean
95% CI
D_t fixation
2
1
0
−1
−2
D_t ASD body
D_t TD body



Object Fixation
Children with ASD relative to
Typically-Developing Norms
percent fixation
35
30
25
20
15
10
5
0
2
3
4
5
6
9
12
15
18
24
ASD object
TD object
$F_{1,34}$ = 12.08, p =.002
mean
95% CI
D_t fixation
2
1
0
−1
−2
D_t ASD object
D_t TD object

Decline in Eye Fixation Predicts Severity of Outcome

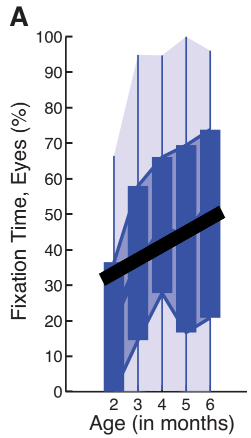




Growth Charts
of Social Engagement to Enable
Early Diagnosis
percent fixation
70
60
50
40
30
20
10
0
2
3
4
5
6
9
12
15
18
24
TD eyes
ASD eyes
mean
95% CI
age (months)
D_t fixation
4
2
0
−2
−4
D_t TD eyes
D_t ASD eyes

Differences Present within the First 6 Months of Life

eyes



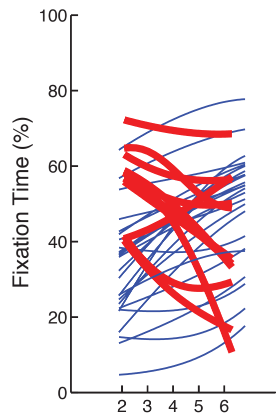
body

Internal Validation

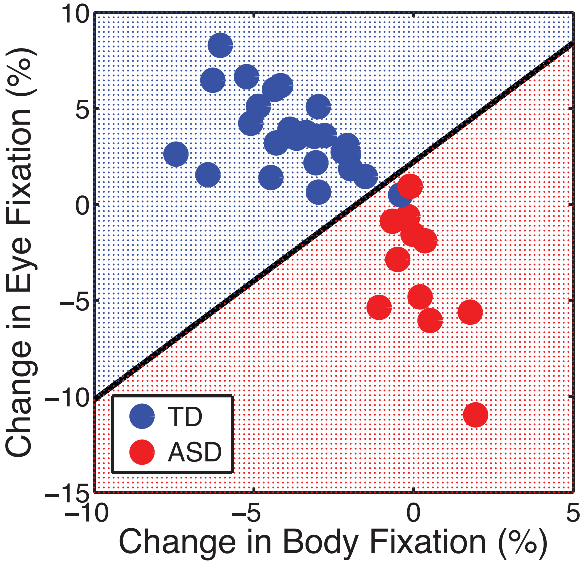
eyes

body

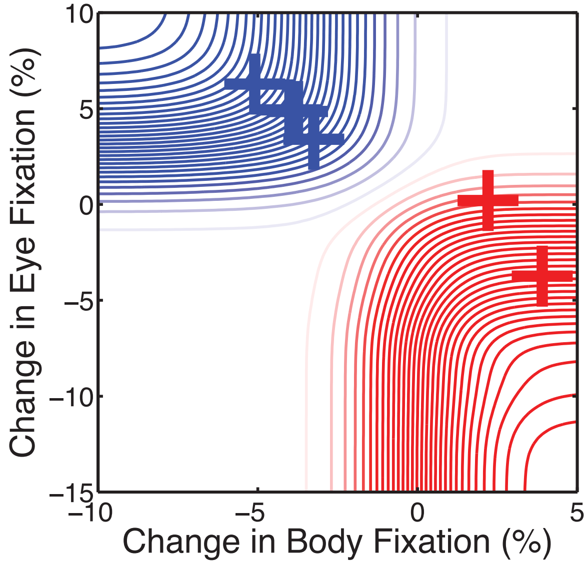
Known Dx LOOCV Known Dx LOOCV



External Validation



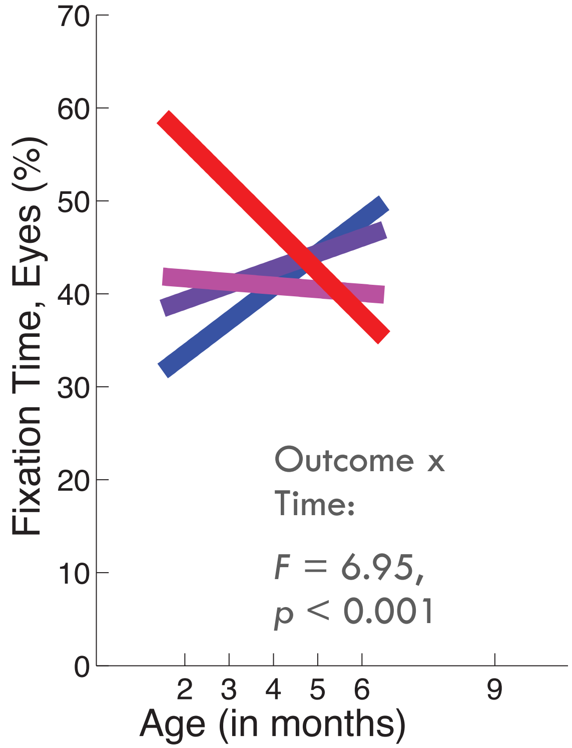
6 Independent
Test Cases

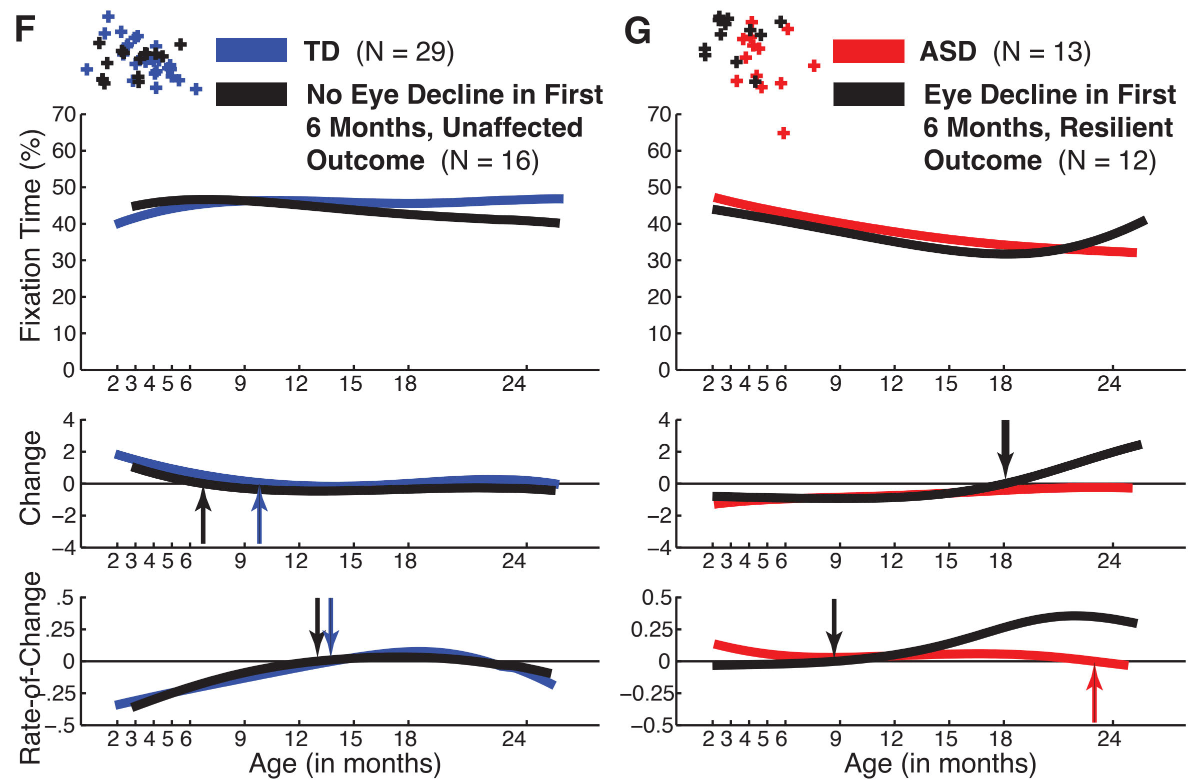


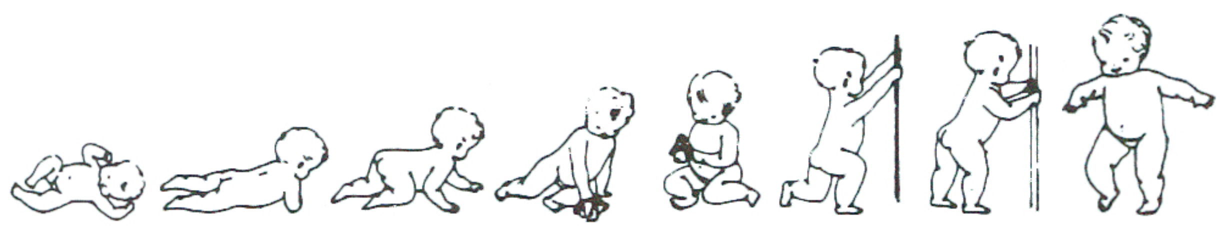
Translational Opportunities

- 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

Developmental Instantiation of a Spectrum of Social Disability: A GLIMPSE INTO SIBLING RESILIENCE (eye fixation)

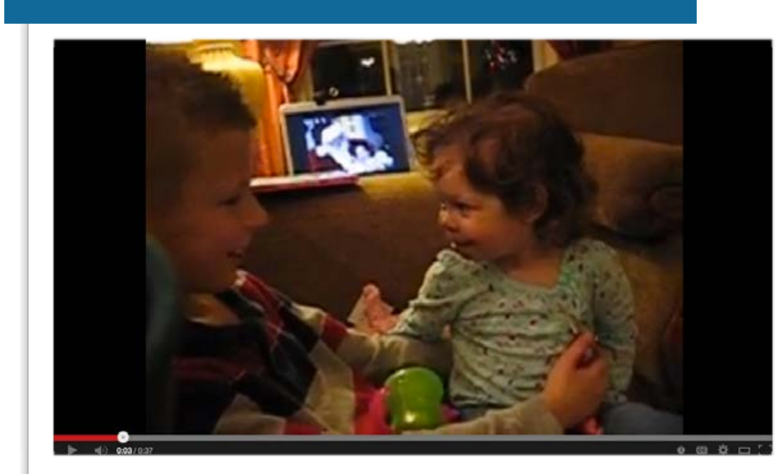






New Scientific Hypotheses

- Genetics: gene expression and methylation studies
- Gene x Environment: alleles more plastic to environmental influences?
- Targeting onset of treatment at these “INFLECTIONABLE” points?
- WILLIAMS SYNDROME

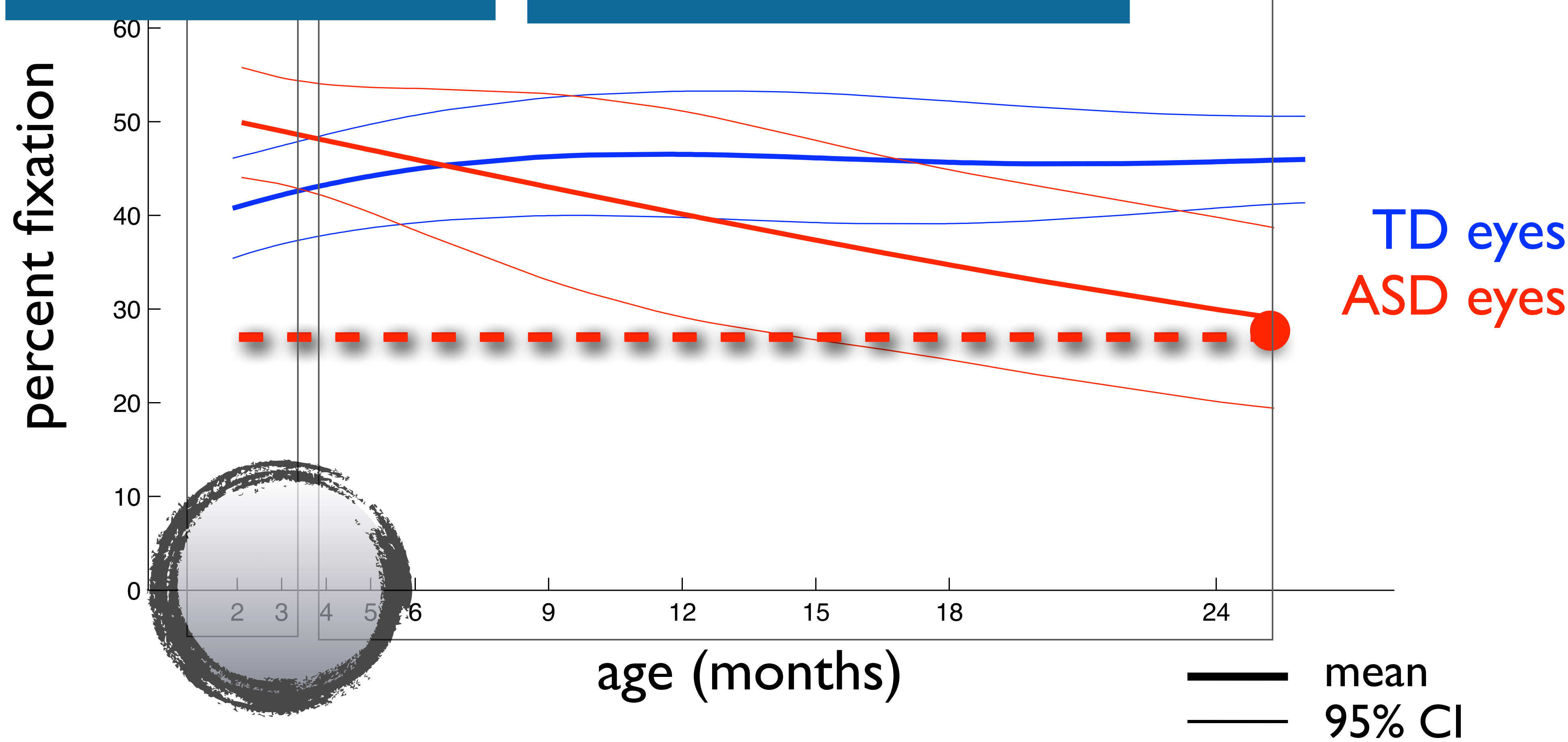


Eye Fixation

Are we wrong? Not one but in fact two curves?

- Reflexive
- Experience Expectant
- Subcortically controlled

- Interactional, Reward-Driven
- Experience Dependent
- Cortically controlled



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A Bioethical Imperative: Access to Early Treatment - Promoting Social Engagement

Reciprocal Social Interaction

The Brain Becomes
Who We Are....

JE LeDoux PhD

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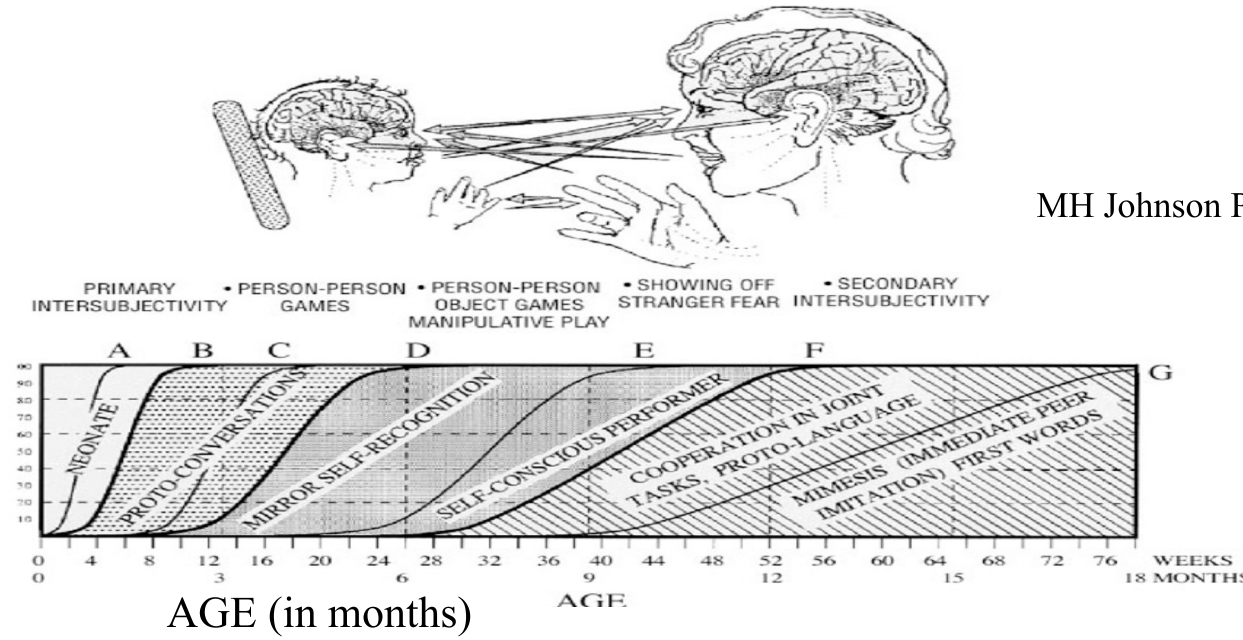
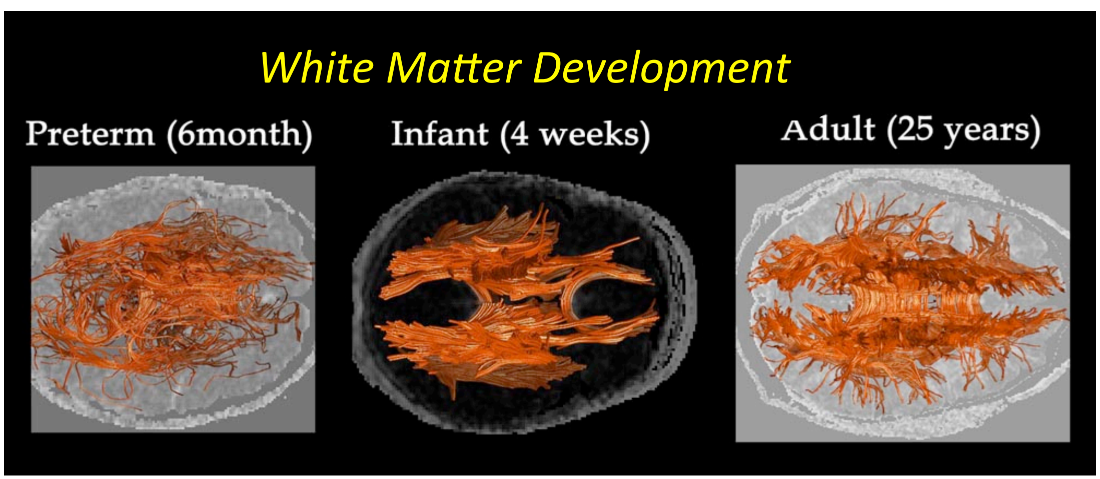
Autism Disrupts the Platform for Brain Development



MH Johnson PhD

birth → 18 months



H-J Park PhD

The Brain Becomes Who We Are....

JE LeDoux PhD

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From reducing age of diagnosis to improving access to early intervention

(National Research Council, 2001)

…so how do we achieve 25 hours per week in which the child is engaged ***actively*** and ***productively*** in meaningful activities?

"Less than 20% of children who will need special services in school in the US are identified before the age of 3 years"

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Augmenting Access to Early Treatment

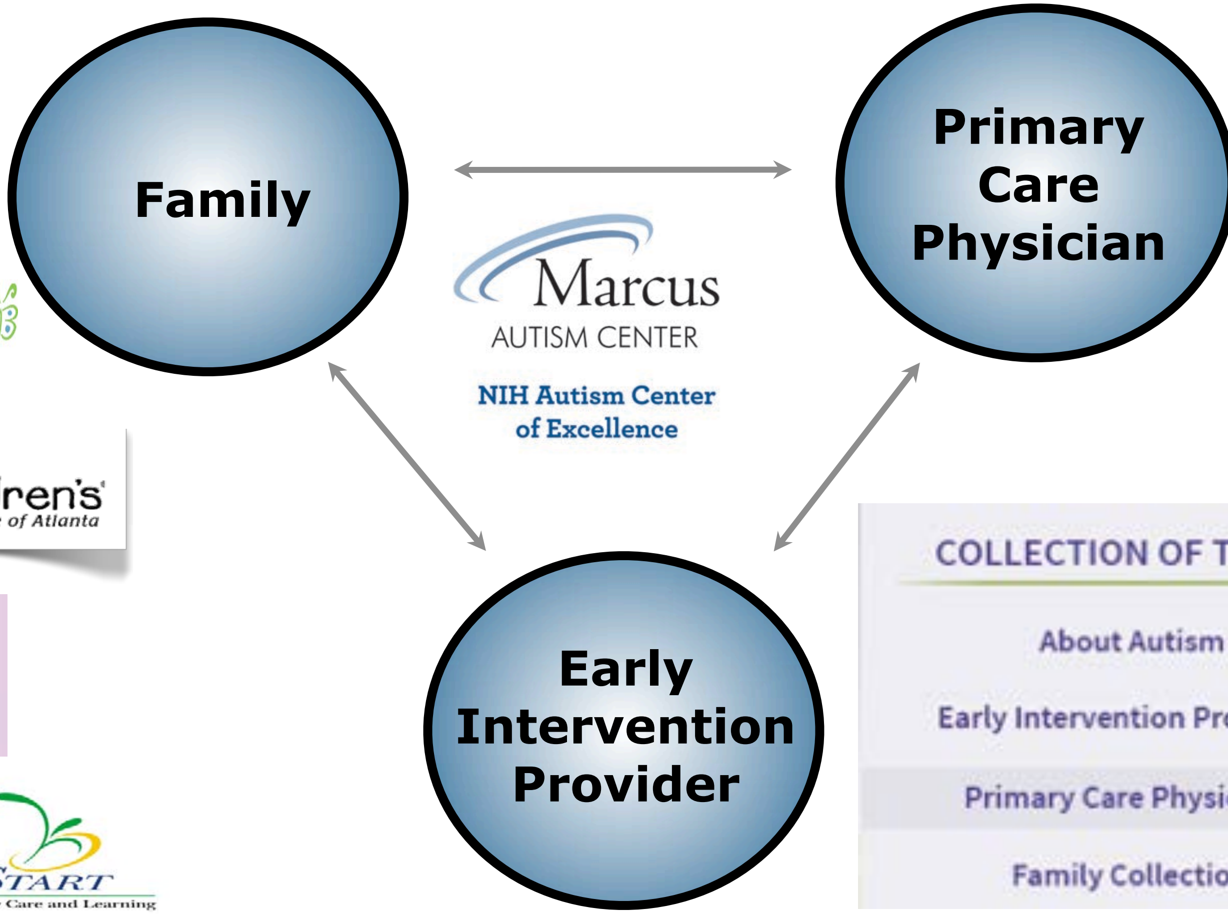
Department of Public Health, State of Georgia

Kids Health First

Children's Healthcare of Atlanta

Early Intervention Because... Babies Can't Wait

Bright from the Start
Georgia Department of Early Care and Learning



Amy Wetherby, PhD

COLLECTION OF TOOLS

About Autism

Early Intervention Providers

Primary Care Physicians >

Family Collection

Jennifer Stapel-Wax, PsyD

Autism Navigator™

Bridging the Gap Between Science and Community Practice


Autism Navigator™
Bridging the Gap Between Science and Community Practice
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Unit 2: Collaborating With Families
Unit 3: Developmental Perspectives
Autism Navigator™ is a unique collection of web-based tools that uses extensive video footage to bridge the gap between science and community practice.
About Autism is a tool for families, professionals, or anyone interested in learning about autism spectrum disorder (ASD). It is available free of charge. Just register and login.
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OUR PARTNERS
Our partners are helping us make an impact on community practice.
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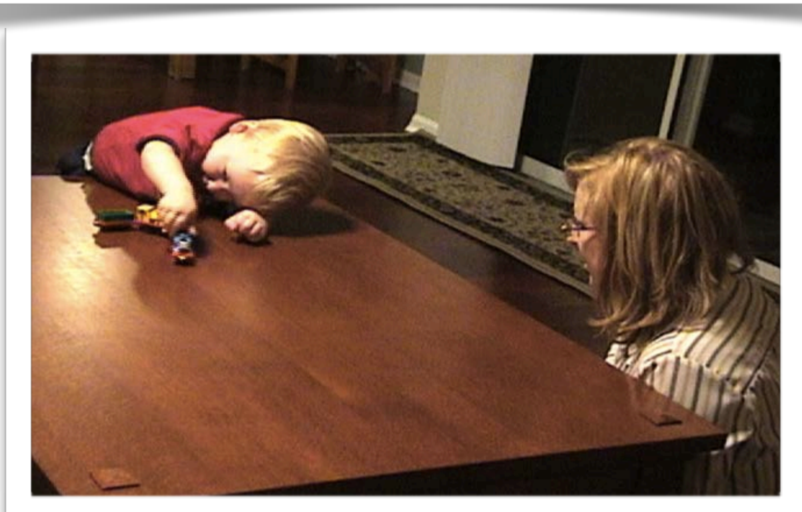
Treating deviations from normative social engagement: Parent-Delivered **Early Social Interaction**



Parent-Delivered ESI

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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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

Autism NAVIGATOR™

Everyday Activities

Play with Toys Blocks, Puzzles, Sand box, Playdough, Cars and Trucks, Ball Games, Baby Dolls	**Play with People** Social Games like Peek-a-boo, Rough and Tumble, Songs & Rhymes
Meals and Snacks Preparation, Eating, Cleanup	**Caregiving** Dressing, Diaper Change, Bath, Washing Hands, Brushing Teeth
Book Sharing	**Family Chores** Mailbox, Laundry, Care for Pets, Plants

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Goals for Early Treatment:

Every waking hour in the home and in the community

Child Behaviors	Parent Behaviors
ACTIVE ENGAGEMENT	**TRANSACTIONAL SUPPORTS**
1. Emotional Regulation	1. Participation & Role
2. Productivity	2. Make Activity Predictable
3. Social Connectedness	3. Follow Child's Attention
4. Gaze to Face	4. Promote Initiations
5. Response to Verbal Bids	5. Balance of Turns
6. Directed Communication	6. Support Comprehension
7. Flexibility	7. Modeling
8. Generative Ideas	8. Expectations & Demands

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Teaching Strategies & Supports to Promote Active Engagement

Supports for better skills

- Model and expand language and play skills
- Extend activity, child's roles, & transitions
- Balance demands and supports

Supports for social reciprocity

- Natural reinforcers
- Waiting for initiation and balance of turns
- Clear message to ensure comprehension

Supports for a common agenda

- Positioning
- Follow child's attentional focus
- Motivating activity with clear roles & turns

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Our ultimate goal

To make autism
an issue of diversity,
not of disability