

# Social Visual Engagement In Children with ASD

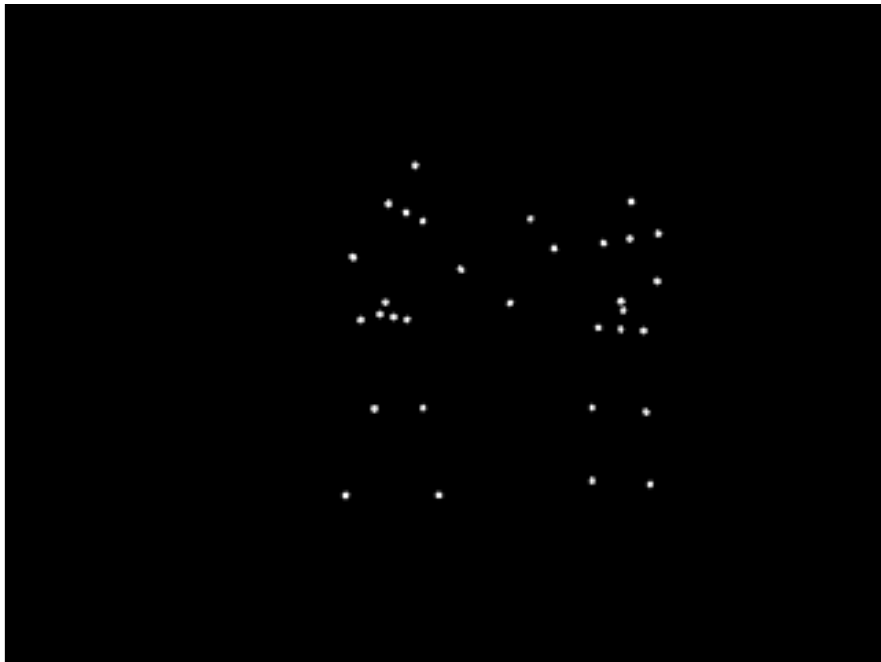
Warren Jones, PhD  
Director of Research, Marcus Autism Center

Children's Healthcare of Atlanta  
Department of Pediatrics  
Emory University School of Medicine

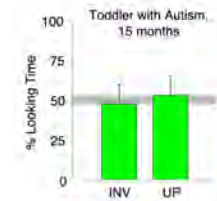


Klin et al. (2004). *American Journal of Psychiatry*, 161(11), 1981-1988.

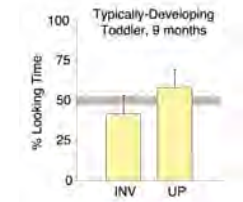
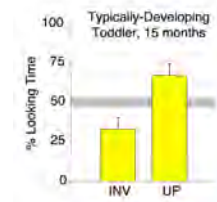




## Attention to Biological Motion



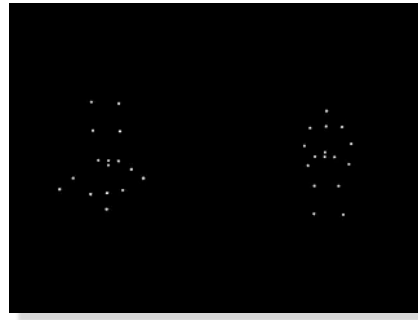
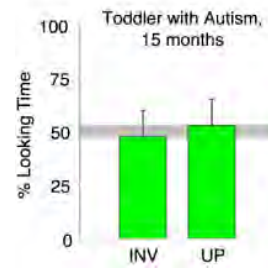
not significantly different from chance,  $p > .05$



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

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## Attention to Biological Motion



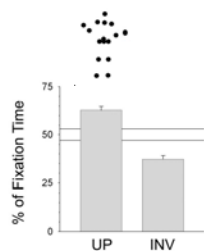
Klin A & Jones W. (2008). *Dev Science*, 1: 40-46.

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

Ami Klin<sup>1</sup>, David J. Lin<sup>1†</sup>, Phillip Gorrindo<sup>1†</sup>, Gordon Ramsay<sup>1,2</sup> & Warren Jones<sup>1,3</sup>



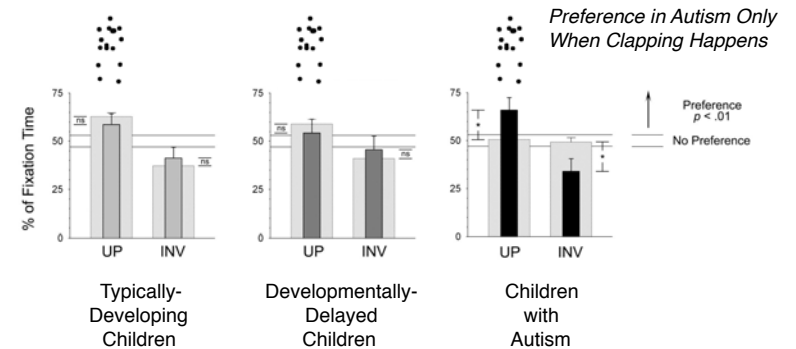
Typically-Developing Children

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

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

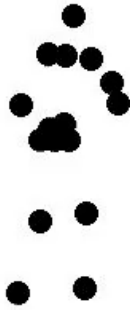
Ami Klin<sup>1</sup>, David J. Lin<sup>1†</sup>, Phillip Gorrindo<sup>1†</sup>, Gordon Ramsay<sup>1,2</sup> & Warren Jones<sup>1,3</sup>



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

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# Physical, rather than social, cues guide looking in toddlers with autism



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

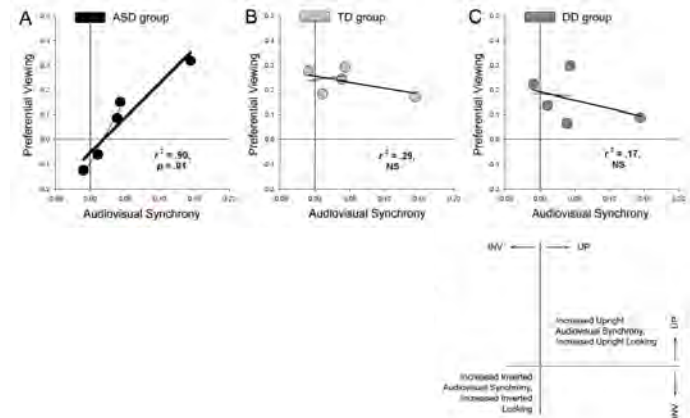
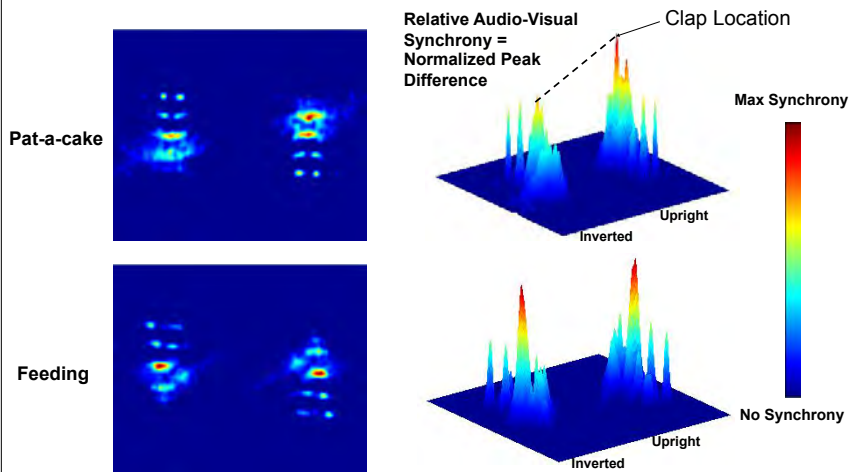
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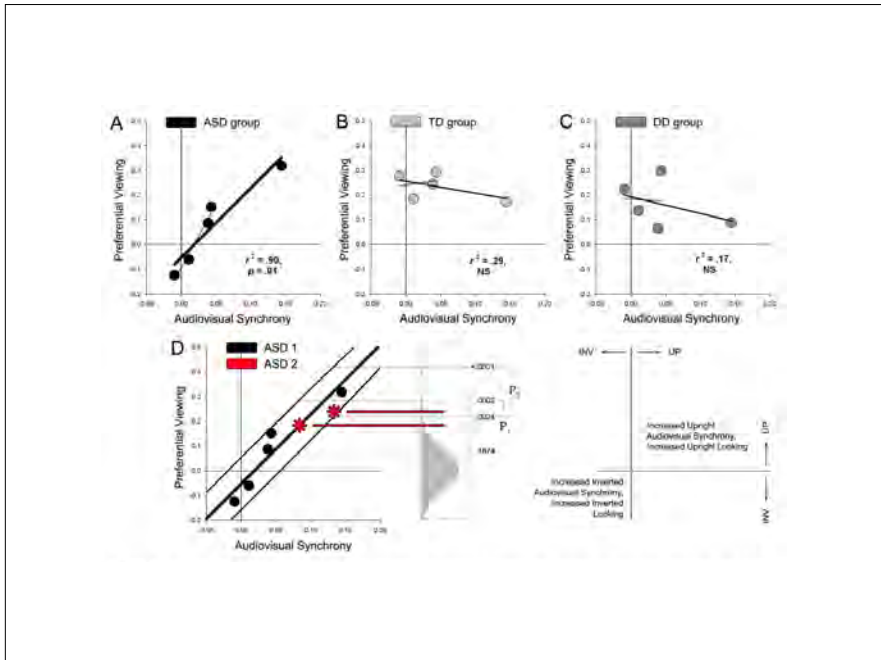
Klin, Lin, Gorrindo, & Jones, 2008



audiovisual synchrony, playback at 1/2 speed


## Cumulative Audiovisual Synchrony






## Watching a Face... But Seeing Physical Contingencies?


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Caregiver



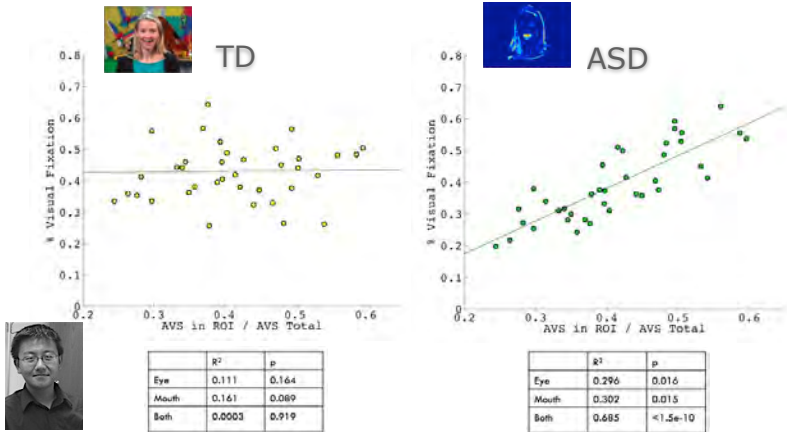
Audiovisual Synchrony



Jennings Xu

Marcus Autism Center

## Looking at Eyes and Mouth As a Function of Audiovisual Synchrony



Jennings Xu

Marcus Autism Center

## Manipulating Physical Contingencies to Assess their Affects on Social Visual Engagement

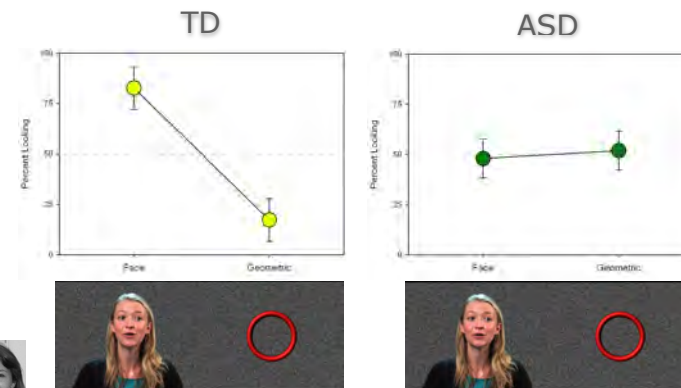


Gordon Ramsay, PhD

- Controlled experimental manipulations of audiovisual synchrony (AVS)
- Examining the role of AVS in perception of physical and social stimuli.
- Determining the sensitivity of ASD and TD infants to physical contingencies in the presence of social contingencies.

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## Effects of Physical Contingencies on Preferential Attention to Faces



Jessie Northrup



David Lin

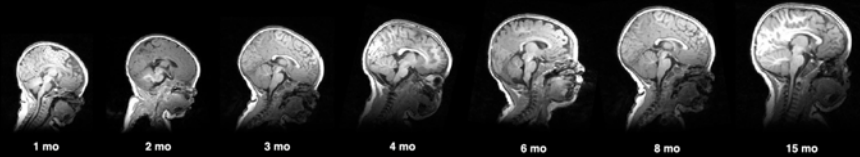
N=30 ASD, N=20 TD; mean(SD) age = 21.3(4.2) months.

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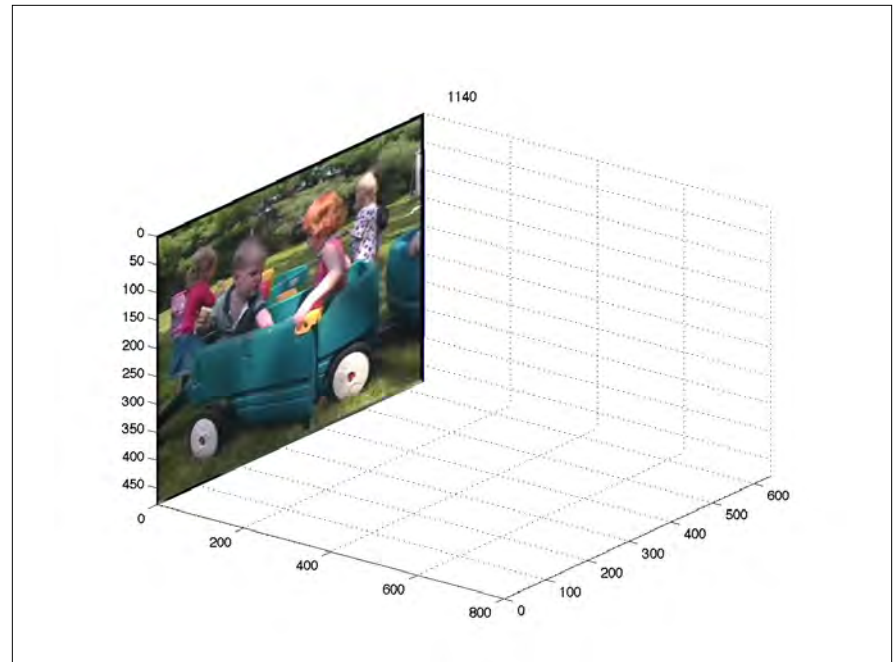


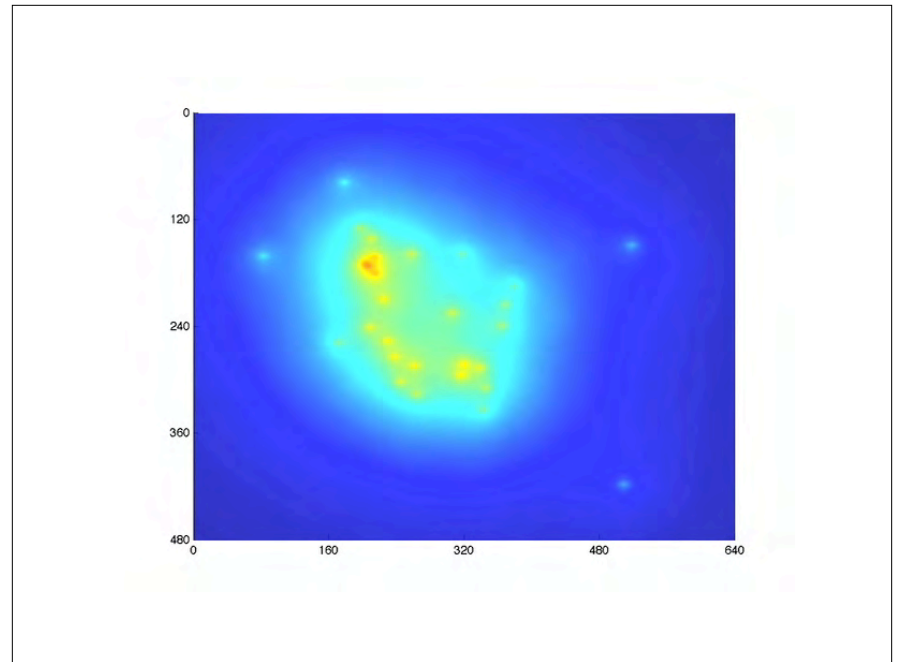
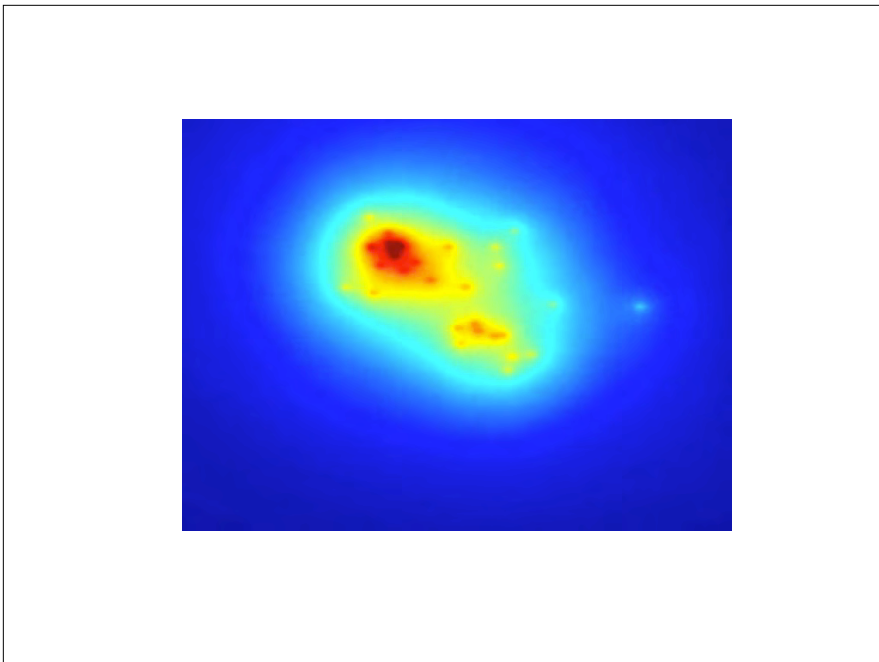
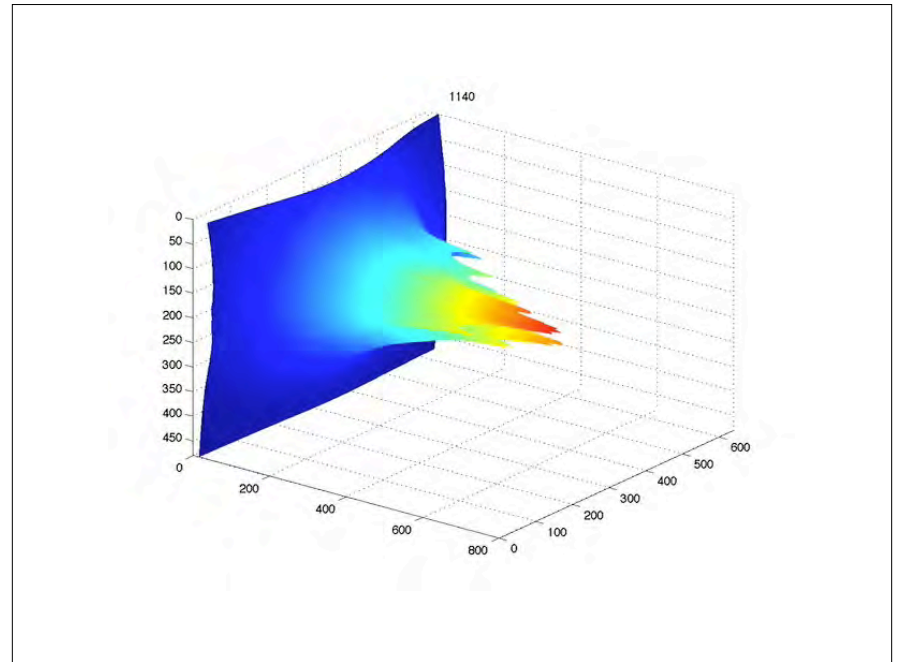
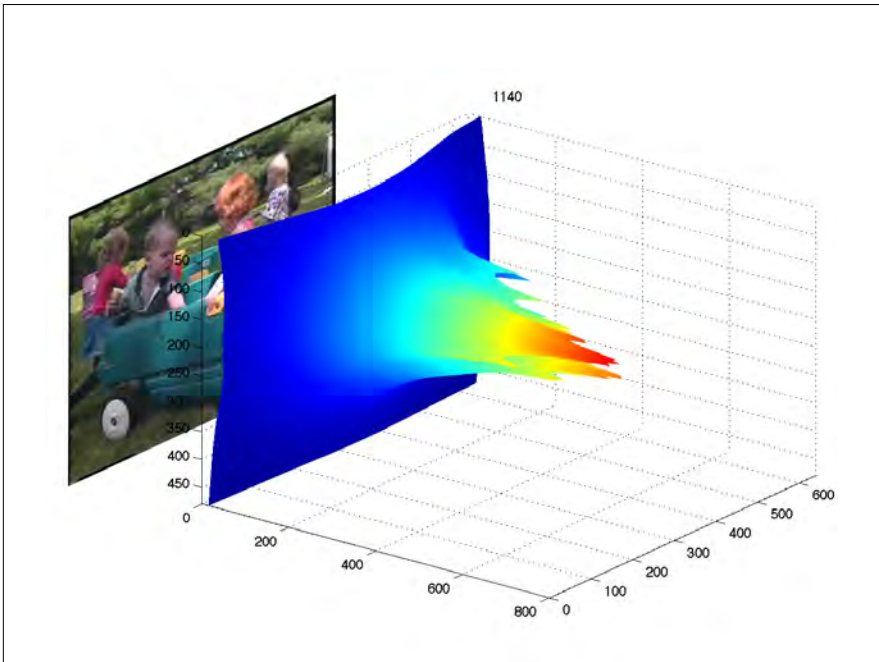
## Social Interaction is the Platform for Brain Development



*Brain size doubles in the 1st year of a baby's life, synaptic density quadruples.*

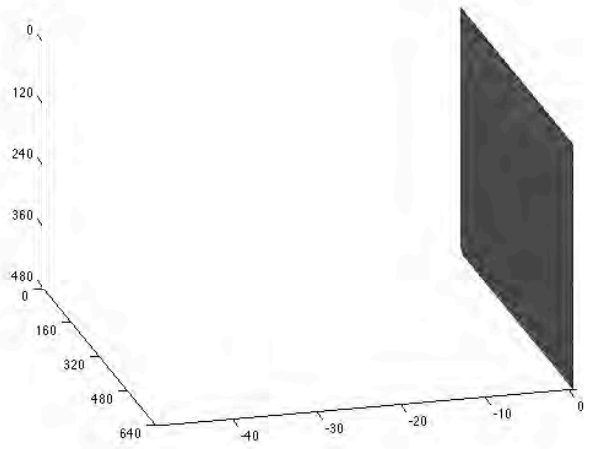
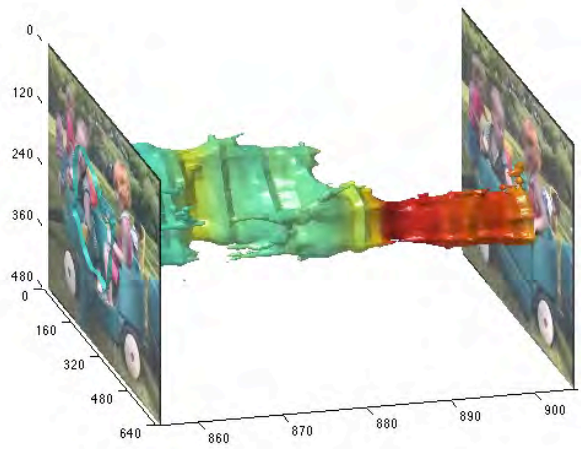
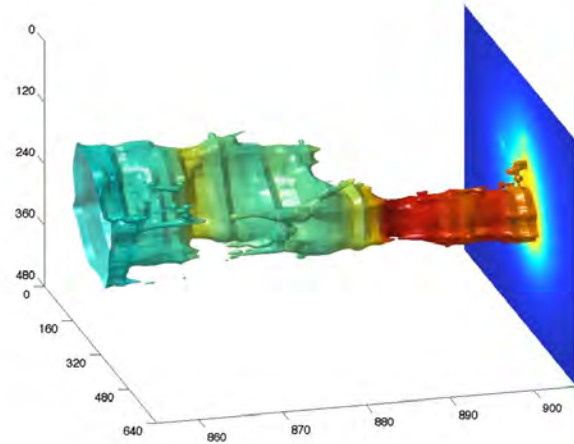
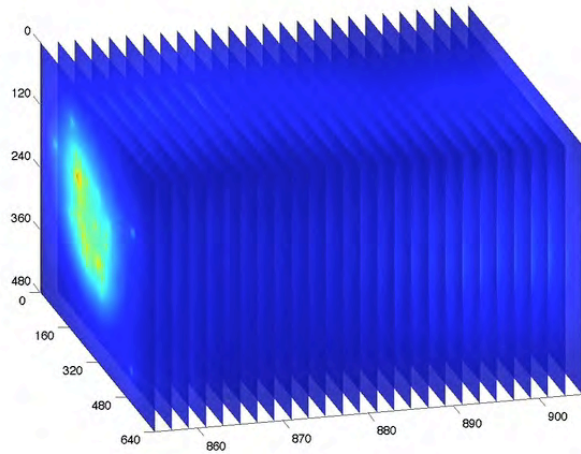
(Gilmore et al, 2007; Pfefferbaum et al, 1994; Huttenlocher, 1979; Petanjek et al, 2011)

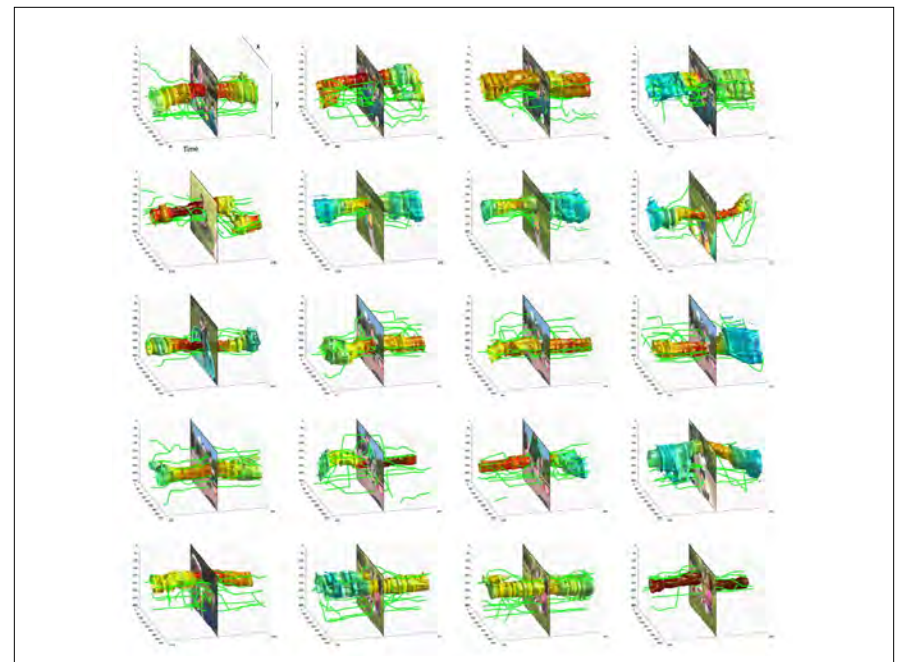
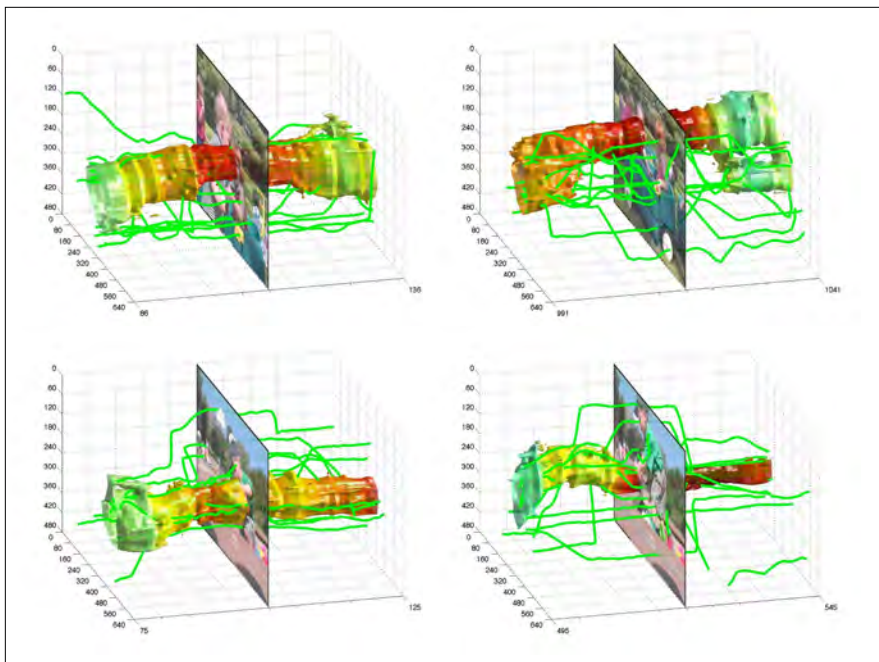
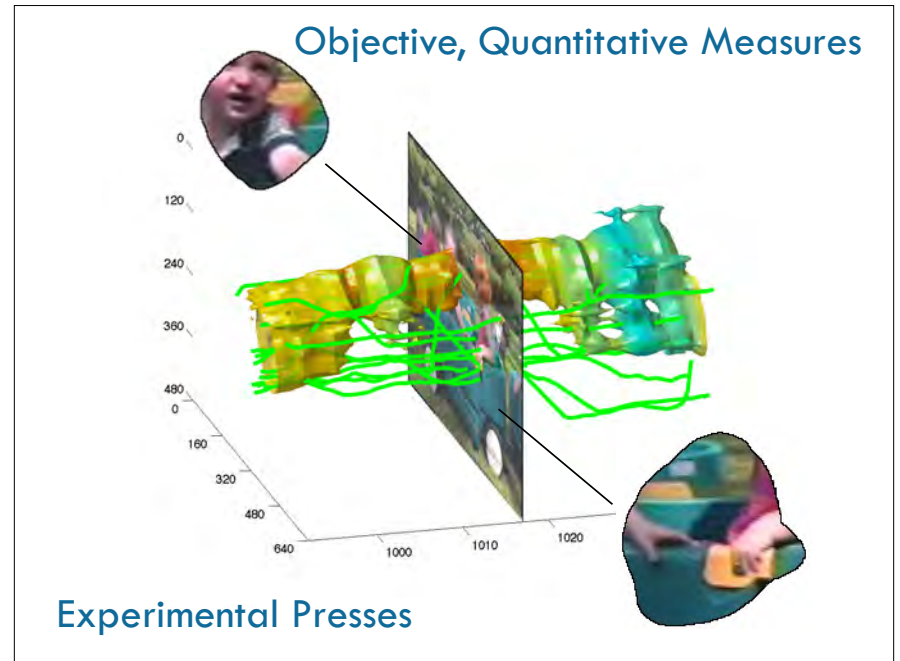
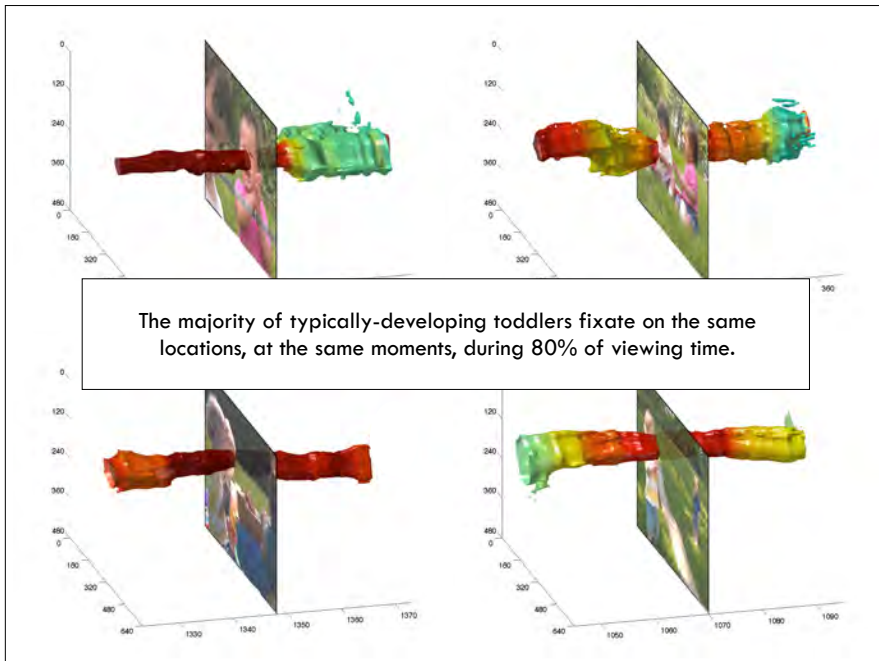




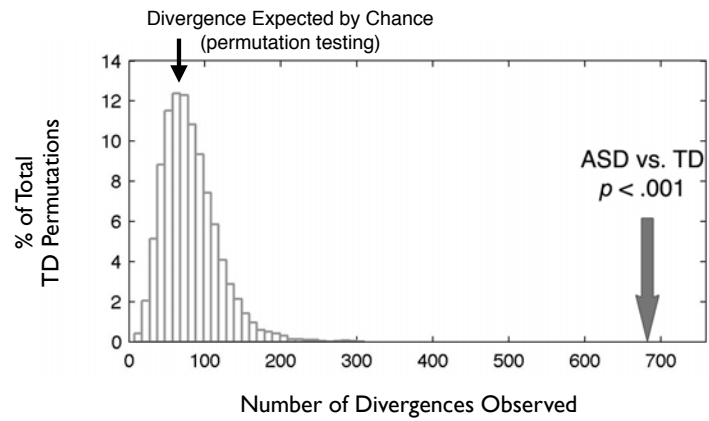


## Derivation of Attentional Funnel





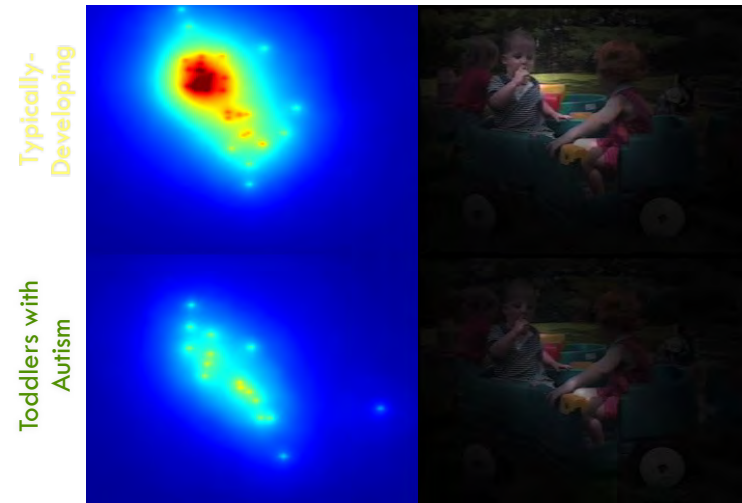
## The accrual of missed opportunities for social learning



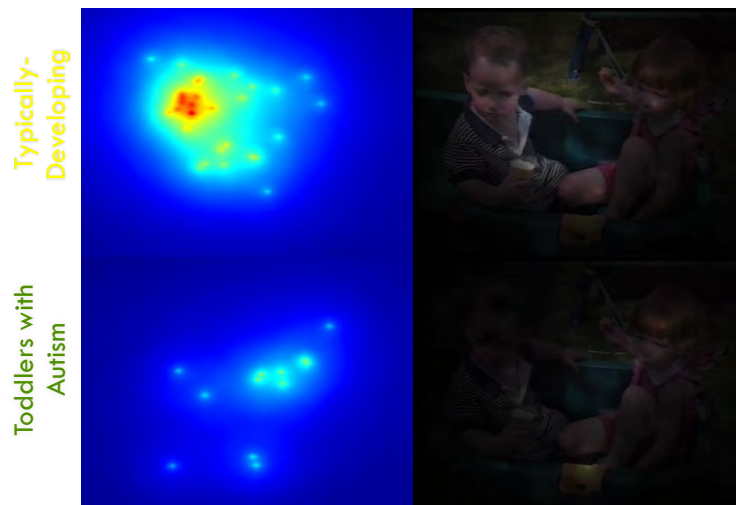
TD, N=44  
ASD, N=22

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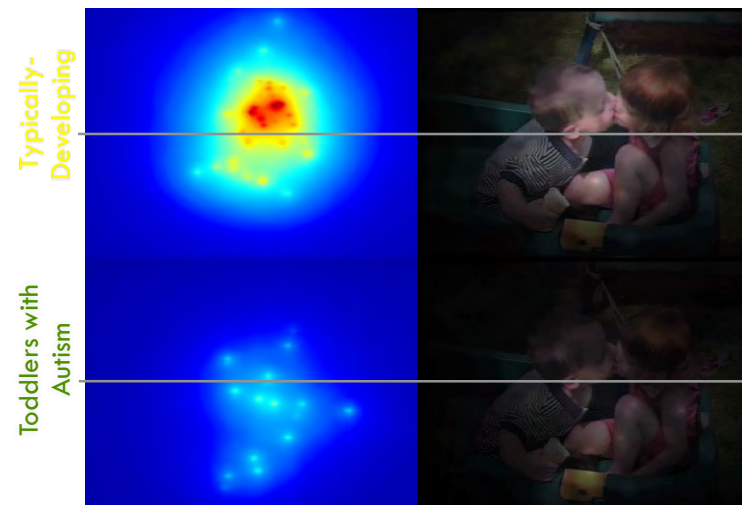
## Scenes of Social Action

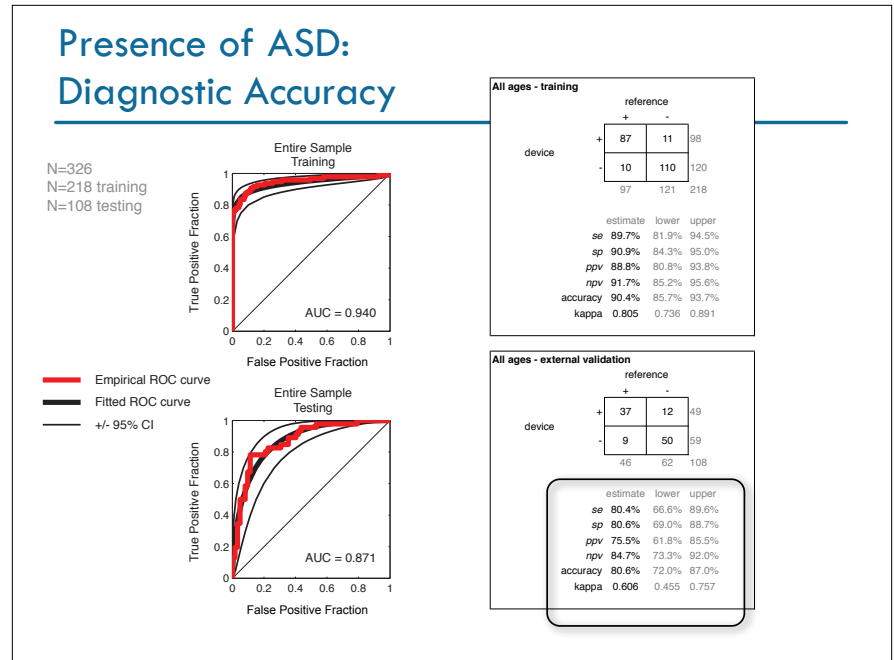
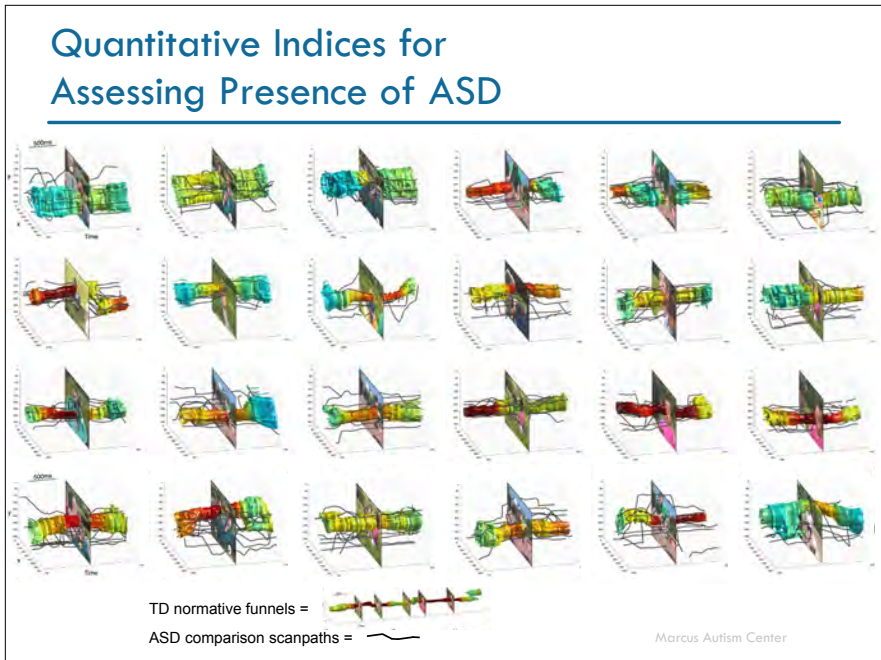
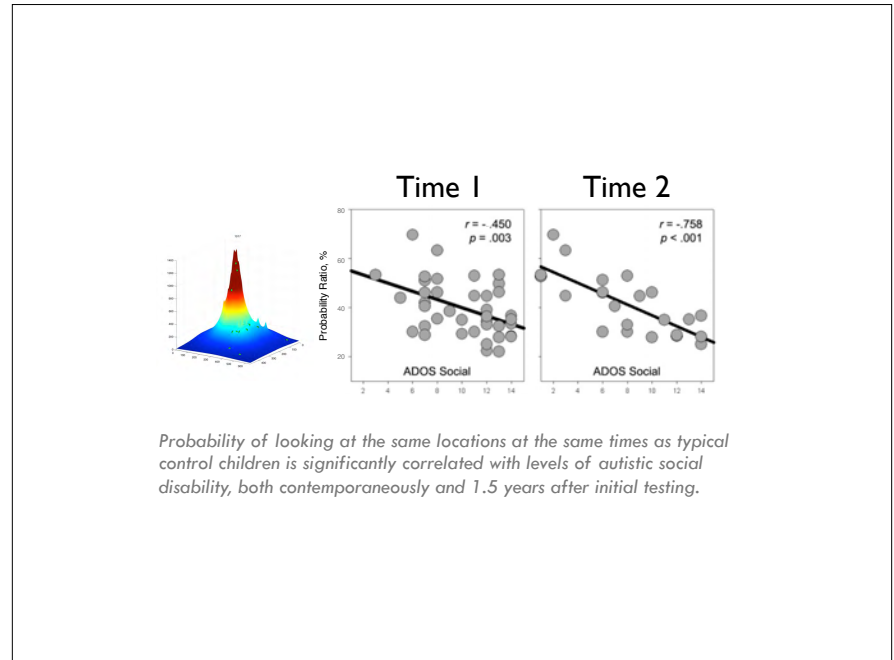
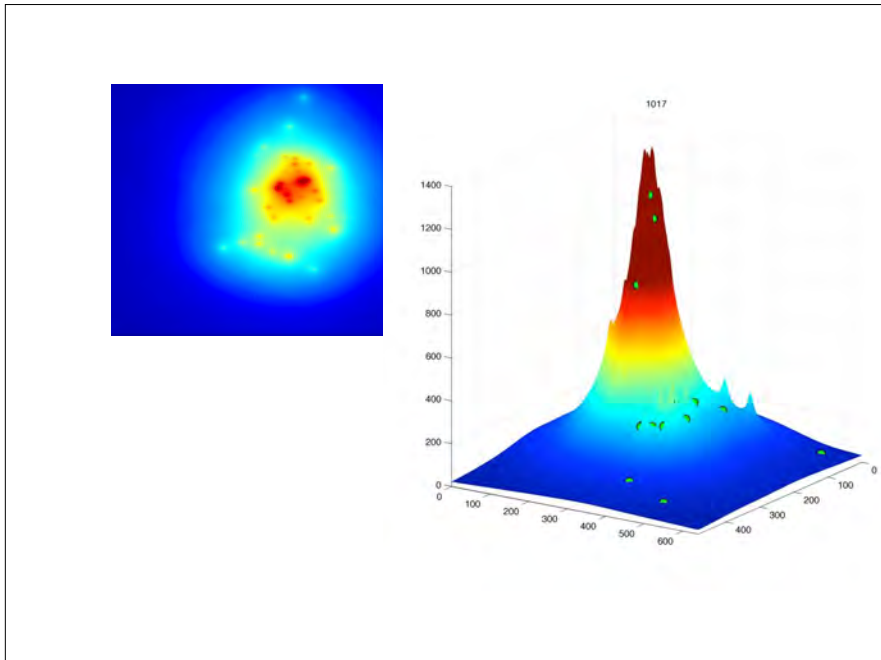


## Scenes of Social Interaction

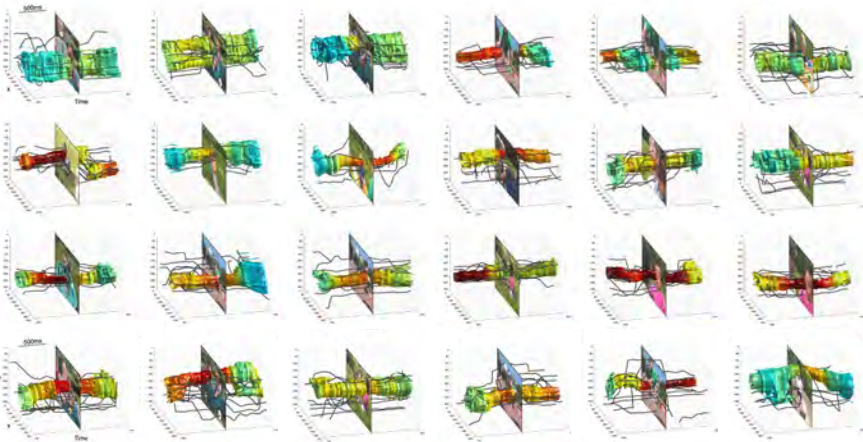




## Scenes of Social Interaction



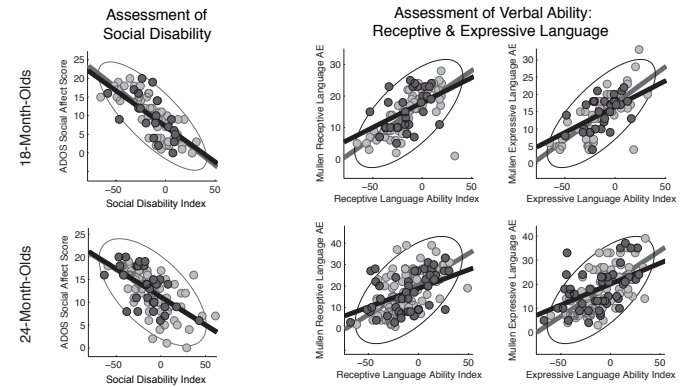


## Quantitative Indices for Assessing Severity of ASD



TD normative funnels =   
 ASD comparison scanpaths = 

## Severity of ASD: Prognostic Indicators



● Training Sample  
 ● Testing Sample

— Training Regression  
 — Testing Regression

testing set: mean  $r_{\text{ADOS Total}} = -0.65, p < 0.001$   
 testing set: mean  $r_{\text{Miller Verbal}} = 0.52, p = 0.001$

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

Measuring the genetic structure of social visual engagement



John Constantino, MD

338 toddlers:

- 82 monozygotic twins (41 MZ pairs)
- 84 dizygotic twins (42 DZ pairs)
- 84 non-sibling comparison children (42 non-sib control pairs)
- 88 non-twins w/ ASD
- age 21.3(4.3) months

Constantino, Kennon-McGill, Weichselbaum, Marrus, Haider, Glowinski, Gillespie, Klaiman, Klin, & Jones. (in press) Infant viewing of social scenes is under genetic control and atypical in autism.

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## Concordance in social visual engagement as a function of zygosity.

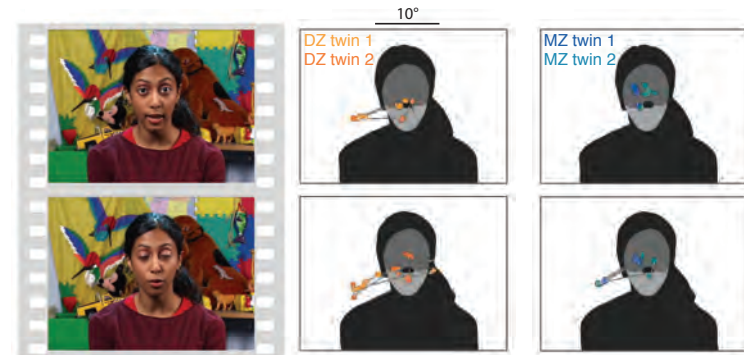


DZ males

Constantino & Colleagues



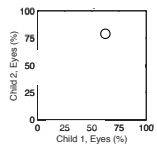
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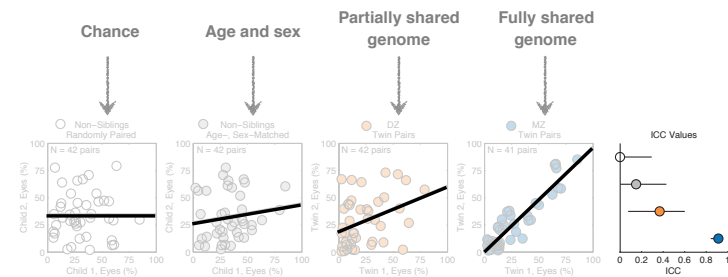
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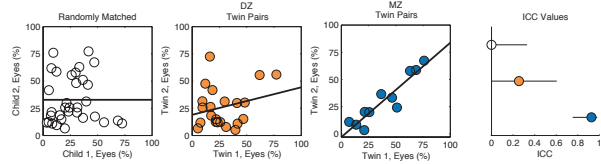
## Individual variation in eye-looking is strongly influenced by genetics.



Constantino, Kennon-McGill, Weichselbaum, Marrus, Haider, Glowinski, Gillespie, Klaiman, Klin, & Jones. (in press) Infant viewing of social scenes is under genetic control and atypical in autism.

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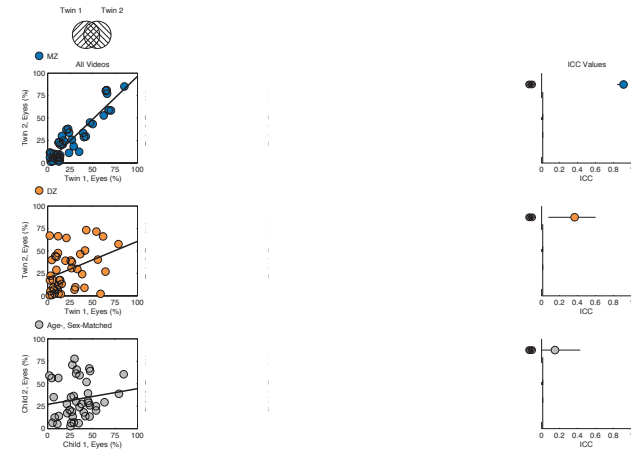
## Strong genetic influence persists across development.



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

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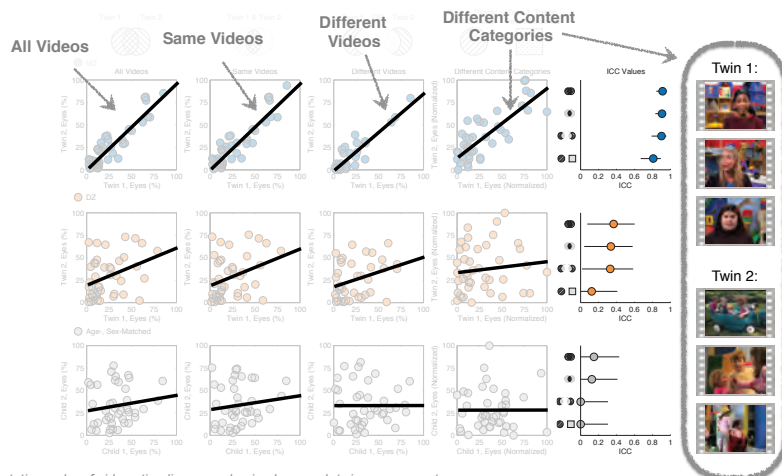
## Strong genetic influence persists across stimulus type, evidence of goal-directed seeking of social information



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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## Strong genetic influence persists across stimulus type, evidence of goal-directed seeking of social information



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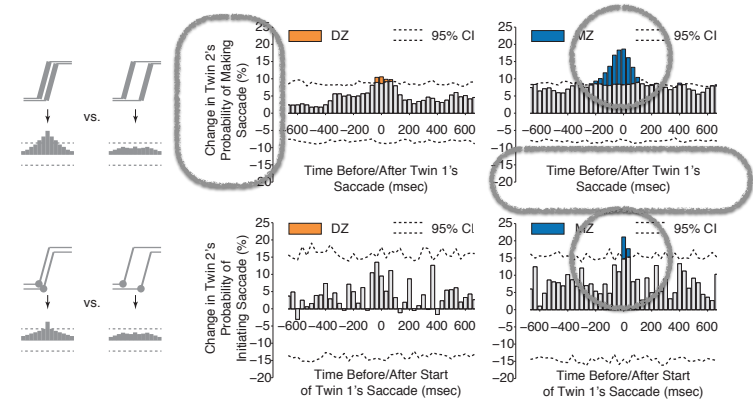
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## Genetic influence exerts its effects on a moment-by-moment basis.





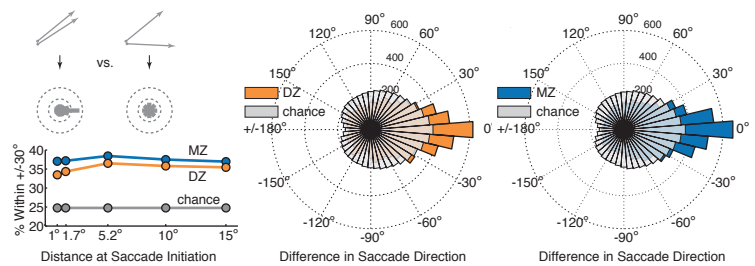
## MZ twins are more likely to...



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

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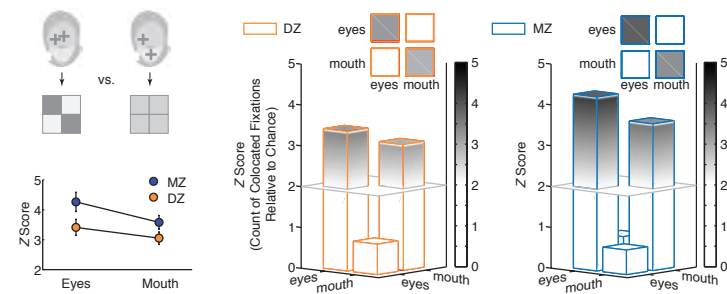
## MZ twins are more likely to...



...move their eyes in the same directions.

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## MZ twins are more likely to...

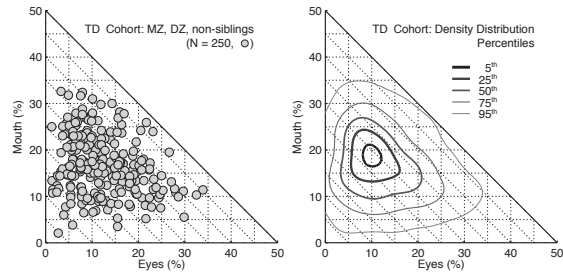


...fixate on the same semantic content  
at the same moments in time.

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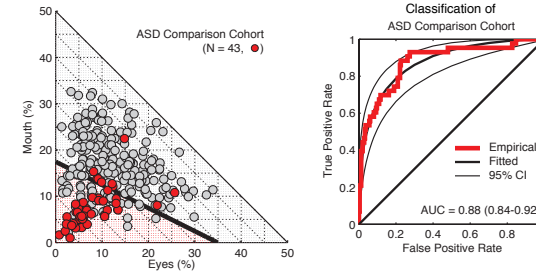
## The markers of social visual engagement that are most highly heritable...



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

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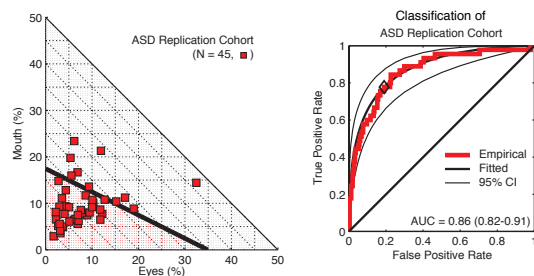
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high **Heritability** (eye- & mouth-looking)

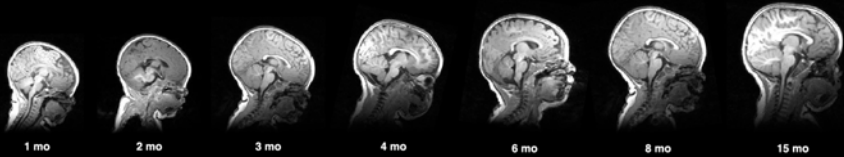
+ high **Probability** (shifting eyes at same moments, in same directions, towards same content)

= profound influence on **human biological niche construction**

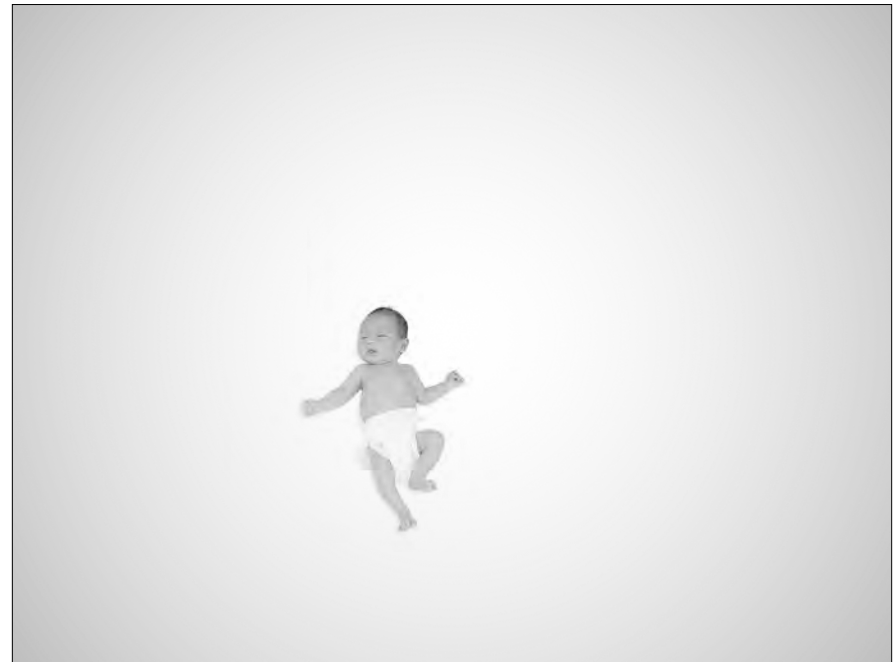
Scarr & McCartney, 1983.



## Social Interaction is the Platform for Brain Development



*"Our brains become who we are." (J LeDoux)*  
*Brain structure and function are physical instantiations of lived experience.*



## Neonates preferentially orient towards stimuli that...

More Preferred



mother's voice    stranger's voice

Less Preferred



complex non-speech    pure tone, structured noise    silence



...**sound** like caregivers.

DeCasper & Fifer, 1980.  
Vouloumanos & Werker, 2007.  
Butterfield & Siperstein, 1970  
Eisenberg, 1976.

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## Neonates preferentially orient towards stimuli that...

More Preferred



mother's scent

Less Preferred



stranger's scent



...**sound** like caregivers.  
...**smell** like caregivers.

Macfarlane, 1975.  
Porter & Winberg, 1999.

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## Neonates preferentially orient towards stimuli that...

More Preferred



biological motion

Less Preferred



inverted biological motion



scrambled biological motion



...**sound** like caregivers.  
 ...**smell** like caregivers.  
 ...**move** like caregivers.

Simion, Regolin, & Bulf, 2008.

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## Neonates preferentially orient towards stimuli that...

More Preferred



face-like



face-like configural

Less Preferred



face-like, scrambled



face-like, inverted



...**sound** like caregivers.  
 ...**smell** like caregivers.  
 ...**move** like caregivers.  
 ...**look** like caregivers.

Goren, Sarty, & Wu, 1975.  
 Johnson, Dzitewicz, Ellis, & Morton, 1991.  
 Simion, Valenza, Umiltà, & Barba, 1998.  
 Valenza, Simion, Cassia, & Umiltà, 1996.  
 Farroni et al, 2005.

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## Neonates preferentially orient towards stimuli that...

More Preferred



mother, engaging



stranger, eyes open

Less Preferred



stranger, eyes averted



stranger, eyes closed



...**sound** like caregivers.  
 ...**smell** like caregivers.  
 ...**move** like caregivers.  
 ...**look** like caregivers.  
 ...**interact** like caregivers.

Bushnell, Sai, & Mullin, 1989.  
 Simion, Valenza, Umiltà, & Barba, 1998.  
 Farroni, Csibra, Simion, & Johnson, 2002.  
 Bartki, Baron-Cohen, et al, 2000.  
 Sai, 1990.  
 Sai, 2005.  
 Walton, Bower, & Bower, 1992.

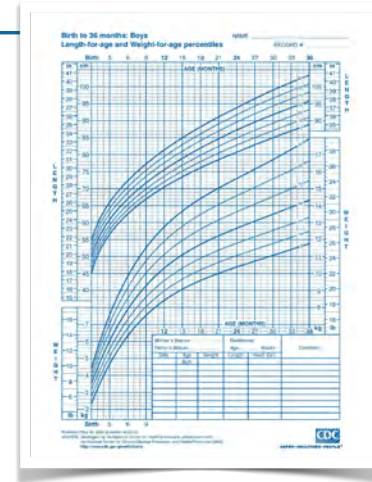
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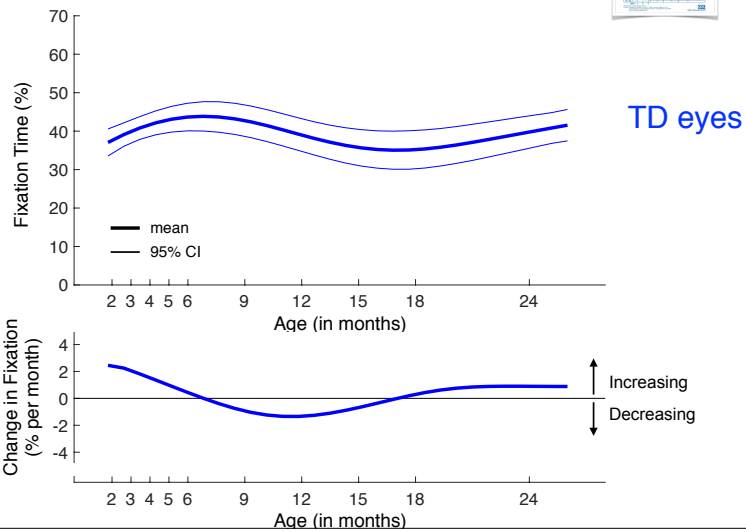
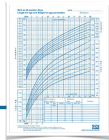
# Typically-Developing 5-Month-Old



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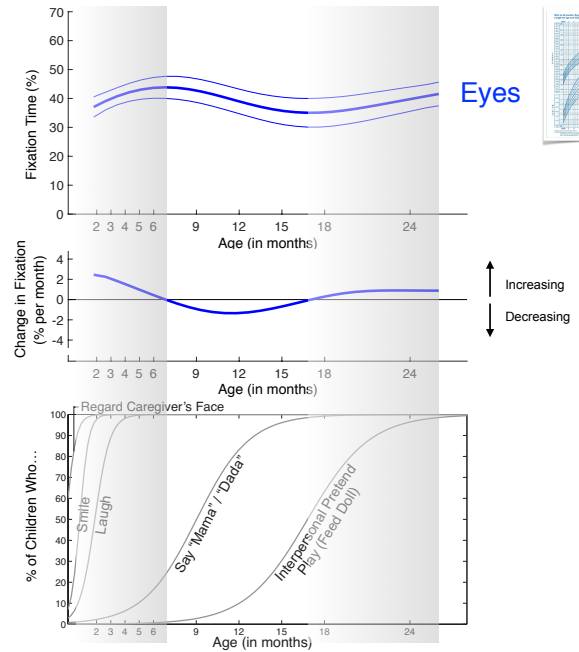


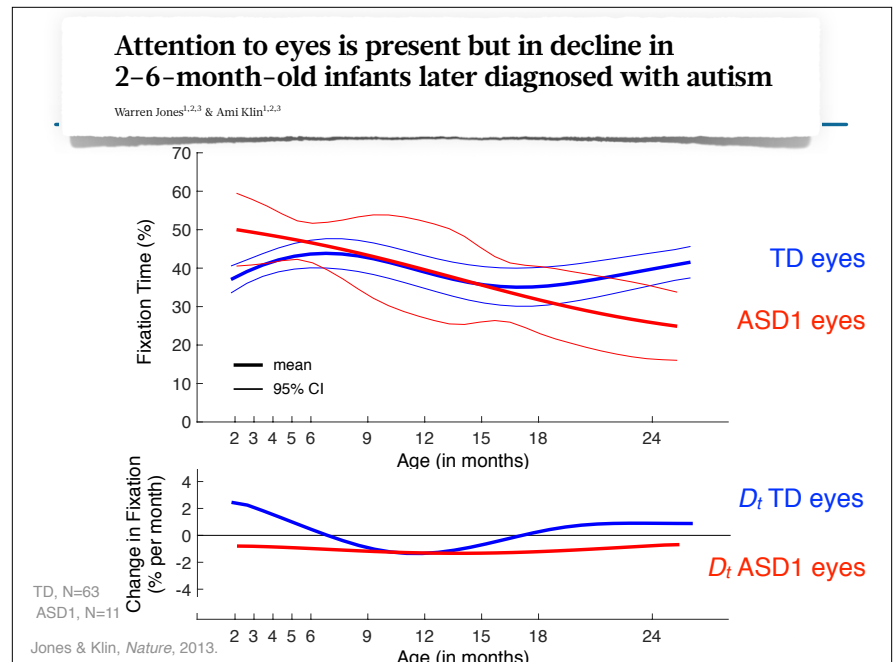
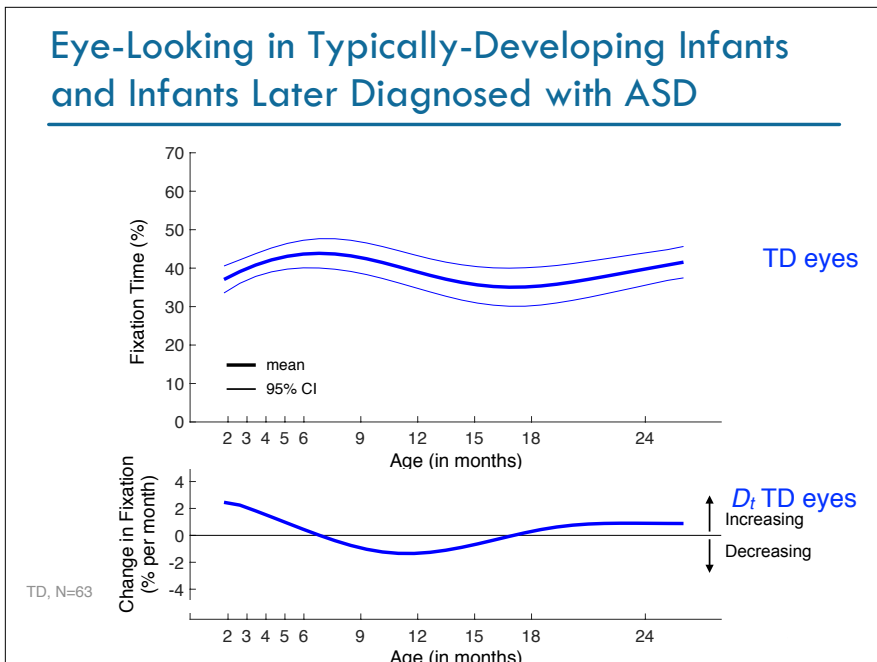
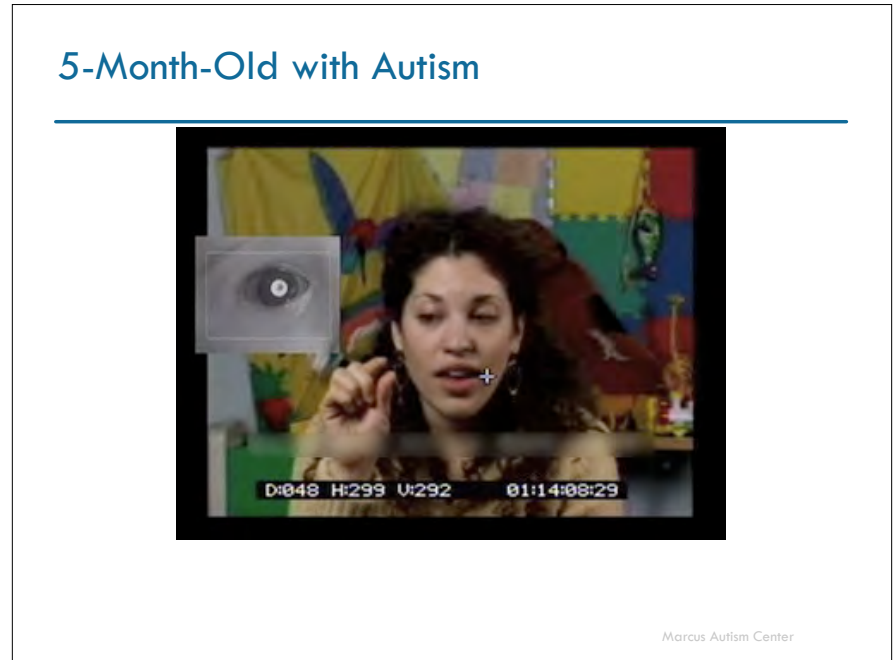
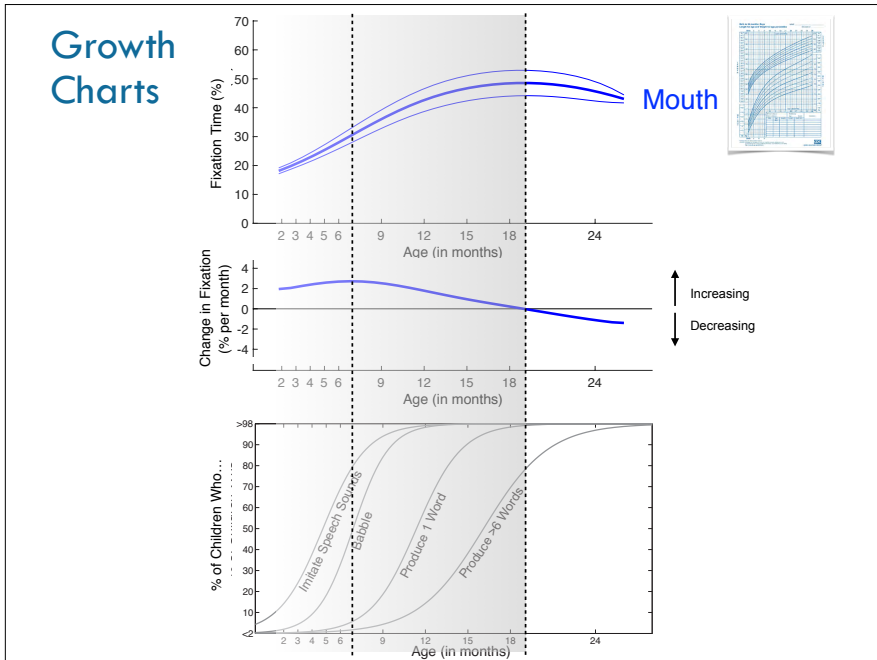
# Normative Growth Charts of Social Visual Engagement



TD, N=63

# Growth Charts



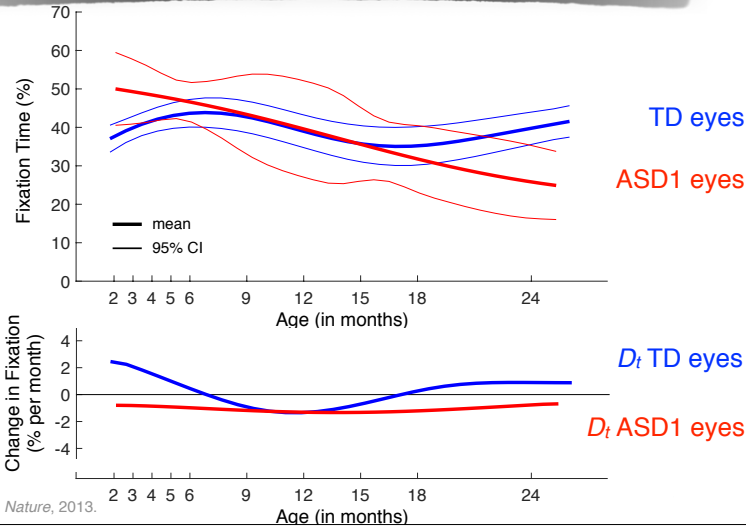


## Attention to eyes is present but in decline in 2-6-month-old infants later diagnosed with autism

Warren Jones<sup>1,2,3</sup> & Ami Klin<sup>1,2,3</sup>



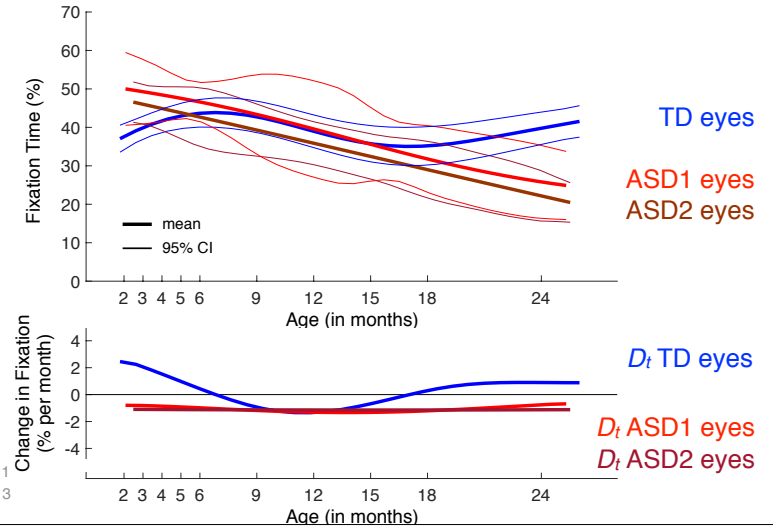
Lindsay Olson



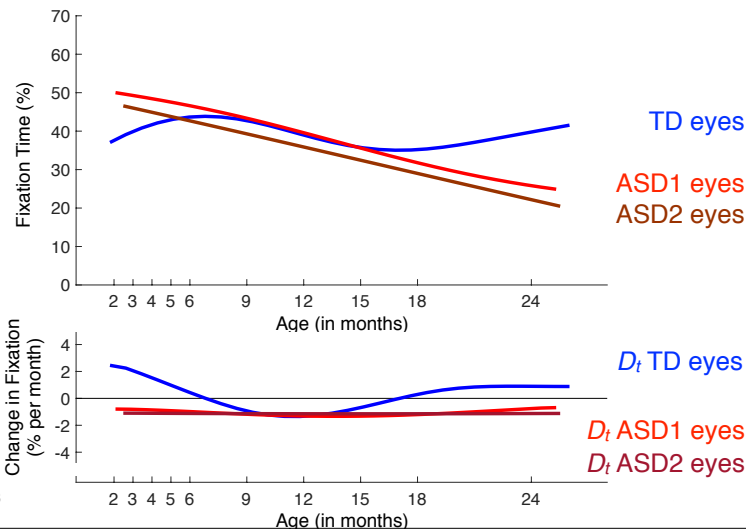
## First Replication Cohort



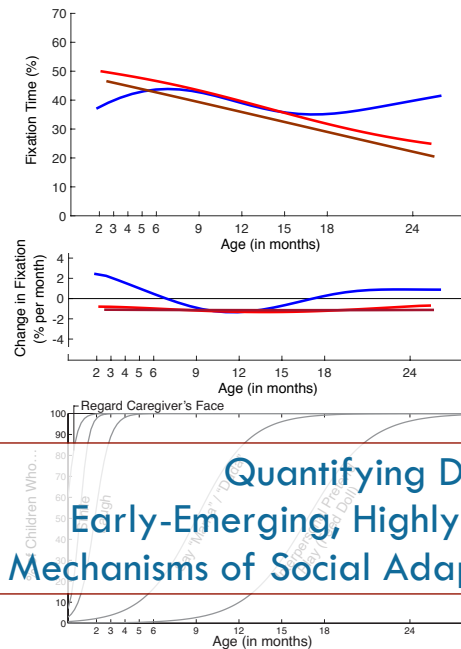
Lindsay Olson



## First Replication Cohort



## Growth Charts



Quantifying Disruption of Early-Emerging, Highly-Conserved Mechanisms of Social Adaptive Action

# Social Visual Engagement & Brain Development in a Model System



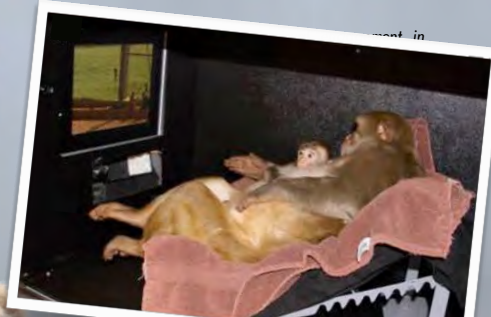
Jocelyne Bachevalier, PhD



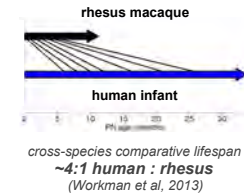
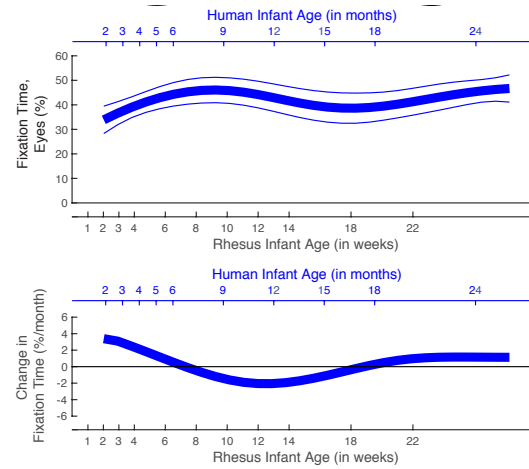
Mar Sanchez, PhD



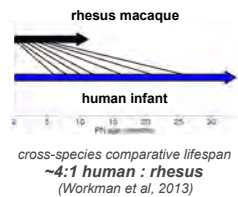
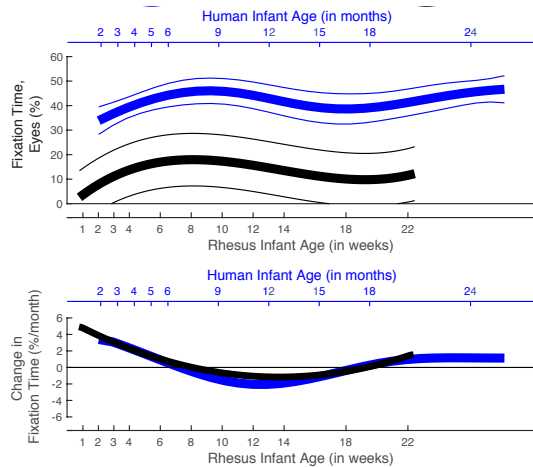
Longchuan Li, PhD



# Social Visual Engagement (Eye-Looking) is Highly Phylogenetically Conserved

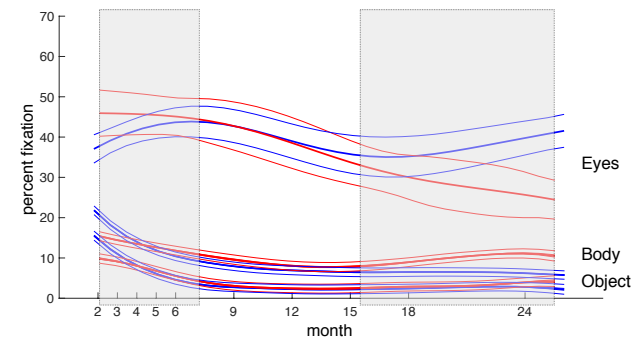


# Social Visual Engagement (Eye-Looking) is Highly Phylogenetically Conserved



N=31 infant rhesus

# Implications for Human Brain-Behavior Development



TD, N=63, 5,375 trials  
 ASD, N=24, 1,410 trials (combined cohorts)

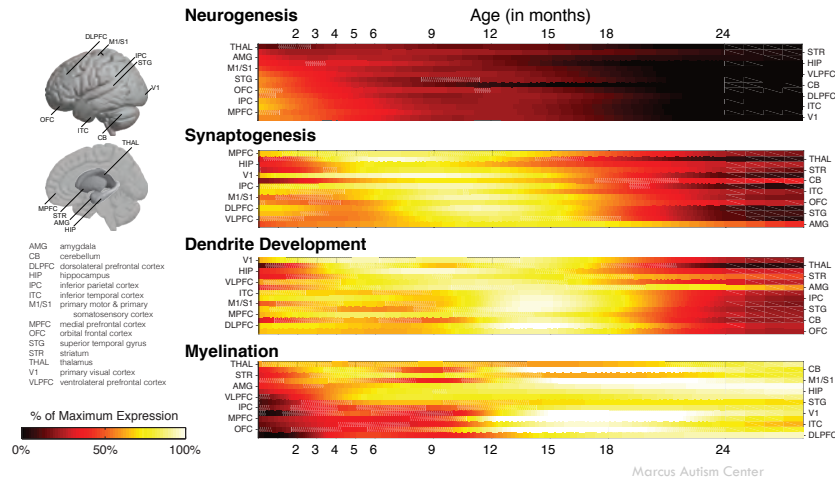
Significant differences in fixation or change in fixation ( $p < 0.05$ )

# Gene Expression in Infant Brain

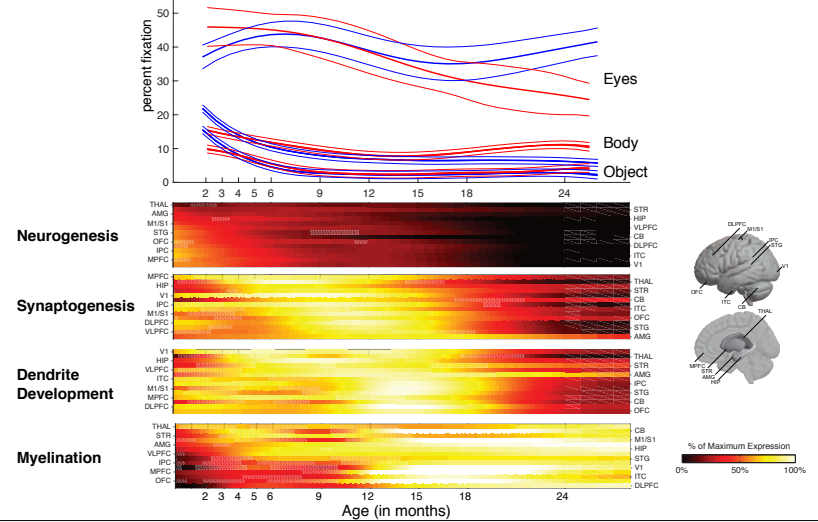
## BRAINSPAN

ATLAS OF THE DEVELOPING HUMAN BRAIN  
 >17,500 genes from fetal week 4 to late adulthood  
 Kang et al (2011), Nature. (Nenad Sestan)

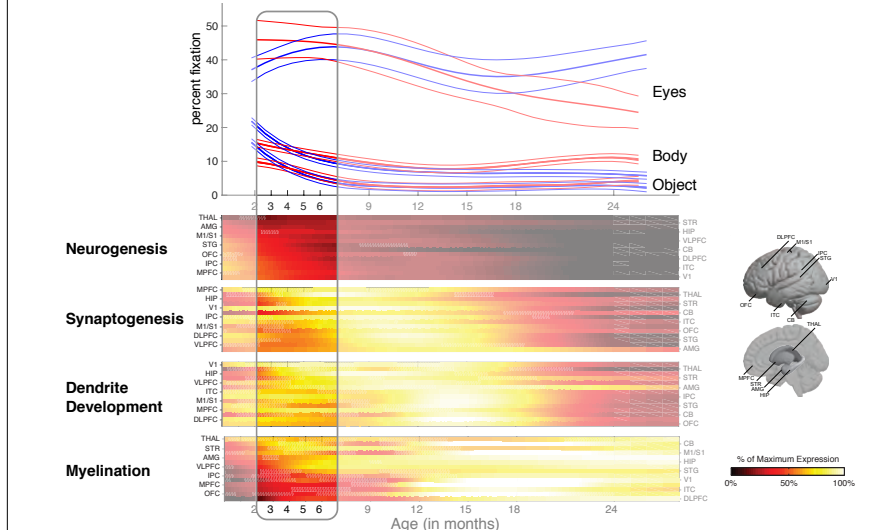
Longitudinal expression of genes associated with...



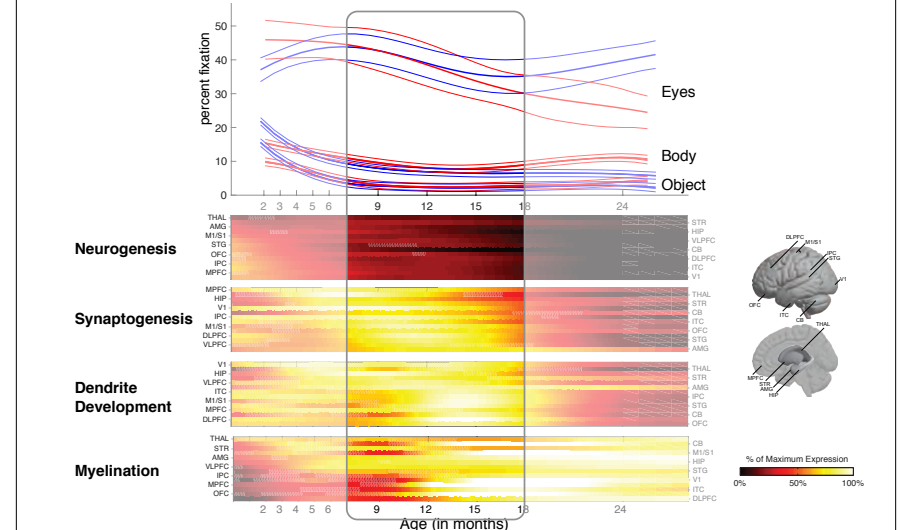
# Atypical Social Visual Engagement: Present Already During Pivotal Windows in Neurodevelopment



# Atypical Social Visual Engagement: Present Between 2-6 Months

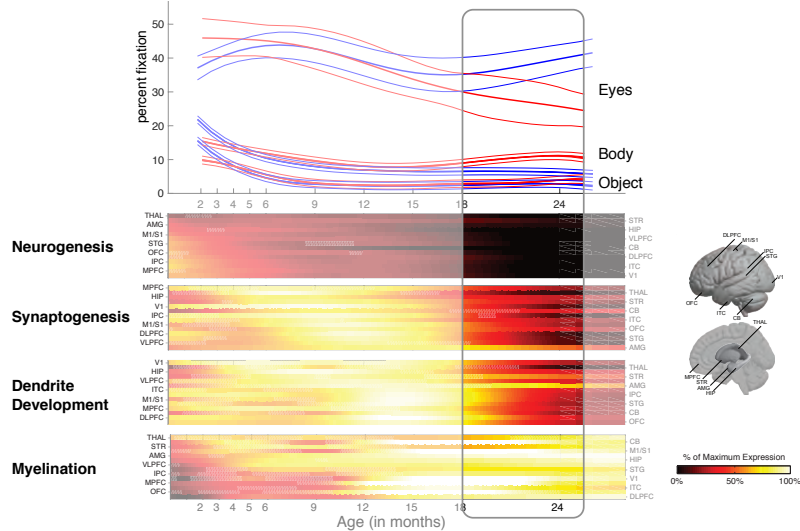


# Atypical Social Visual Engagement: Precedes Waves of Synaptogenesis & Dendrite Development

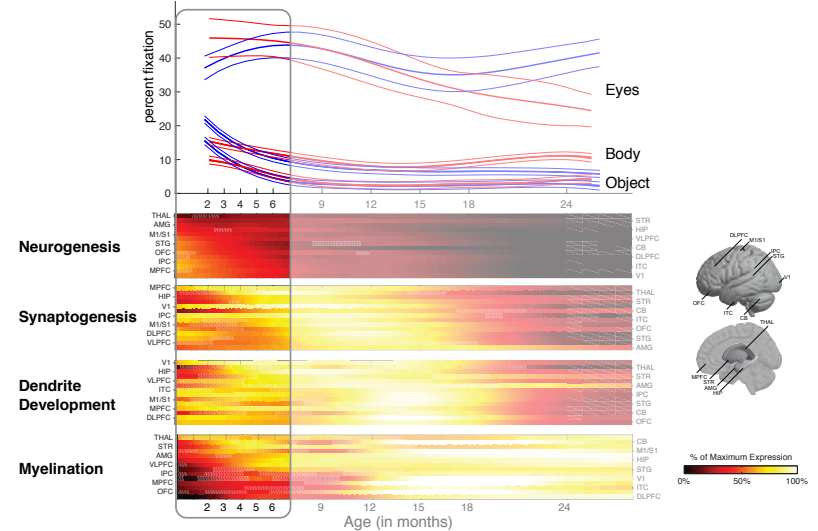




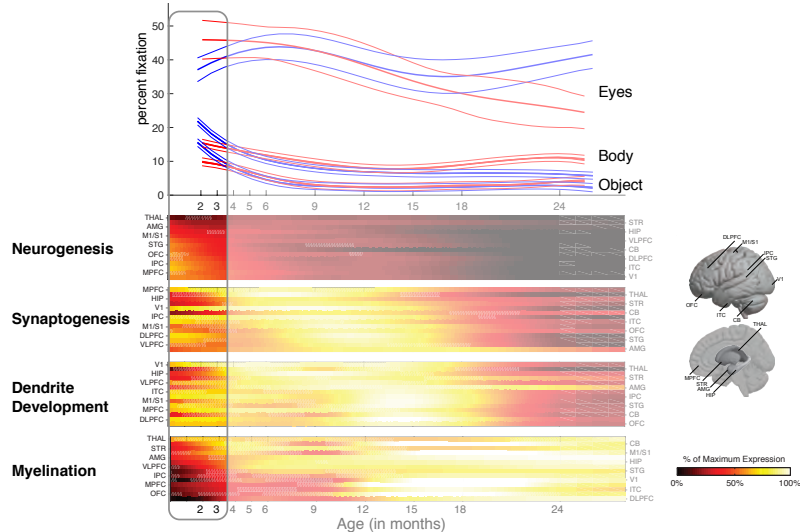
## Atypical Social Visual Engagement: 2<sup>nd</sup> Wave of Behavior Differences Manifests at 18-24 Months



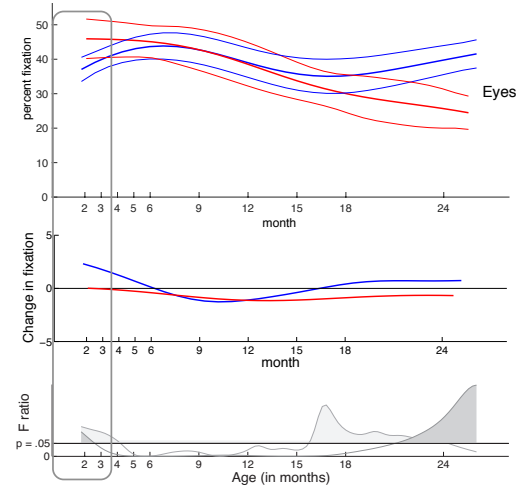
## Atypical Social Visual Engagement: Critical Window in Infants' First 6 Months



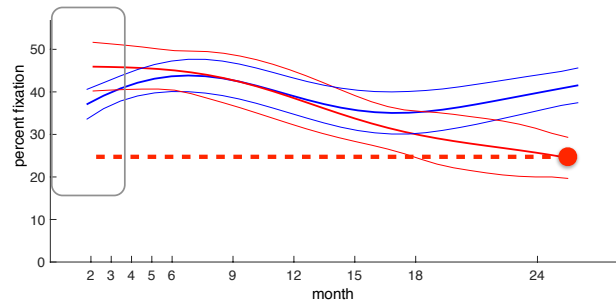
## Atypical Social Visual Engagement: Pivotal Transitions at ~2 Months



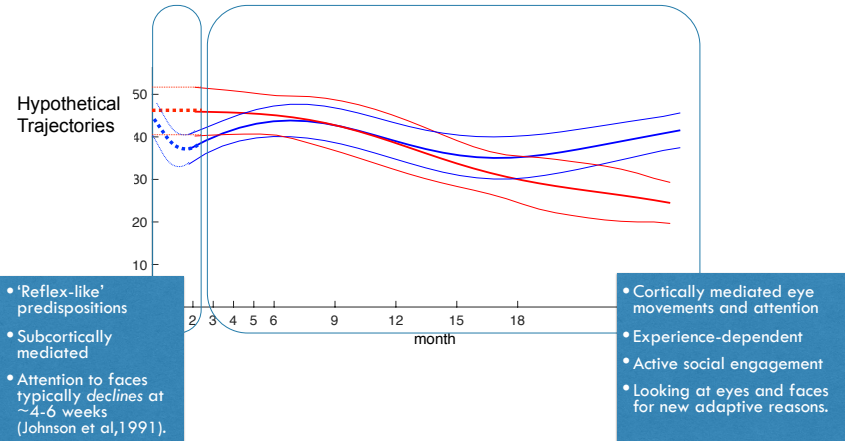
## Pivotal Transitions at ~2 Months: New Hypotheses and Opportunities



## Pivotal Transitions at ~2 Months: New Hypotheses and Opportunities



## Pivotal Transitions at ~2 Months: New Hypotheses and Opportunities



## Dynamic Transitions in Typical Infancy

### Abilities Present Shortly After Birth



- Reflex-like predispositions
  - Orienting to faces and eyes (Johnson et al., 1991)
  - Endogenous smiling (Emde, 1972)



Subcortically mediated

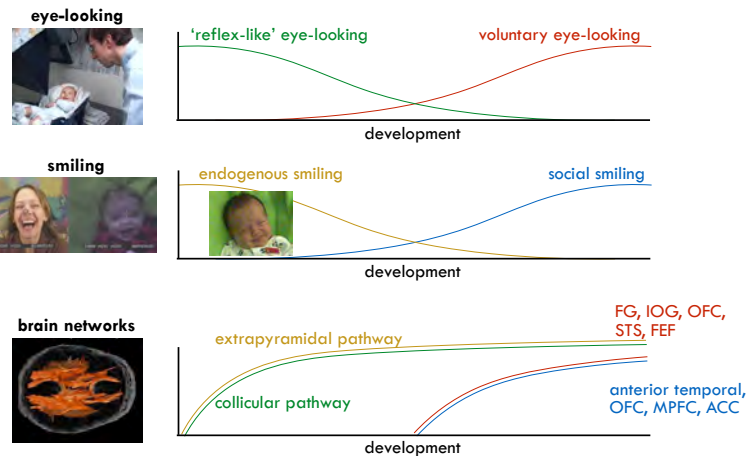
### Typical Transitions by ~2 months



- Decline in reflex-like behavior (Johnson et al., 1991)
- Increased alertness & control over own movements (Wolff, 1987; Bronson, 1974)
- Active and intentional exploration (Rochat, 2001)
- Engagement in contingent social interaction
  - Increased looking to eyes (Haith et al., 1997; Jones & Klin, 2013)
  - Emergence of social smiling (Wolff, 1987; Lavell & Fogel, 2002; Messinger & Fogel, 2003)

Cortically mediated

## Associated Changes in Brain and Behavior



## How to link these pivotal transitions in behavior to the neural bases of autism?

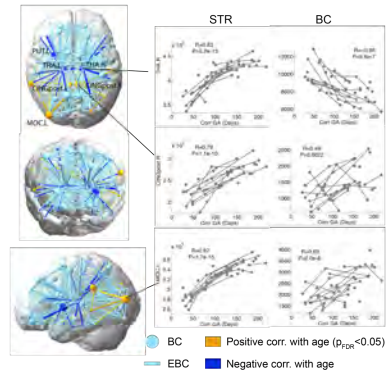
Change in social adaptive action and brain connectivity in infants' first 6 months



Longchuan Li, PhD



Sarah Shultz, PhD



Significant positive (orange) and negative (blue) changes of nodal importance (BC) over development: 27 days to 218 days in human infants.

## The Search for Endophenotypes

✓ **Quantitative**

✓ **Specific**

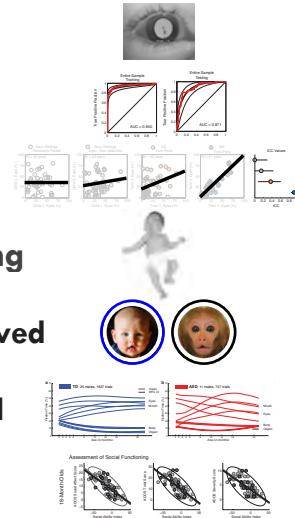
✓ **Heritable**

✓ **Early-Emerging**

✓ **Highly-Conserved**

✓ **Developmental**

✓ **Individualized**



## 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

## Thank You

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- The children and families for their participation.
- The National Institute of Mental Health
- The Simons Foundation
- The National Institute of Child Health and Human Development
- The Marcus Foundation
- The JB Whitehead and Woodruff Foundations
- Autism Science Foundation



Marcus Autism Center

## Thank You

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## Thank You

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