

Neuroimaging Studies of Autism: A Review of the Existing Literature and New Directions

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The Social Brain and Social Perception

The Social Brain:

the complex network of areas that enable us to recognize other individuals and to evaluate their mental states (e.g. intentions, dispositions, desires, and beliefs) (Brothers, 1990)

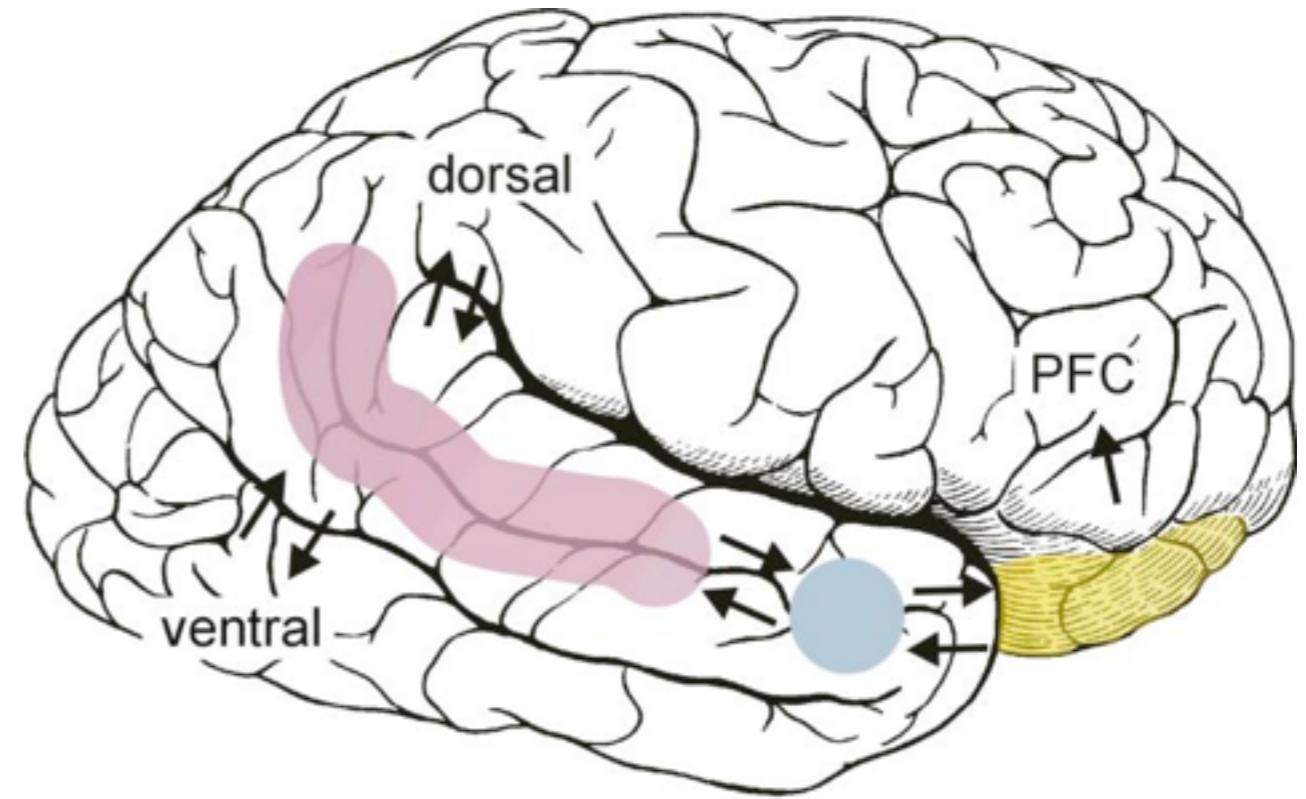


Figure from Allison, Puce, & McCarthy, 2000, TICS

The Social Brain and Social Perception

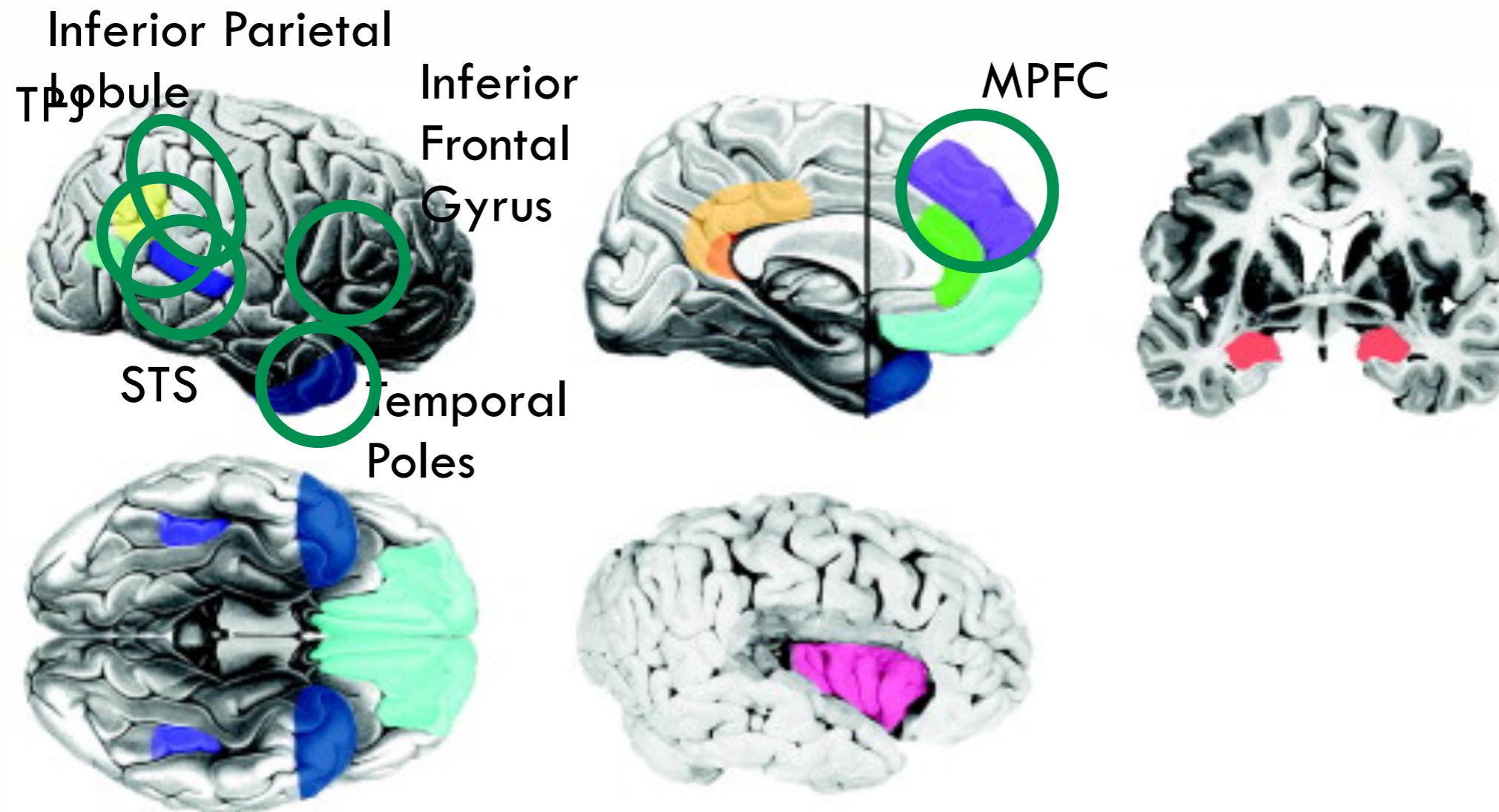


Figure from Kennedy & Adolphs, 2012, TICS

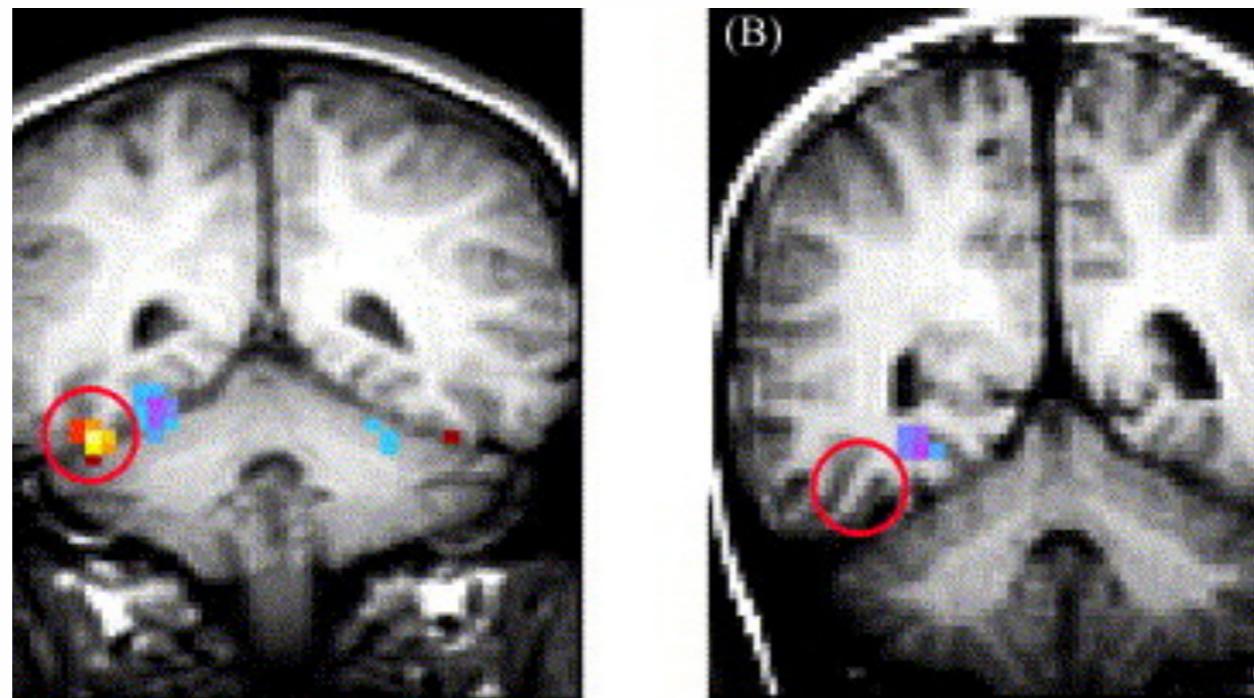
Neural Mechanisms Underlying Core Behavioral Deficits in ASD

- Face processing
- Responding to biological motion
- Understanding and interpreting the intentions of others (TOM)
- Reward processing

Social Brain Dysfunction in ASD

Neural Mechanisms Associated with Face Processing in ASD:

- The fusiform gyrus and the amygdala of individuals with ASD responds *less* to faces compared with typically-developing controls (e.g. Schultz et al., 2000)



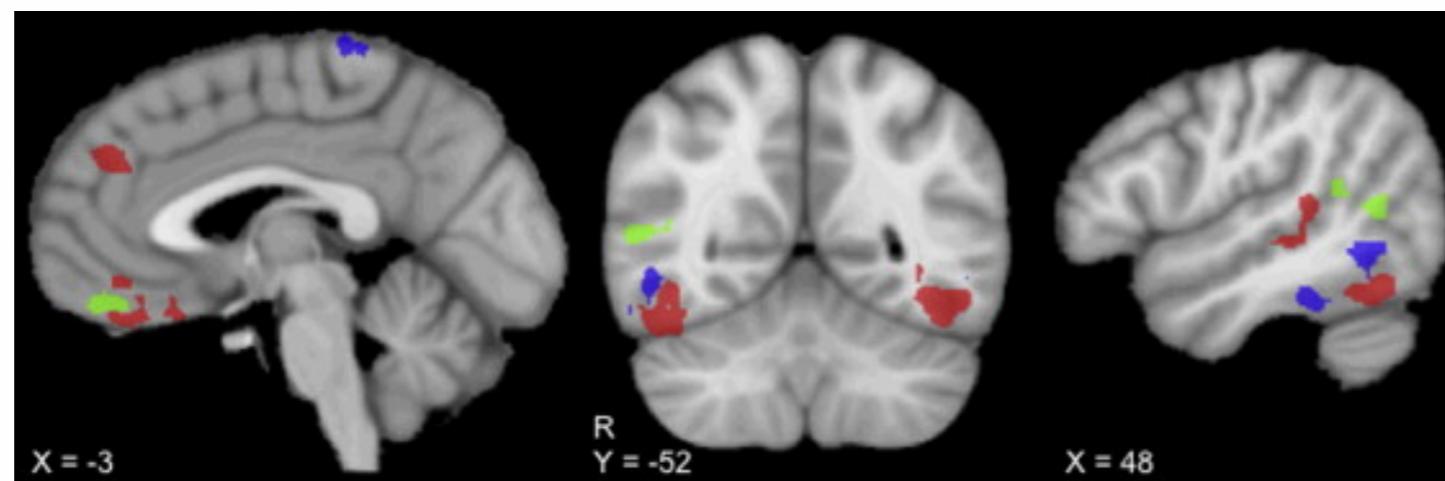
Schultz, 2005, *Intl. J. Dev. Neuro.*

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Social Brain Dysfunction in ASD

Neural mechanisms associated with perception of biological motion in ASD:

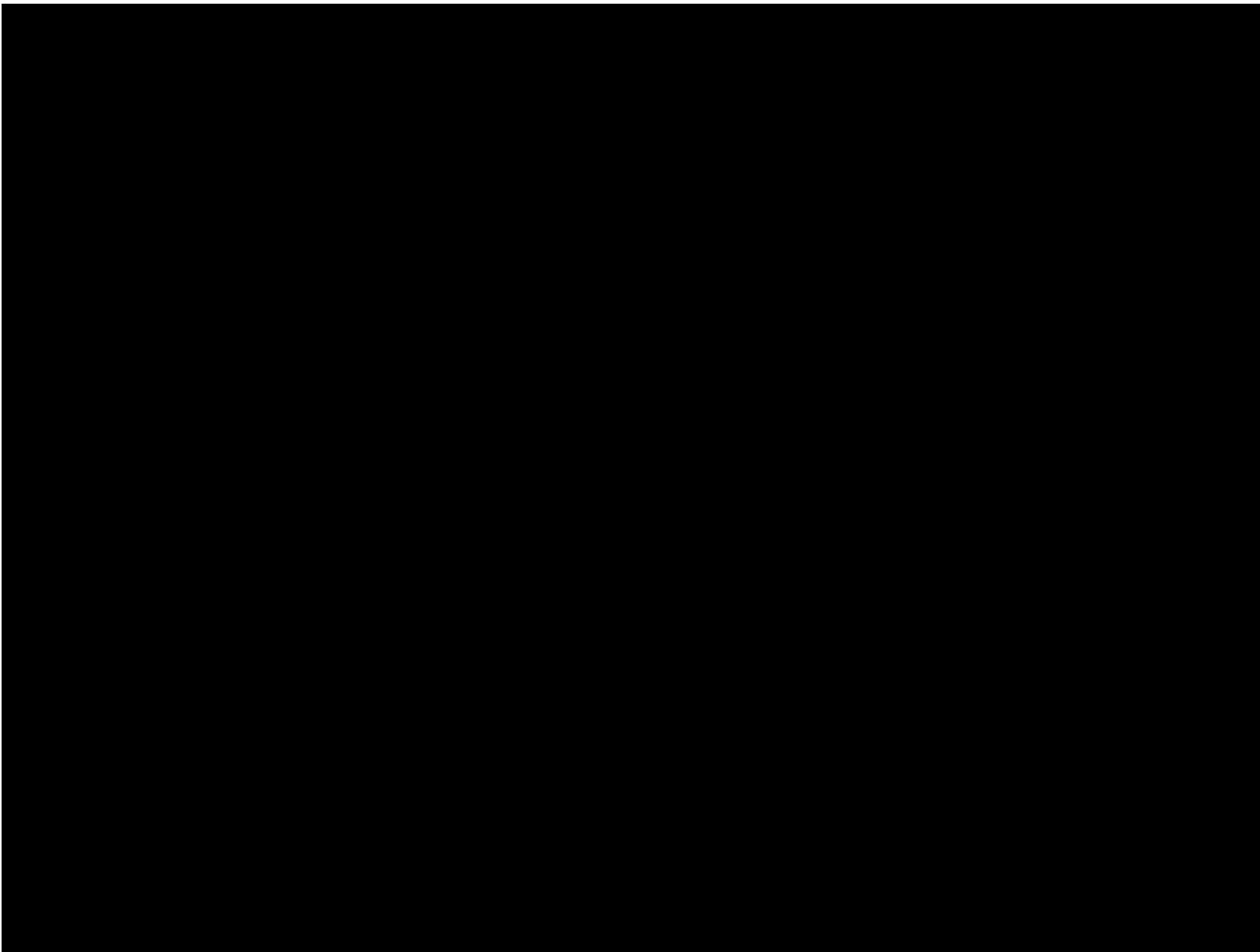
- Individuals with ASD show *reduced STS activation when viewing biological motion* (Herrington et al., 2007; Frietag et al., 2008)
- The STS shows *reduced sensitivity to the intentions underlying actions* in ASD (Pelphrey et al., 2005)
- *Sibling studies reveal potential ‘compensatory mechanisms’ for processing biological motion* (Kaiser et al., 2010)



red: state activity
blue: trait activity
green:
compensatory
activity
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Social Brain Dysfunction in ASD

Neural mechanisms associated with mentalizing in ASD



Social Brain Dysfunction in ASD

Neural mechanisms associated with mentalizing in ASD

- Individuals with ASD show reduced activation in MPFC, STS and temporal poles when viewing animations that elicit mentalizing in typical viewers (Castelli et al., 2002)
- Theory of mind tasks yield abnormal patterns of activation in the MPFC (Happé et al., 1996)
- Activation of the mirror neuron system is decreased in ASD (Dapretto et al., 2006)

Social Brain Dysfunction in ASD

Neural mechanisms associated with reward processing in ASD

- ASD participants show reduced striatal activation in response to social reward (e.g Delmonte et al. 2012)
- Individuals with ASD show atypical activation in the anterior cingulate, frontal cortex and ventral striatum in response to monetary reward (e.g. Kohls et al. 2013)
- Participants with ASD show normative activation in reward-related circuitry when viewing participant-specific restricted interest objects (Cascio et al. 2014)

Connectivity

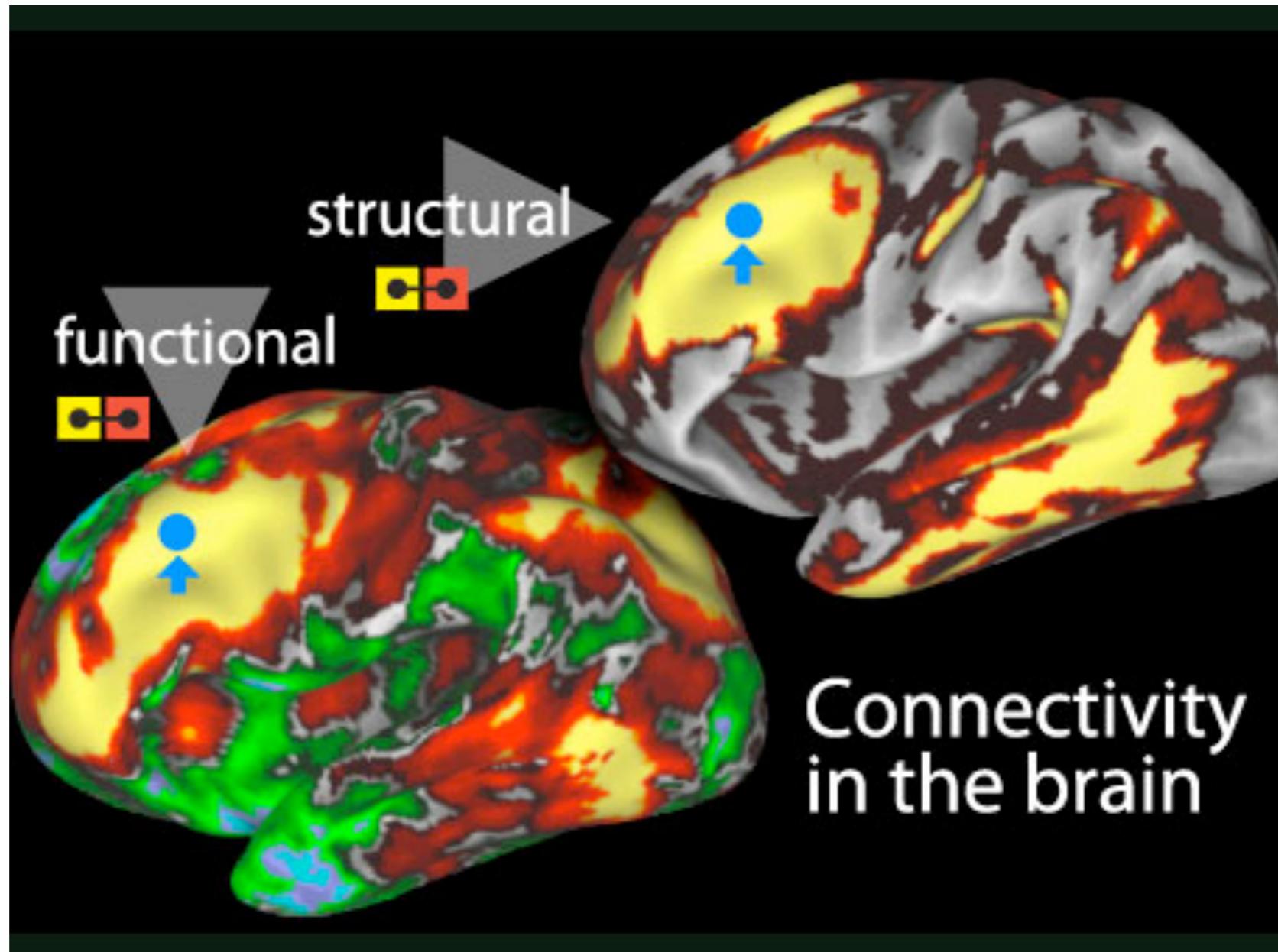
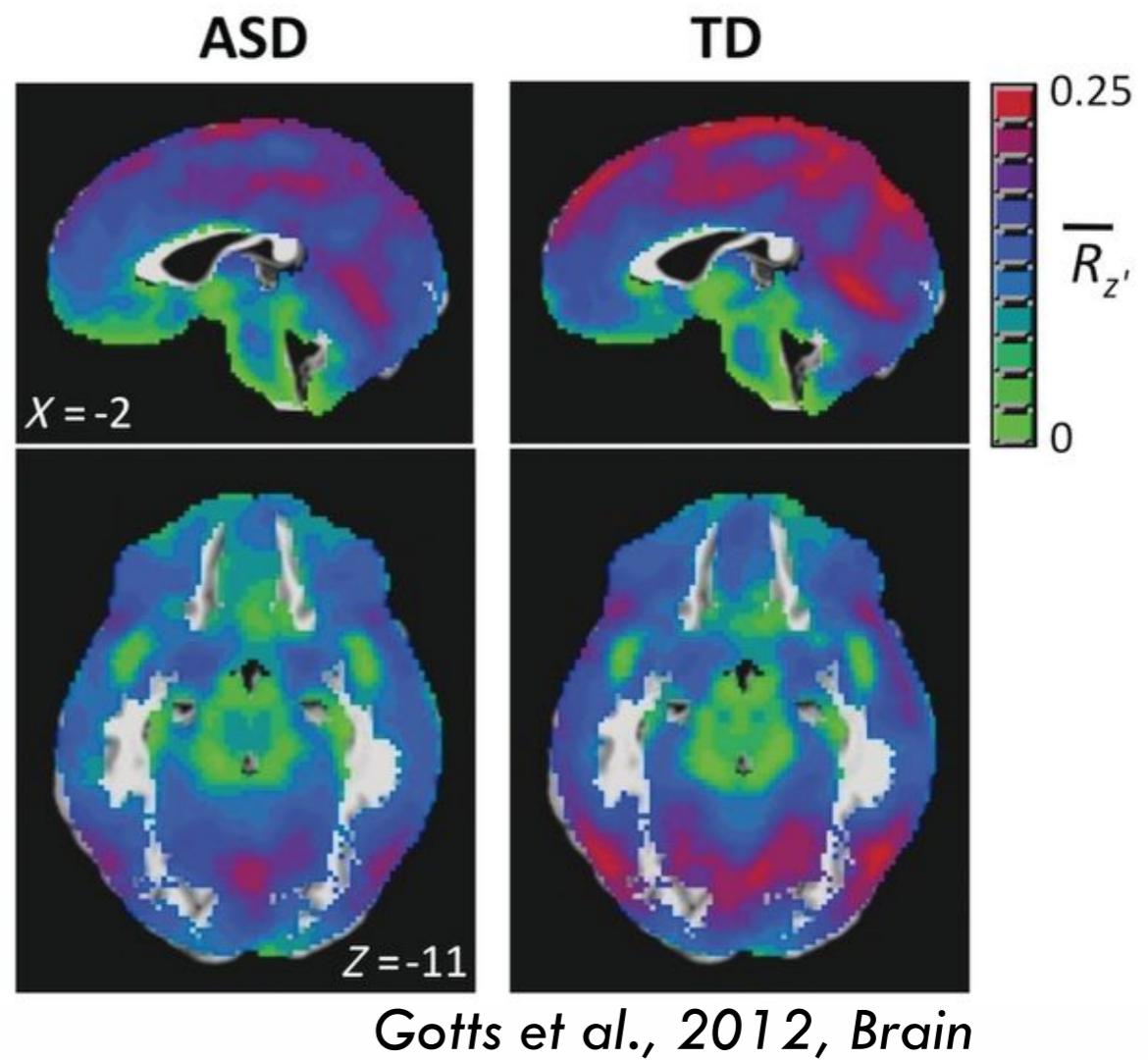


Image from the Human Connectome Project

Autism: A disorder of brain connectivity?

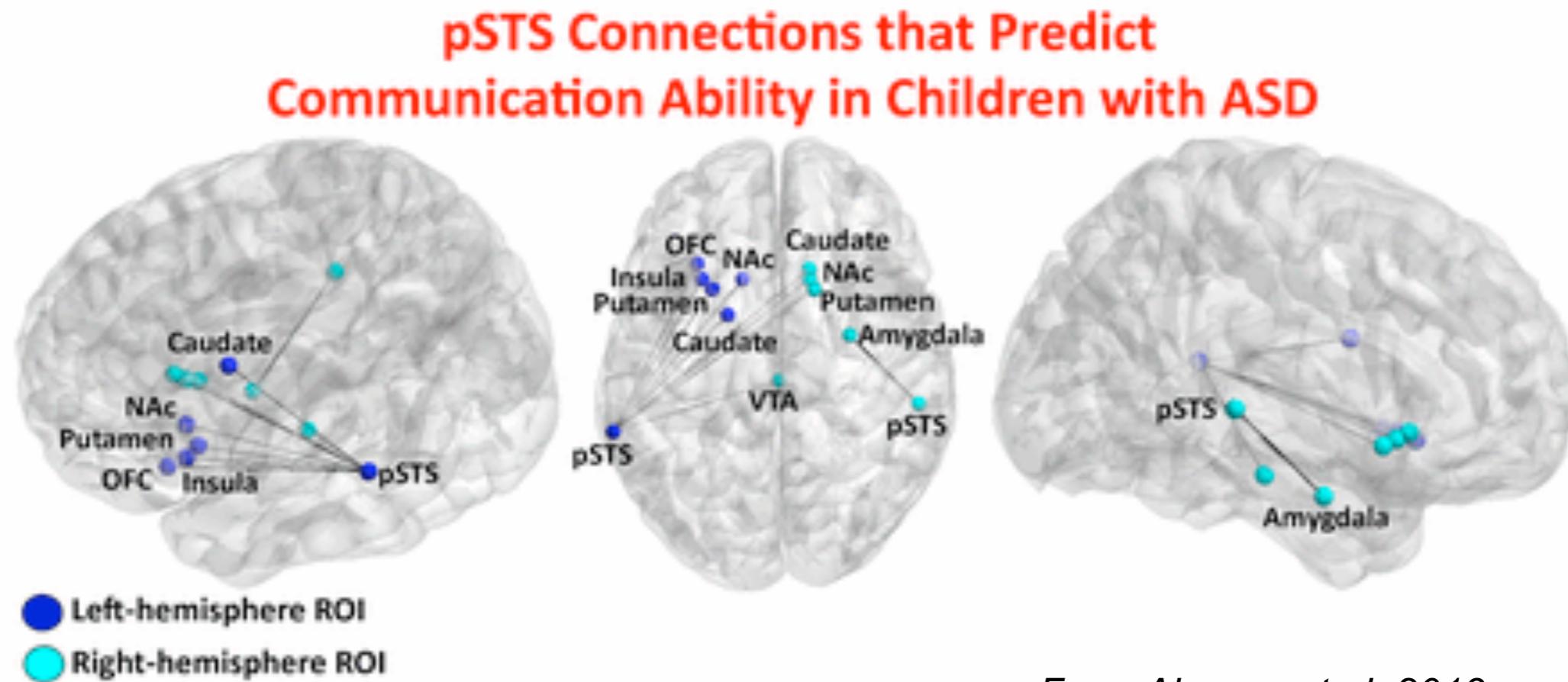
- ASD may be characterized by high local connectivity and reduced long-range connectivity (Just et al., 2004)
- Abnormal connectivity has been reported between components of the social brain rather than everywhere in the brain (Gotts et al. 2012)



Gotts et al., 2012, Brain

Autism: A disorder of brain connectivity?

- Children with ASD show under connectivity between voice-selective regions and reward networks (Abrams et al. 2013)



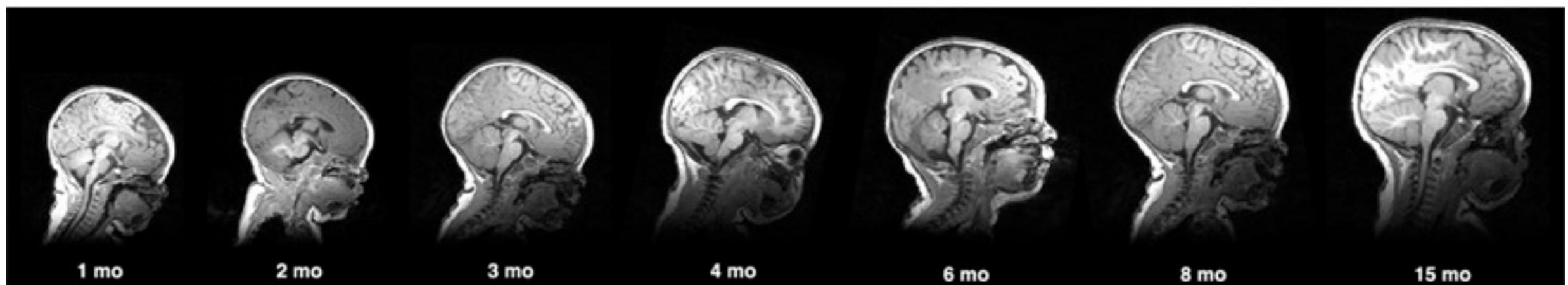
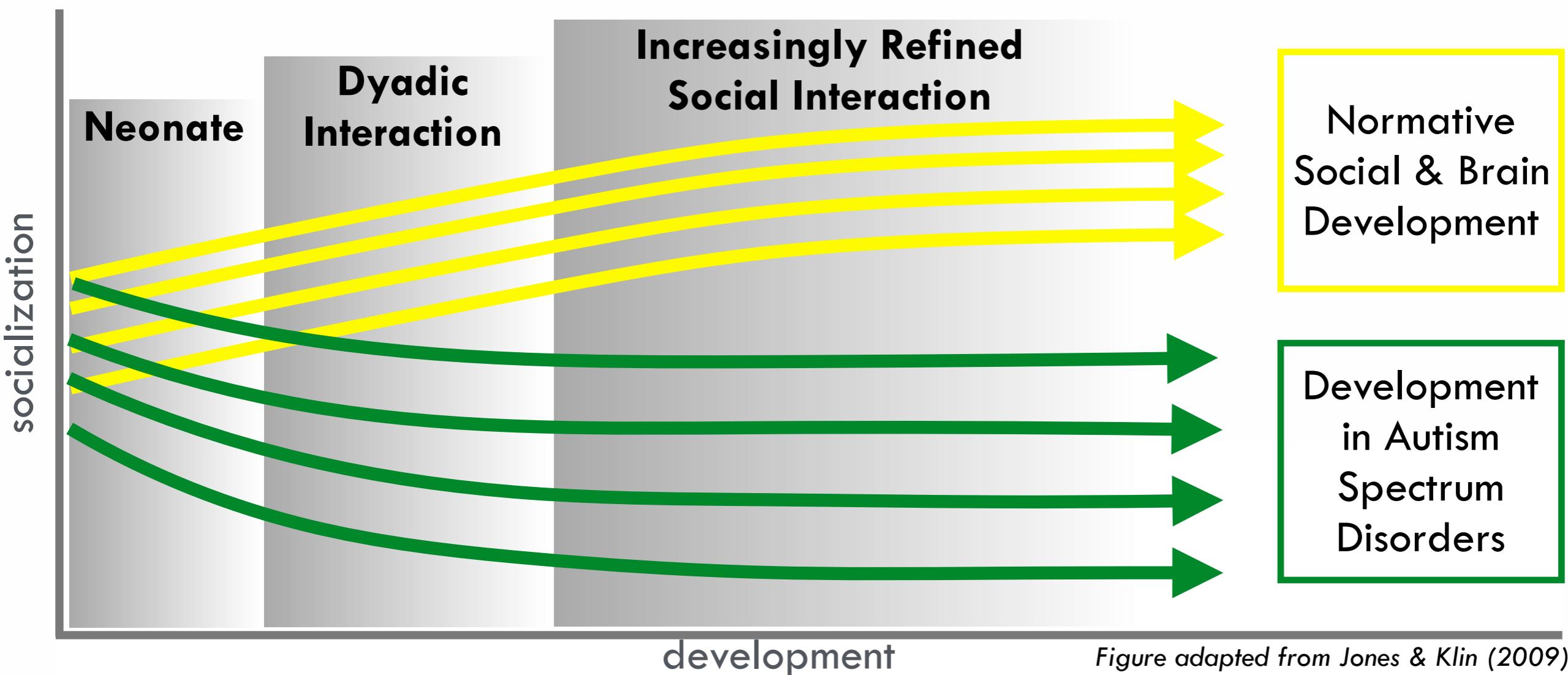
From Abrams et al. 2013

A Developmental Perspective on the Social Brain

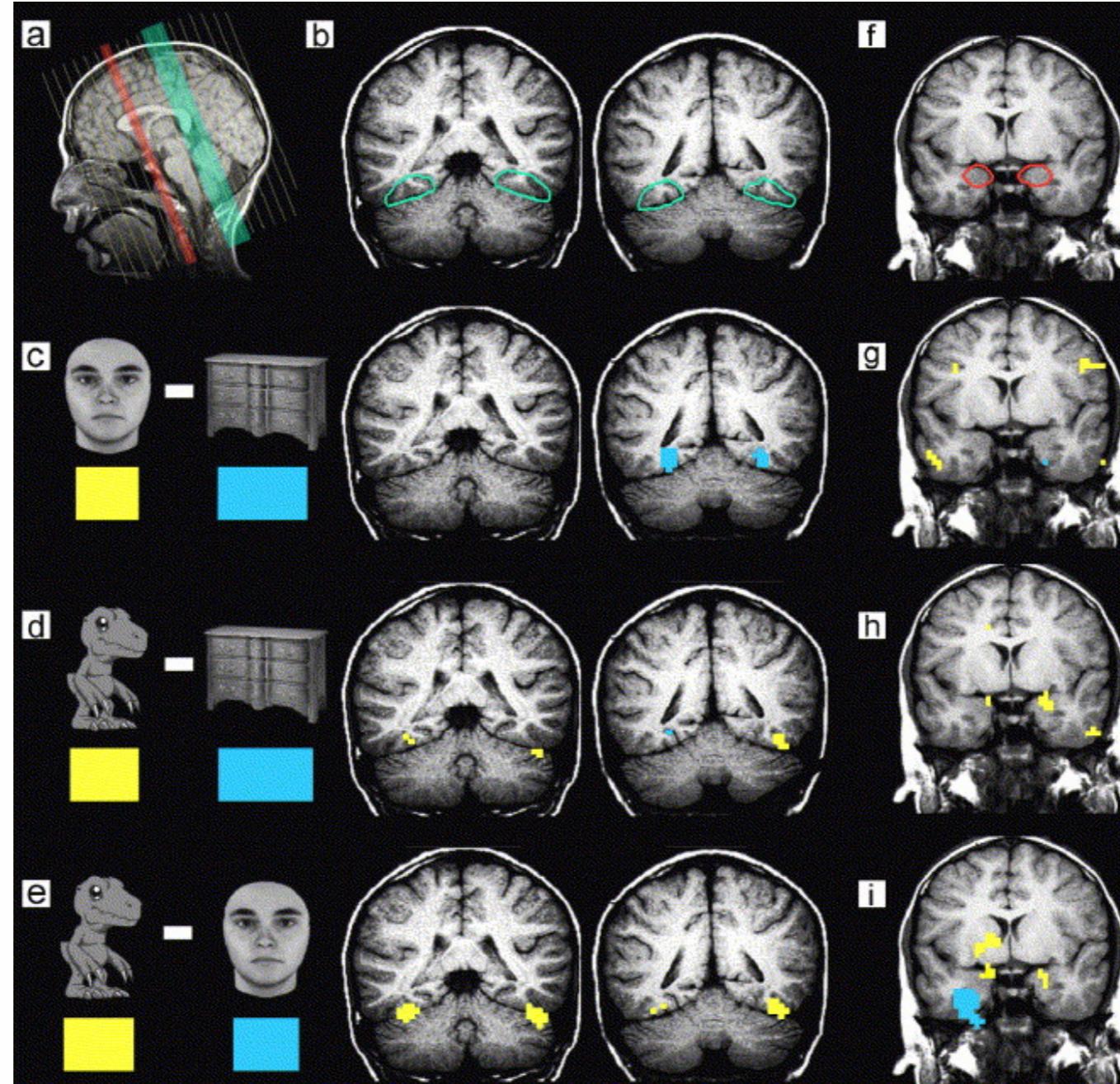
How should we interpret findings of brain dysfunction in ASD?

- Does social brain dysfunction cause the symptoms characteristic of ASD?
- Or, are the observed brain differences the *result* of having ASD?

A Developmental Perspective on the Social Brain



Brain and behavior mutually shape and constrain one another



Grelotti et al., 2005, *Neuropsychologia*

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A Developmental Perspective on the Social Brain

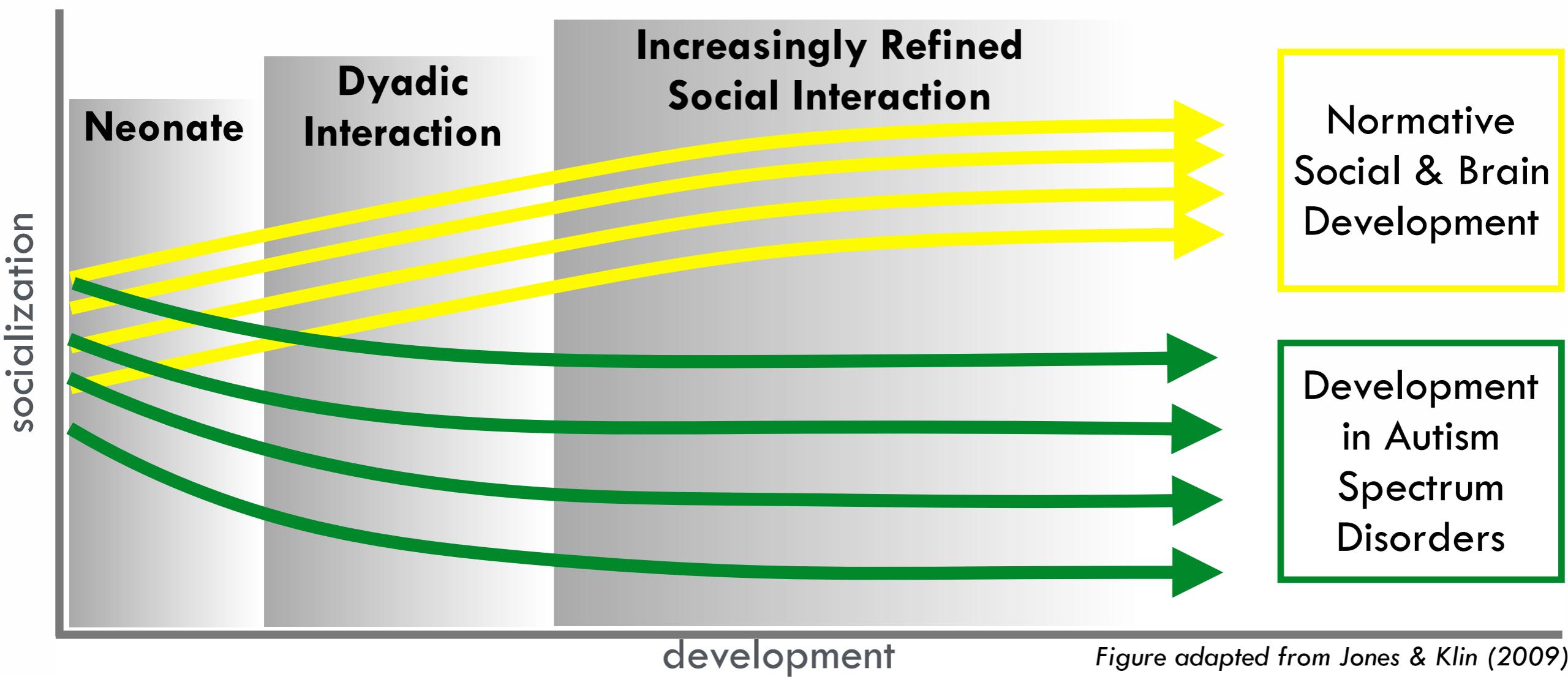
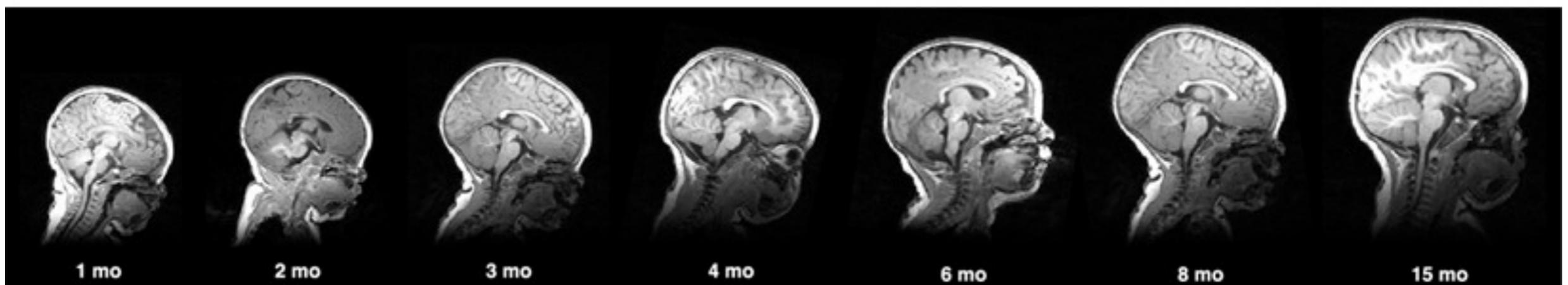


Figure adapted from Jones & Klin (2009)

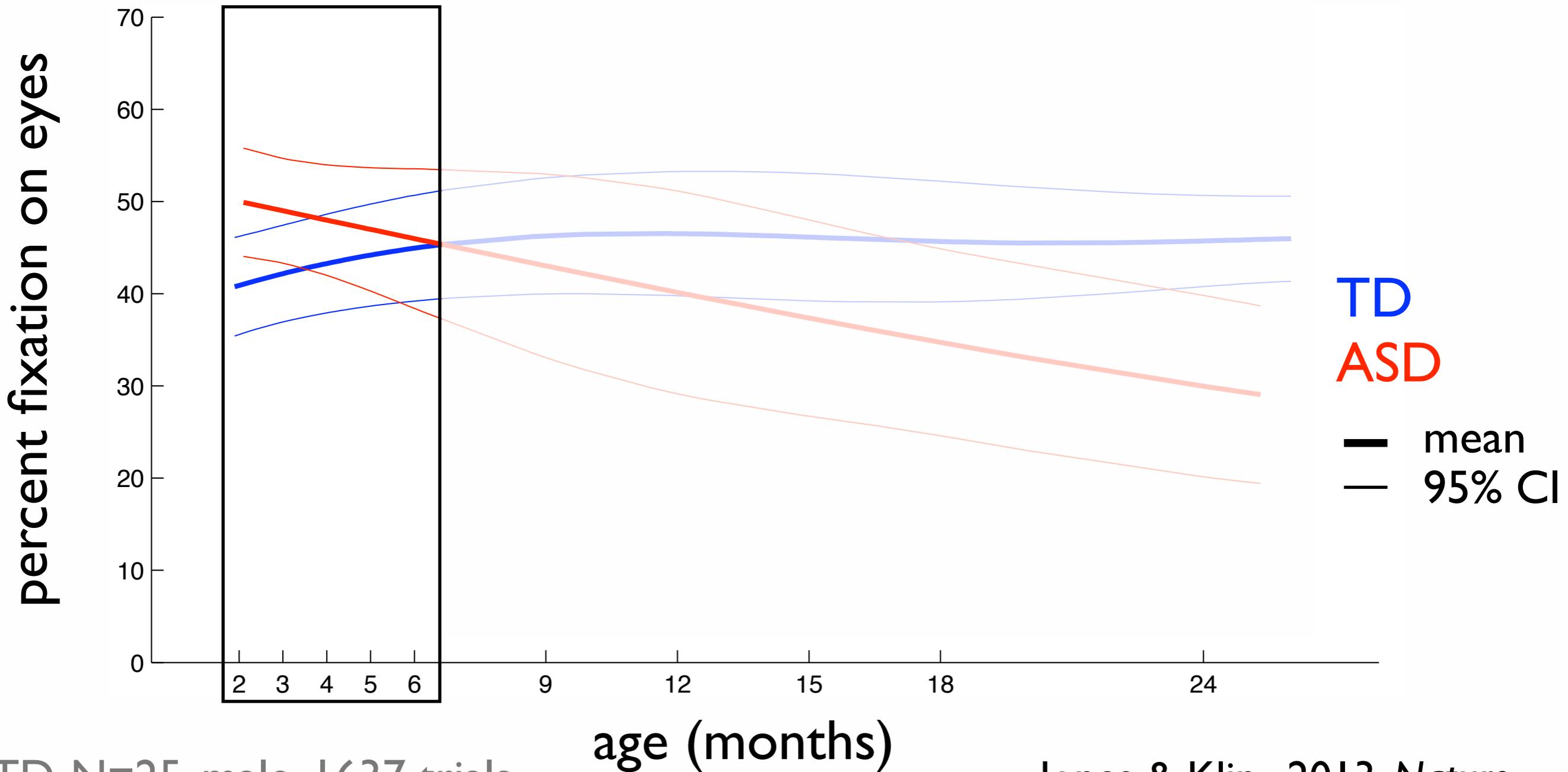


Neuroimaging Studies of Infants at High and Low-Risk for ASD



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Eye Fixation in Infants with ASD Relative to Typically-Developing Norms



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

Jones & Klin, 2013, *Nature*

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The Development of Smiling

- Birth to ~2 months
 - newborns smile spontaneously in the absence of external stimulation
 - occurs most often during sleep or during transitions to wakefulness (Emde, 1972)
- ~2 months
 - social smiling (smiling that is linked to the actions or vocalizations of a communicative partner) emerges (Emde, 1972)

Social Smiling in 2- to 5-Month-Old Infants



Rachel Sandercock



Caregiver Behavior

- Neutral
- Talking
- Smiling
- Smiling and talking

Infant Affect

- Neutral
- Fussy
- Smiling

Infant Gaze

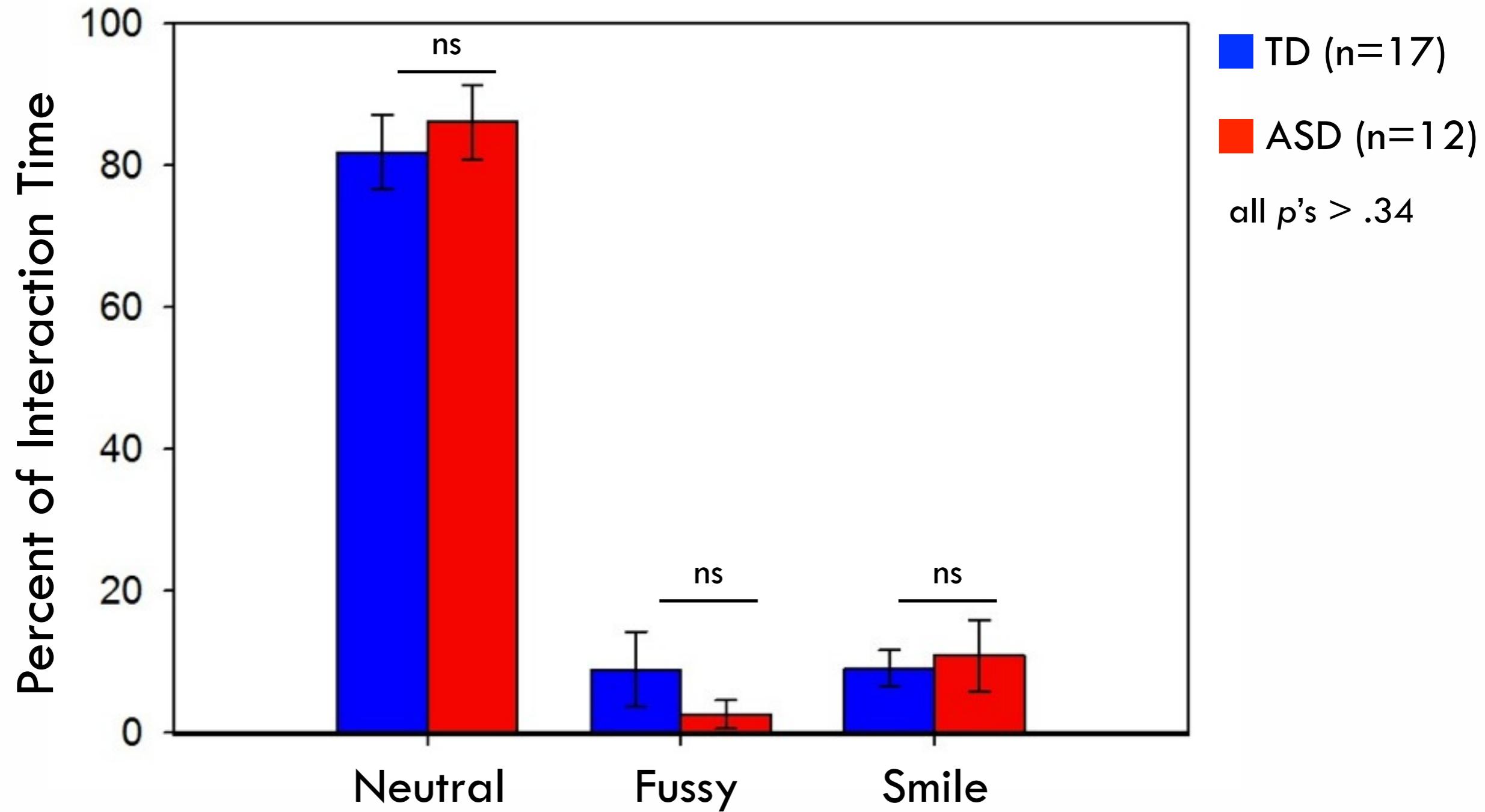
- Towards caregiver
- Away from caregiver

Participants

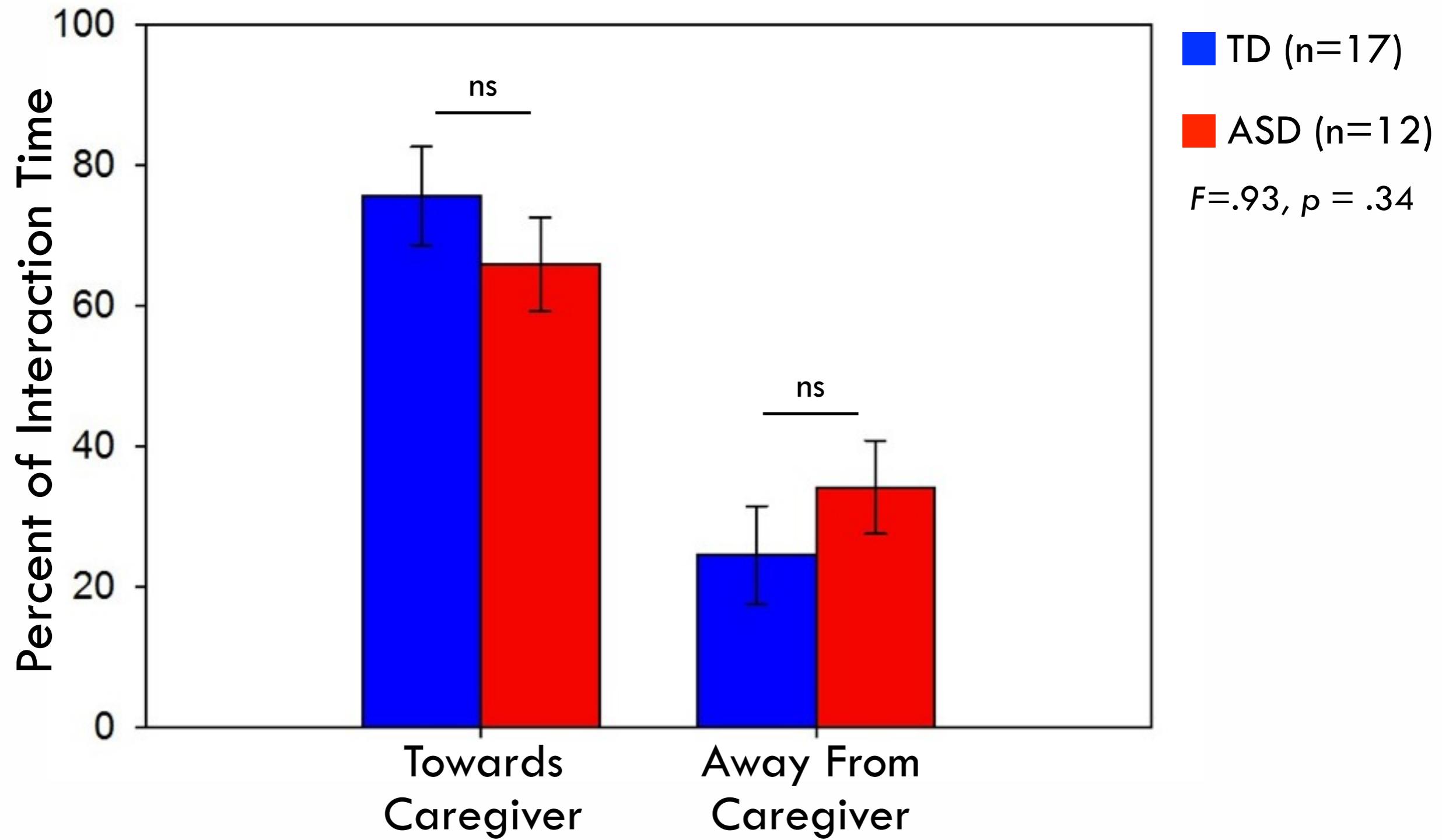
- Infants at high- and low-risk for ASD were enrolled at birth
- Live interactions were recorded at **2 to 5 months** of age
- Diagnostic status was ascertained at **24 months** and confirmed at **36 months**

	TD (n=17)	ASD (n=12)	F values and significance
sex (M/F)	10/7	9/3	
age at testing (months)	3.48(.98)	3.87(.62)	1.47, <i>p</i> =.24
nonverbal function at 24 months	31(5.32)	25.36(5.50)	7.12, <i>p</i> <.05
verbal function at 24 months	29.97(4.06)	22.72(6.19)	13.56, <i>p</i> <.01
ADOS 1 score at 24 months	3.38(3.03)	11.91(5.61)	26.22, <i>p</i> <.001

Infant Behavior During Infant-Caregiver Interactions

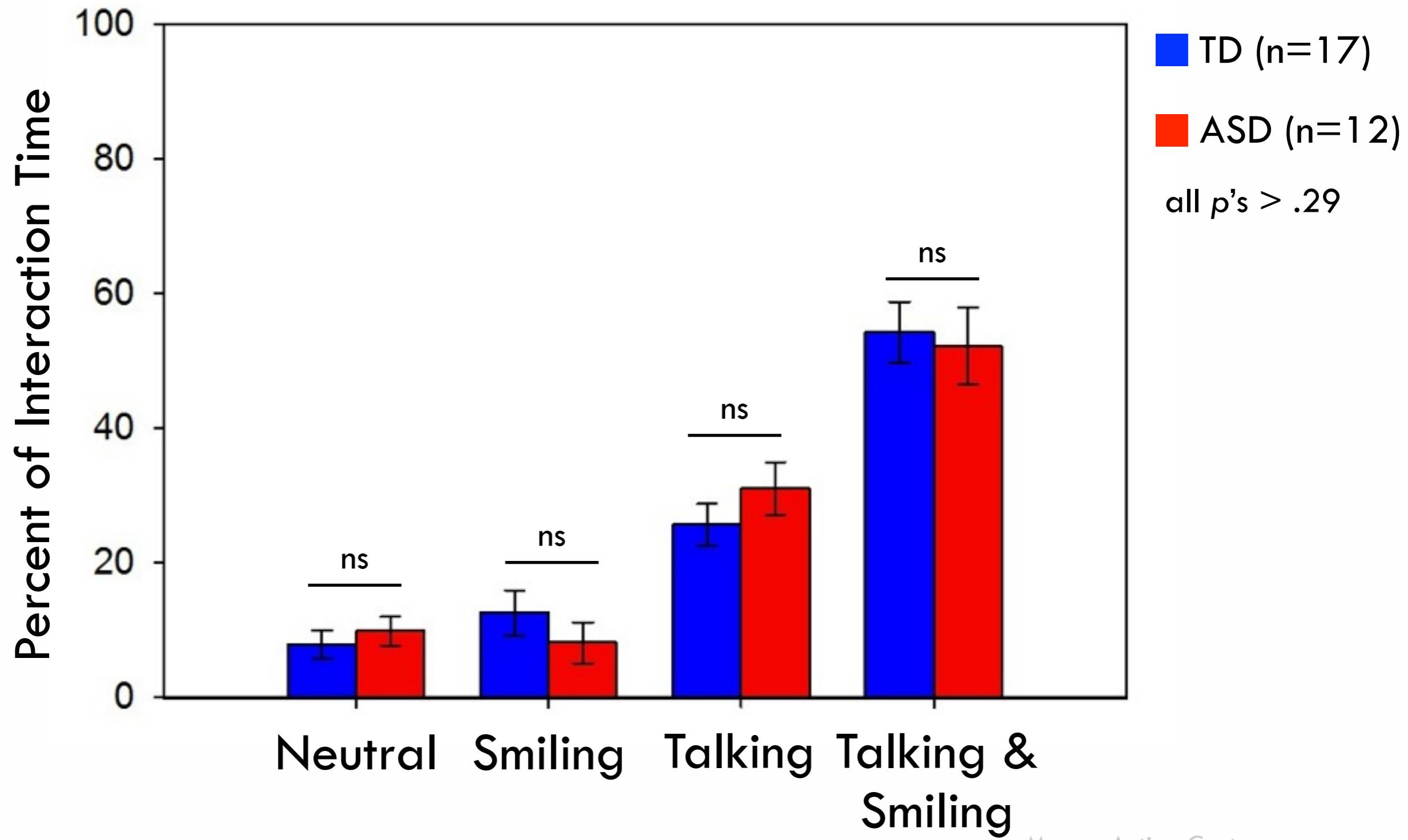


Infant Gaze During Infant-Caregiver Interactions



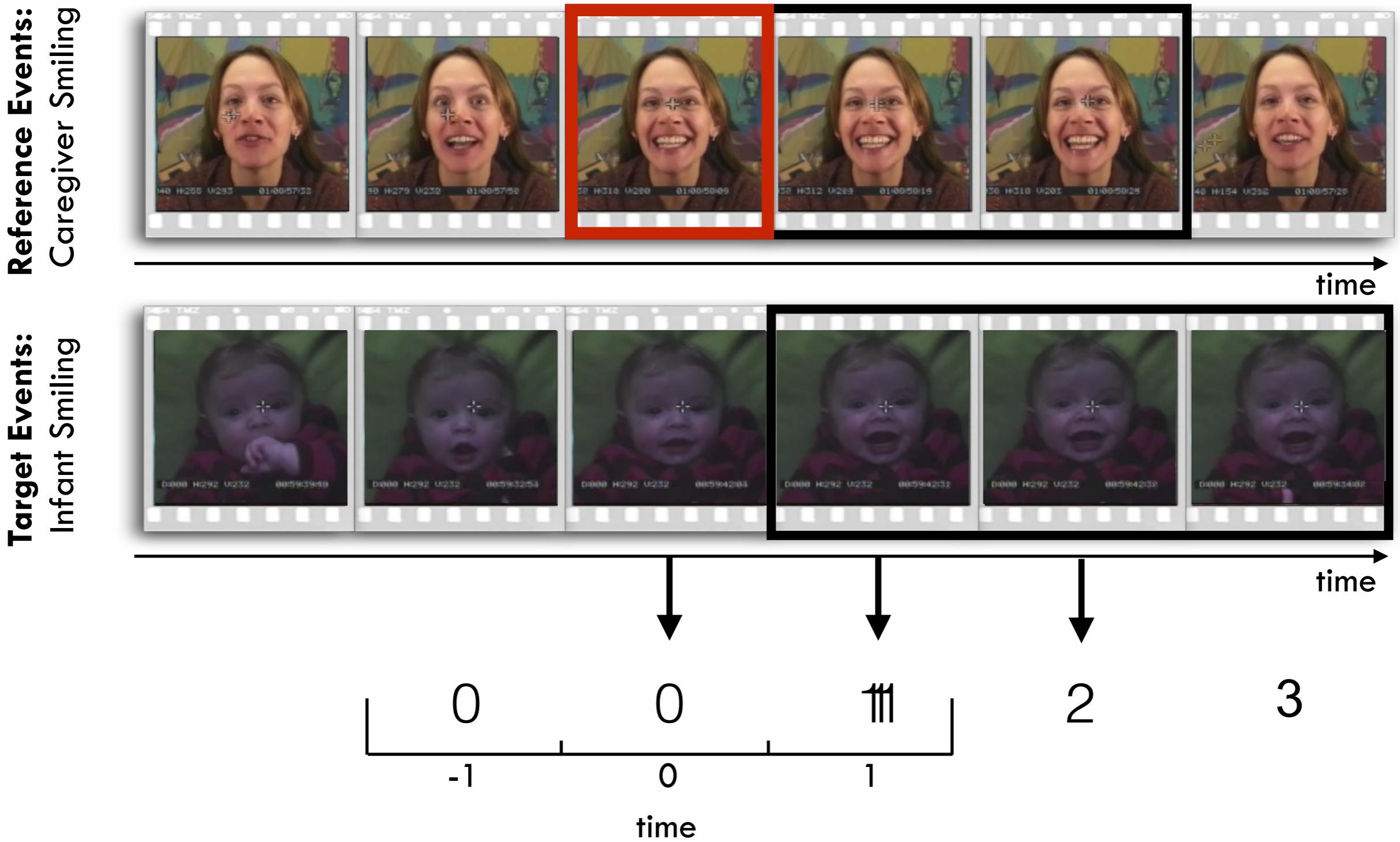
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Caregiver Behavior During Infant-Caregiver Interactions



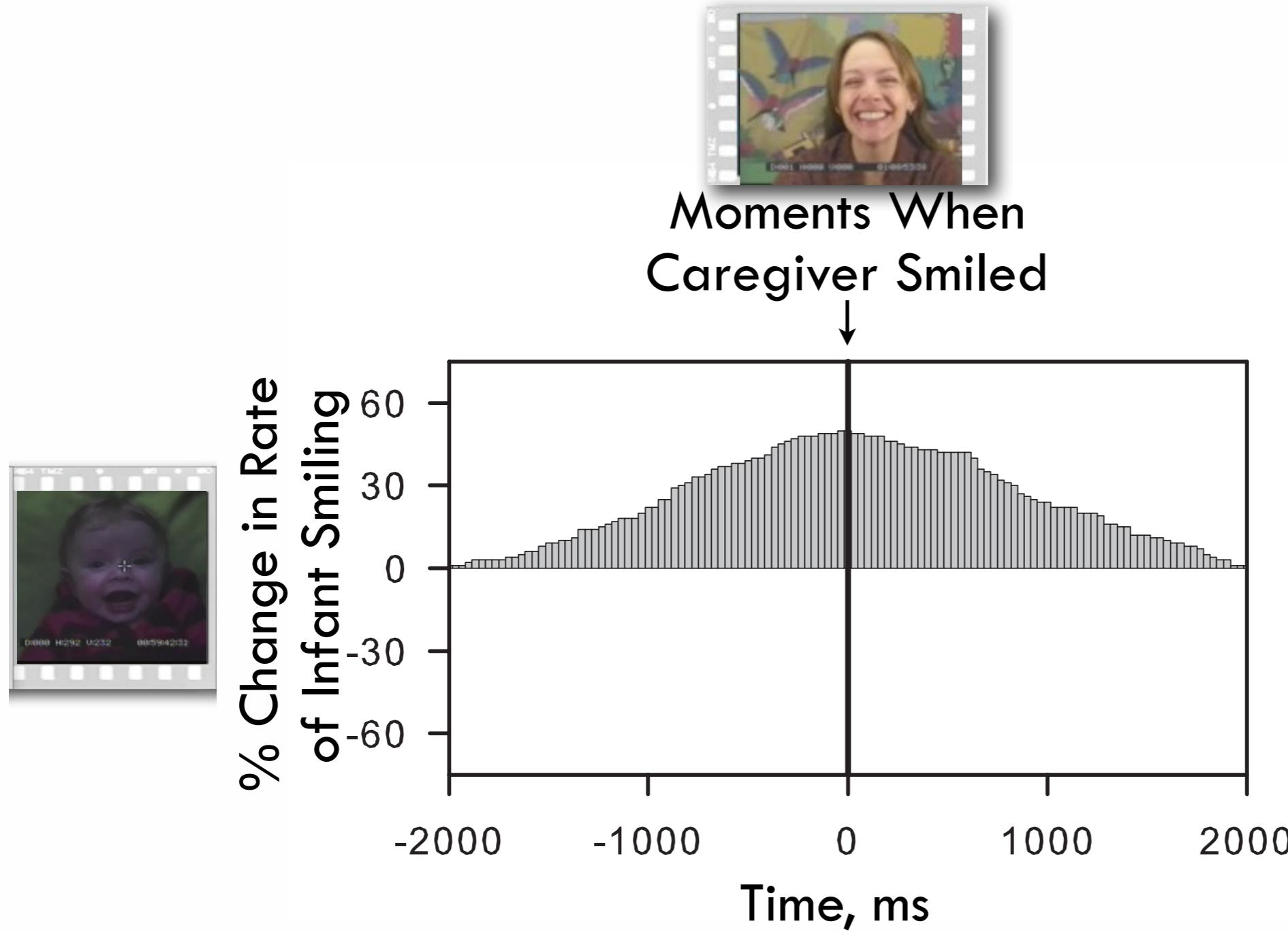
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Measuring Contingency Between Infant Smiling and Caregiver Actions: Peristimulus Time Histograms

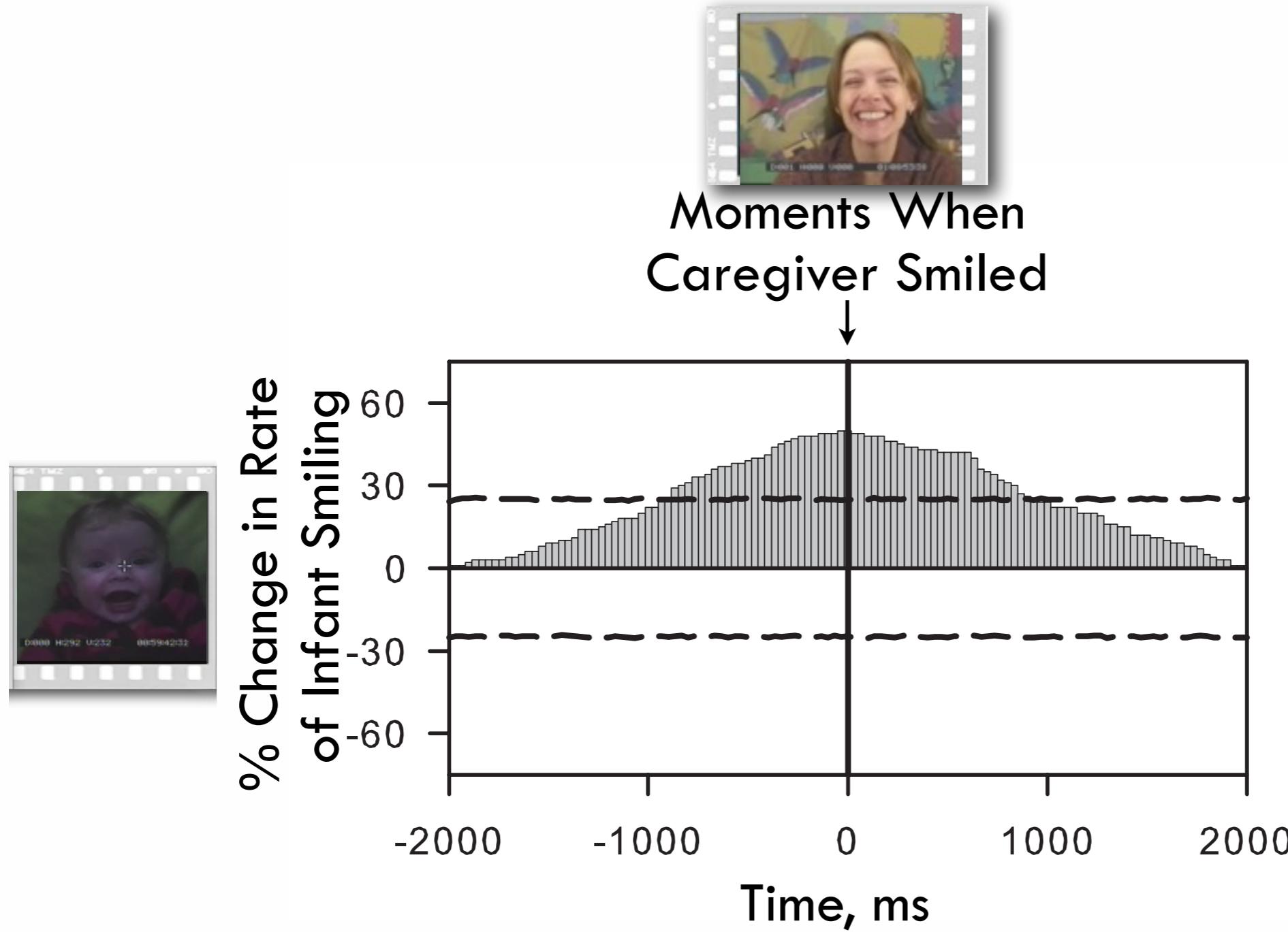


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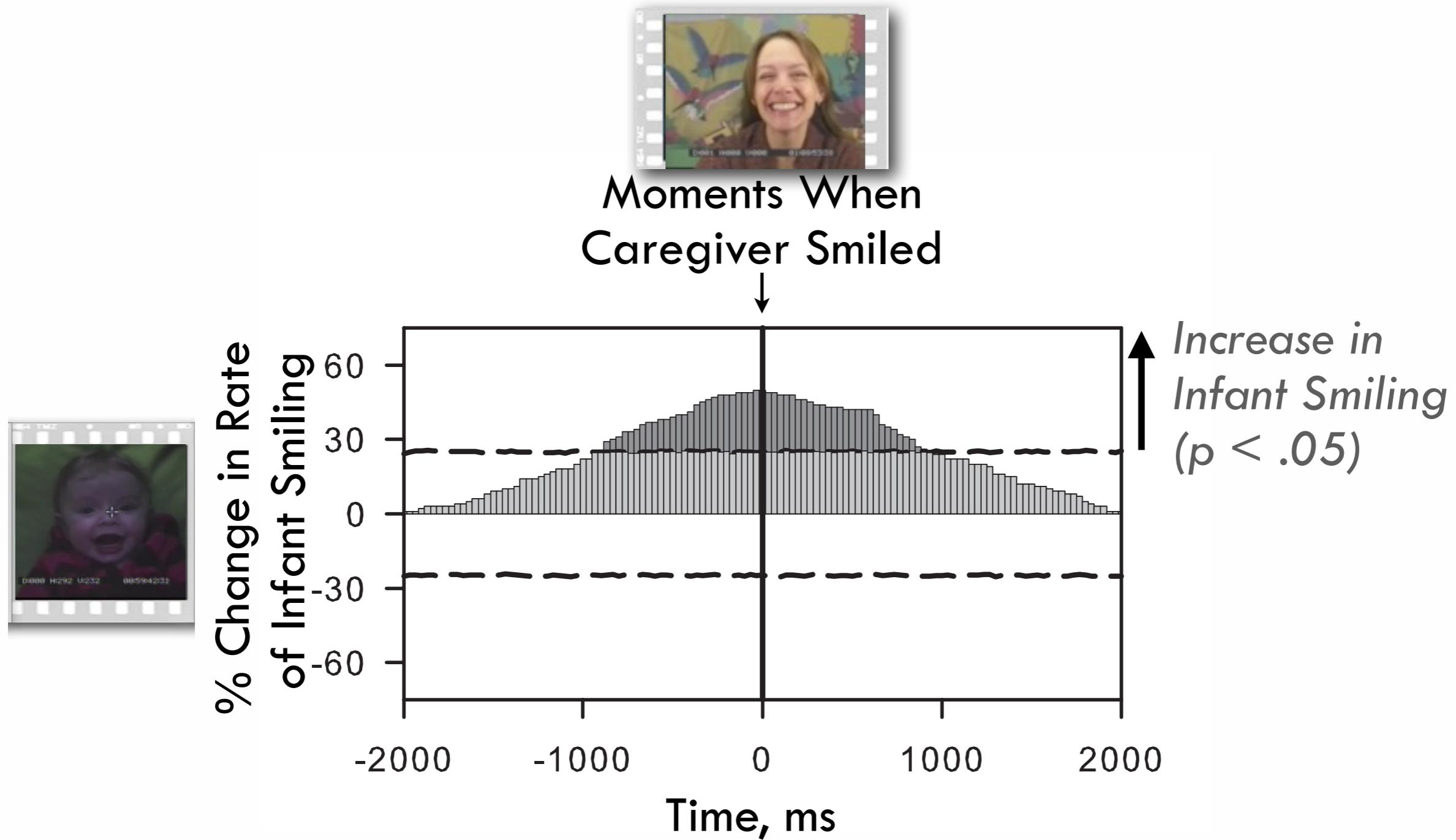
Measuring contingency between infant smiling and caregiver actions



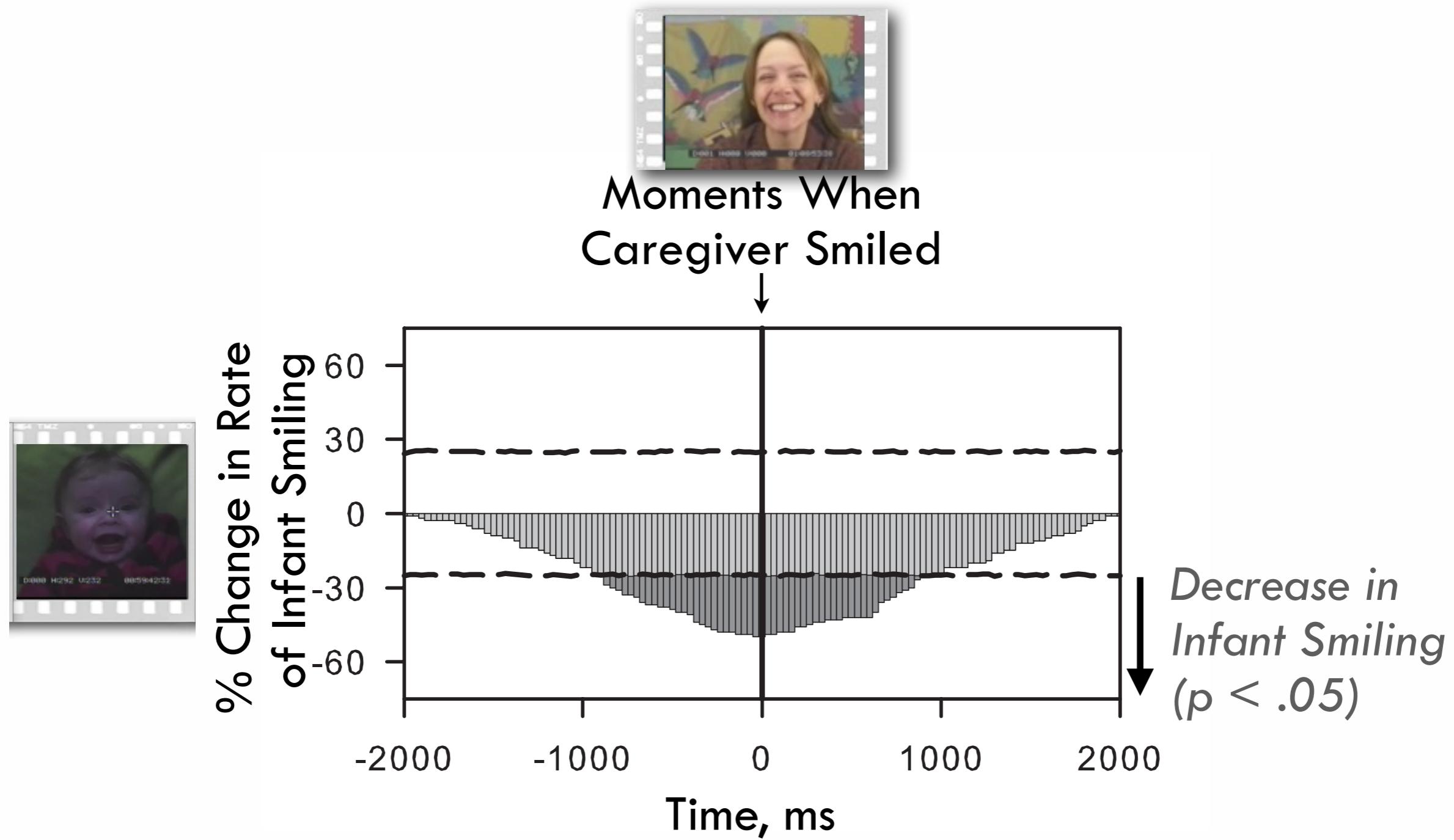
Measuring contingency between infant smiling and caregiver actions



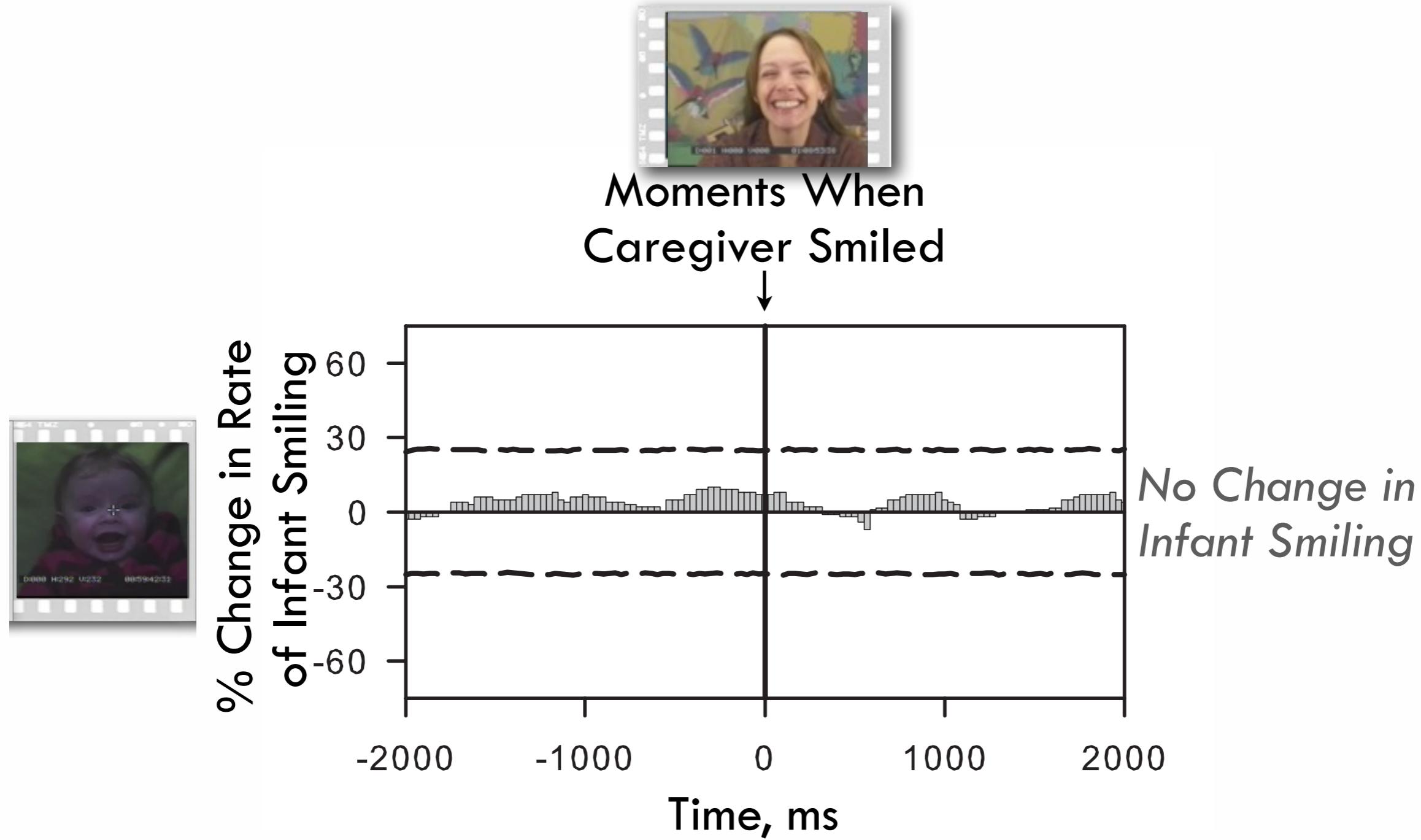
Measuring contingency between infant smiling and caregiver actions



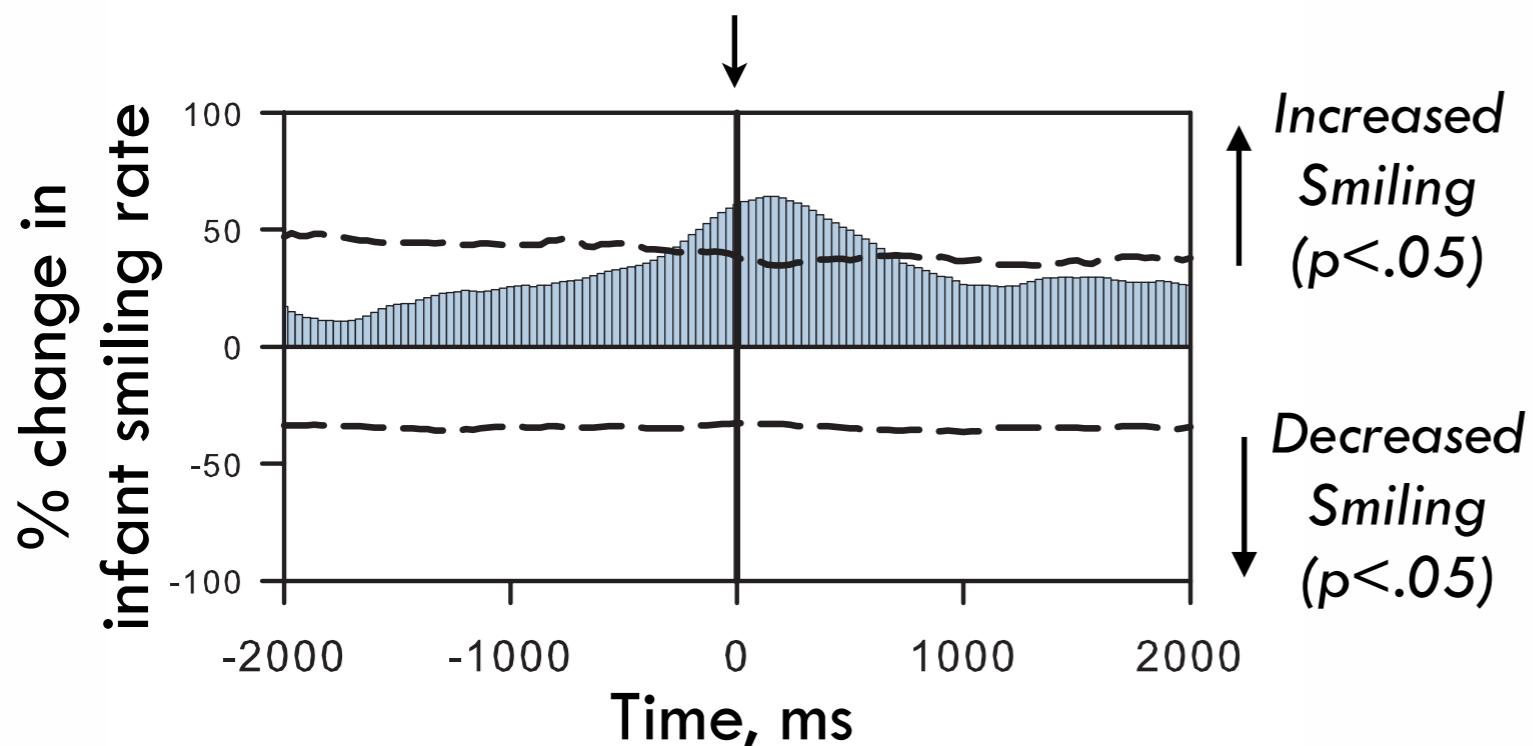
Measuring contingency between infant smiling and caregiver actions



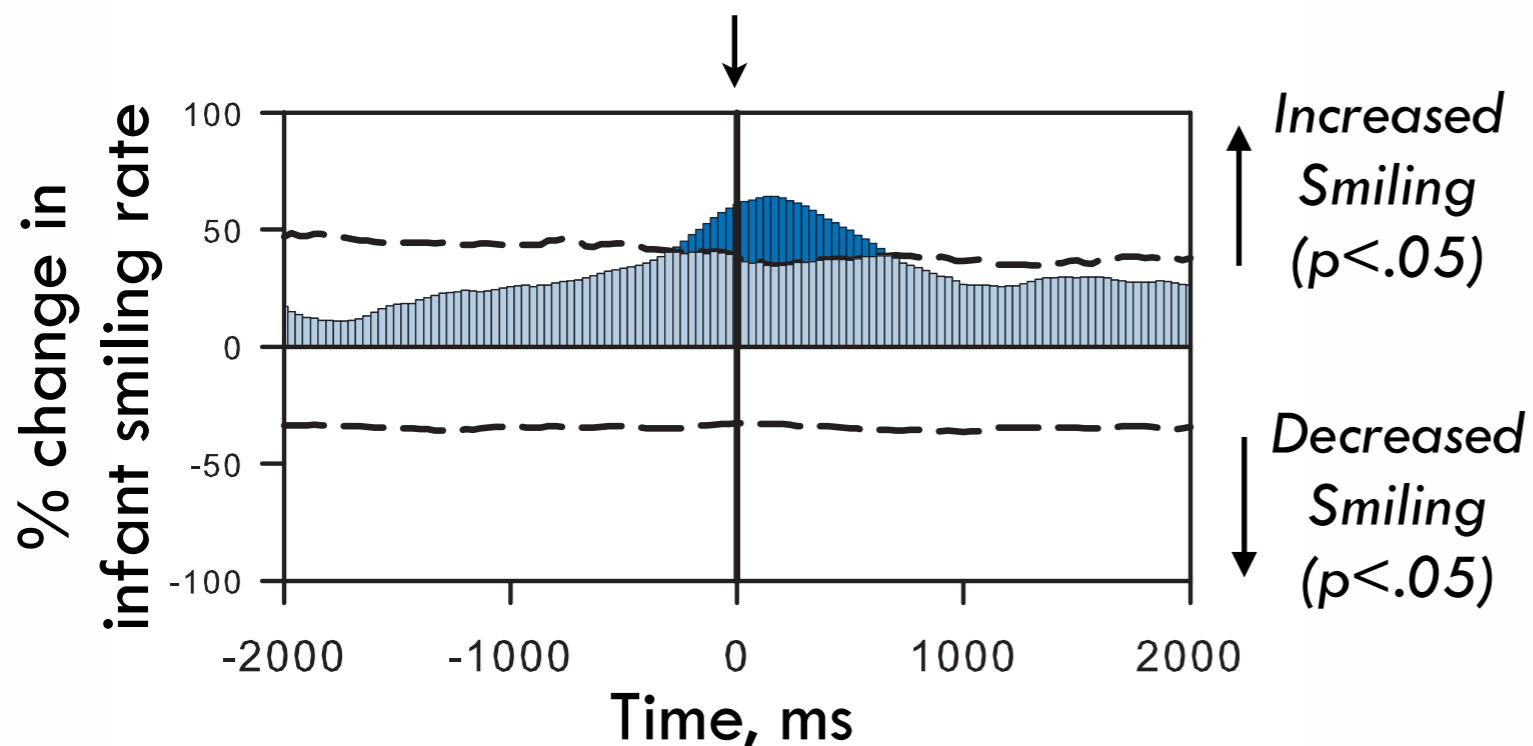
Measuring contingency between infant smiling and caregiver actions



Moments When Caregiver Smiled

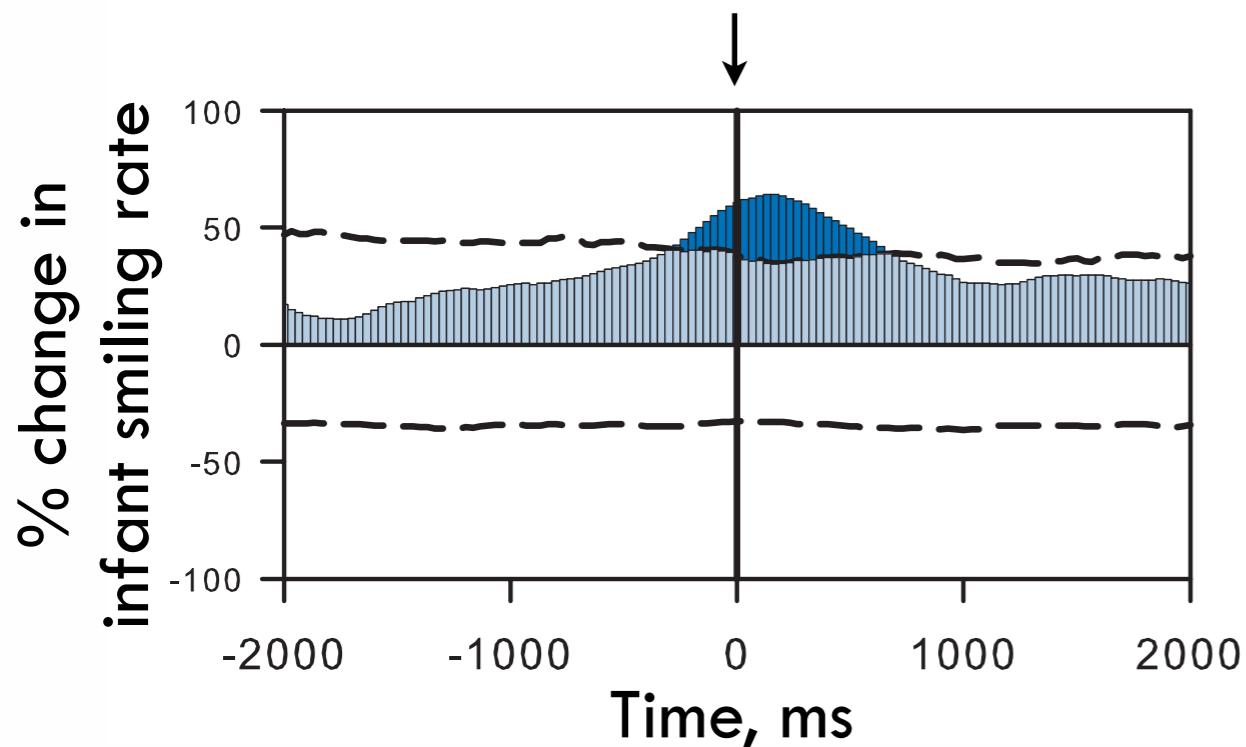


Moments When Caregiver Smiled

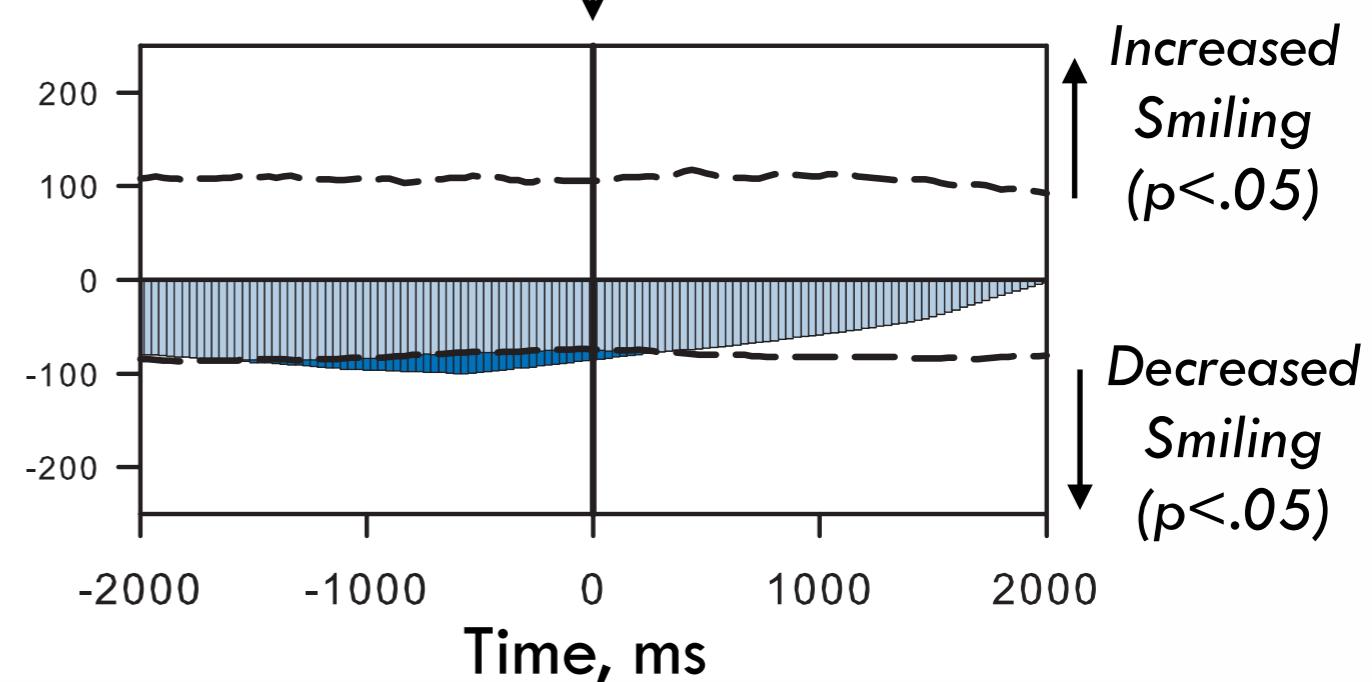


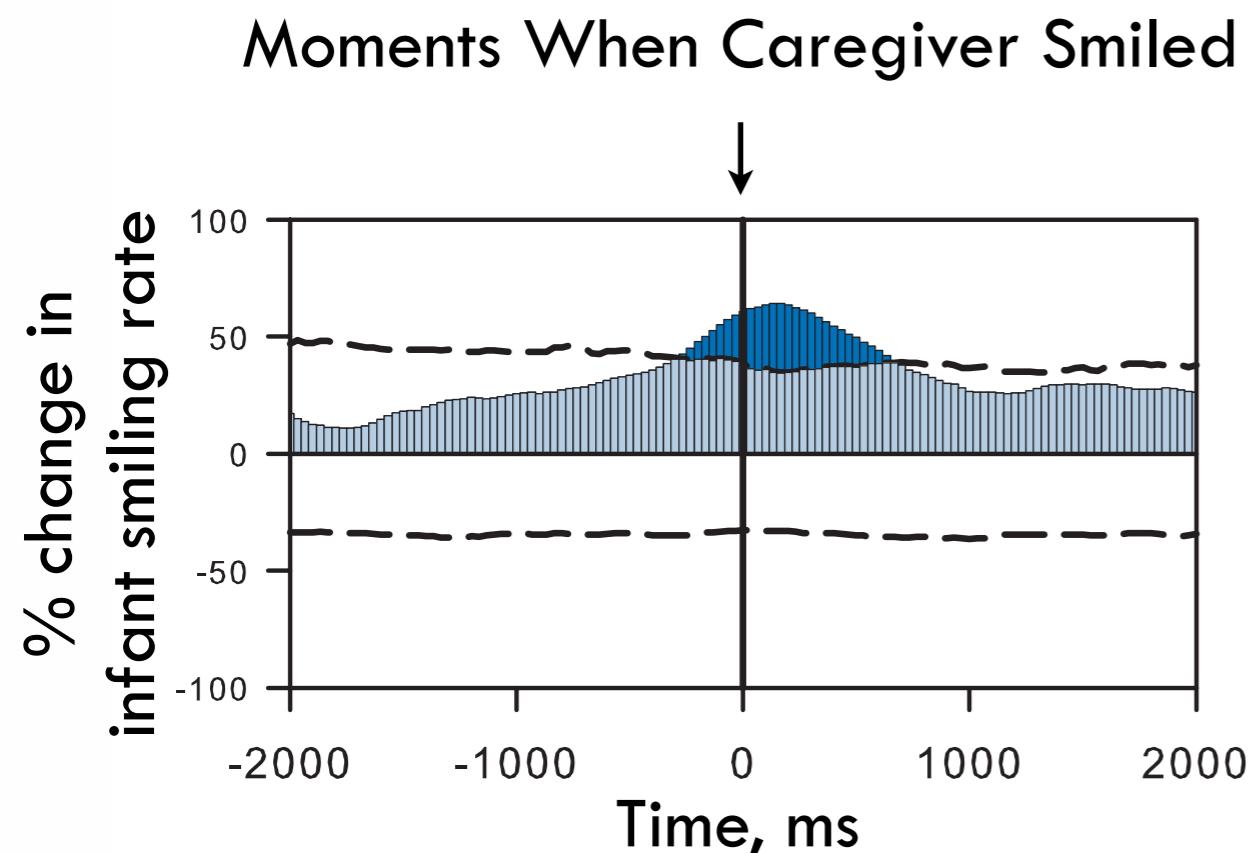
TD

Moments When Caregiver Smiled

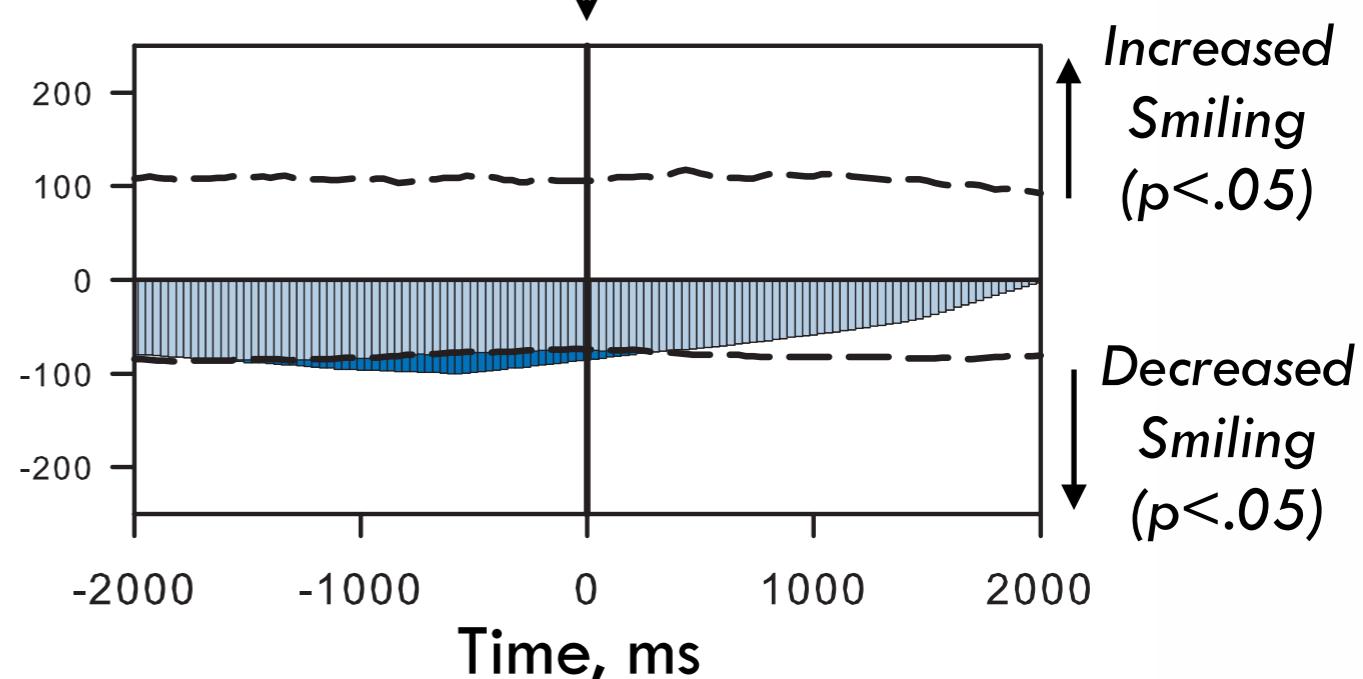
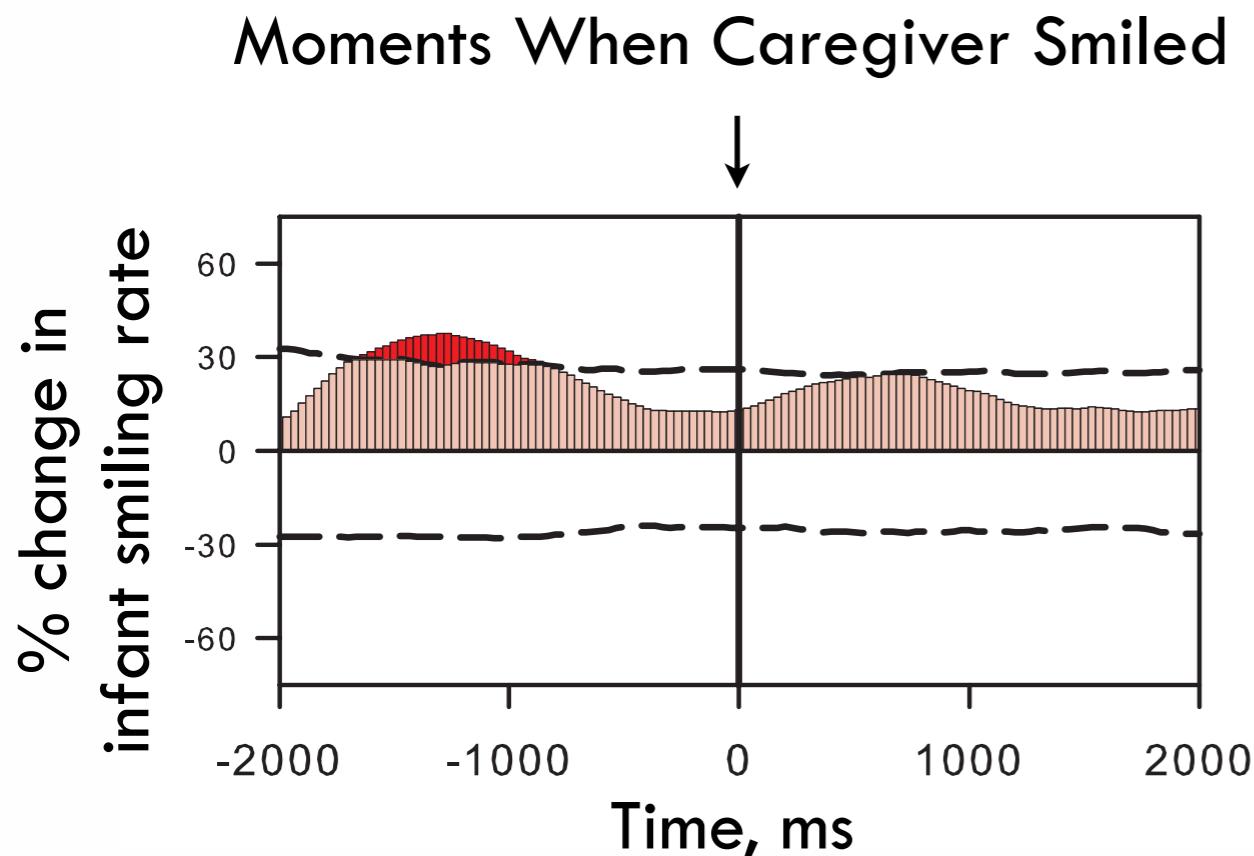


Moments When Caregiver Talked *Without* Smiling

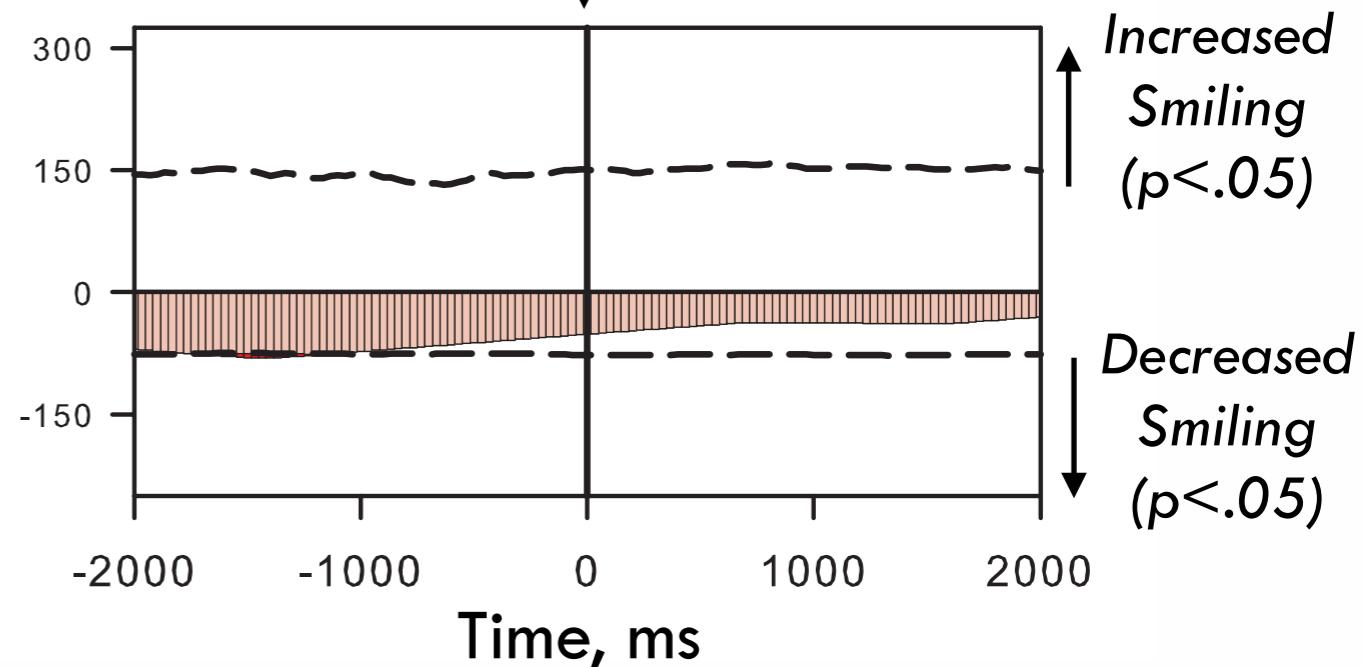


TD

Moments When Caregiver Talked Without Smiling

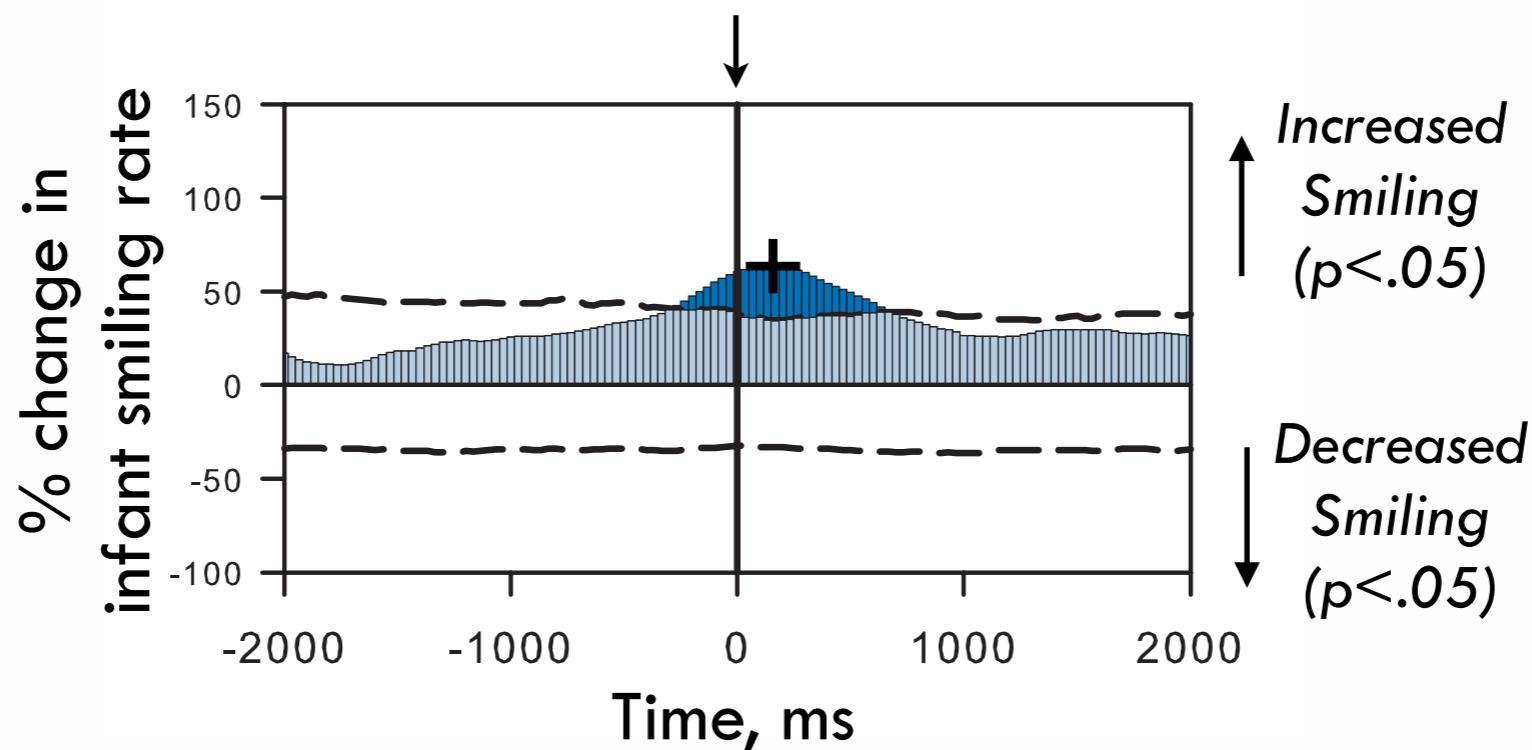
**ASD**

Moments When Caregiver Talked Without Smiling



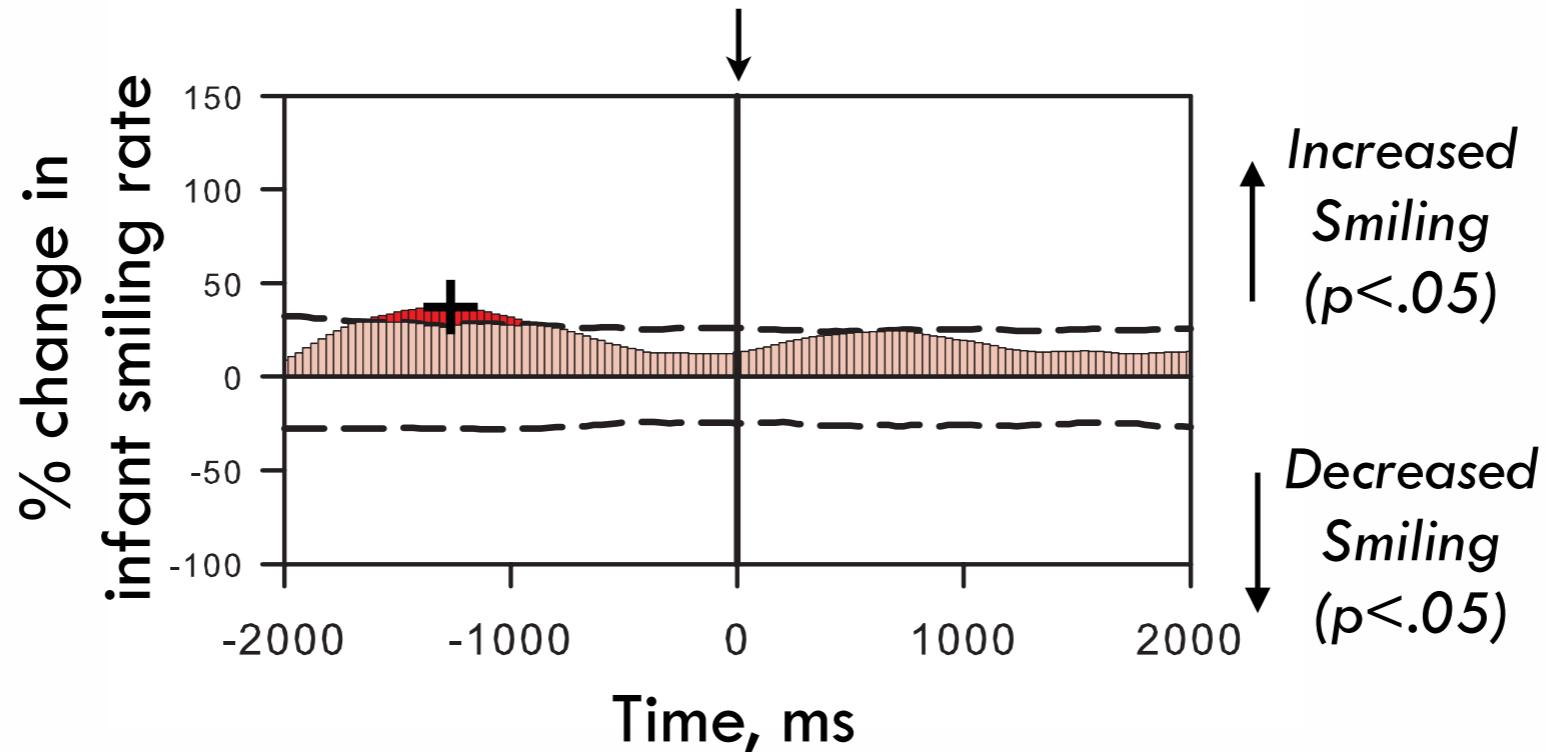
TD

Moments When Caregiver Smiled



ASD

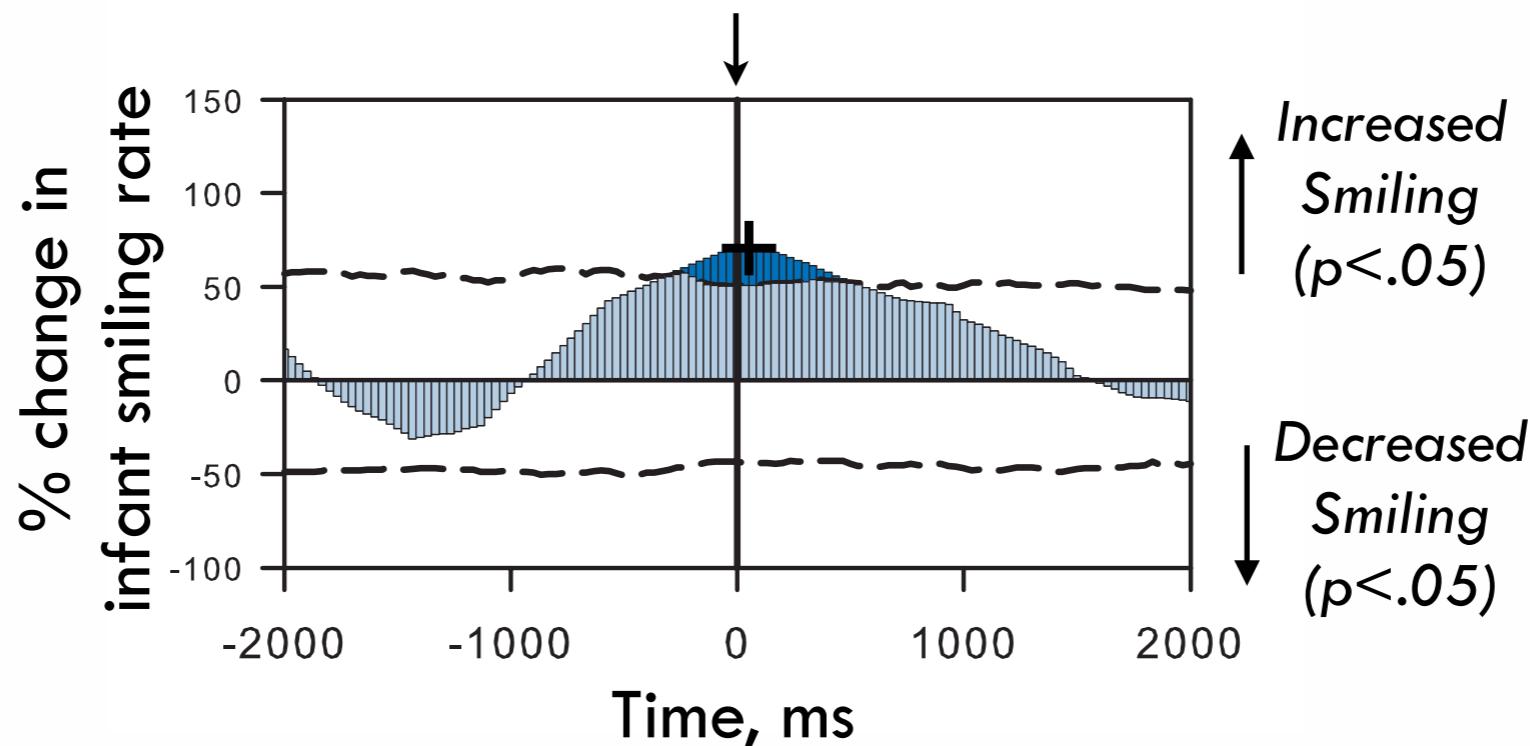
Moments When Caregiver Smiled



TD

Bootstrap Sample # 1

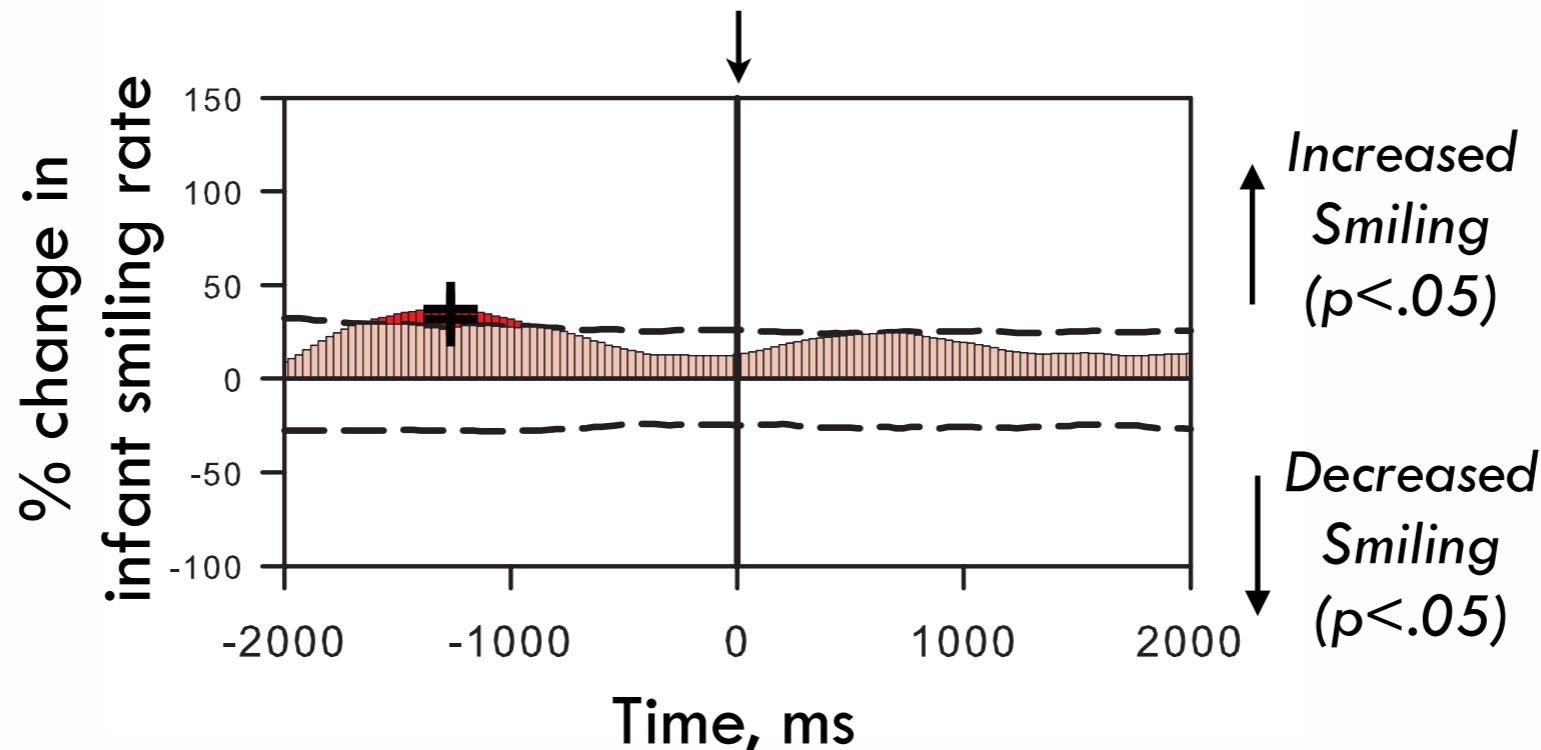
Moments When Caregiver Smiled



ASD

Bootstrap Sample # 1

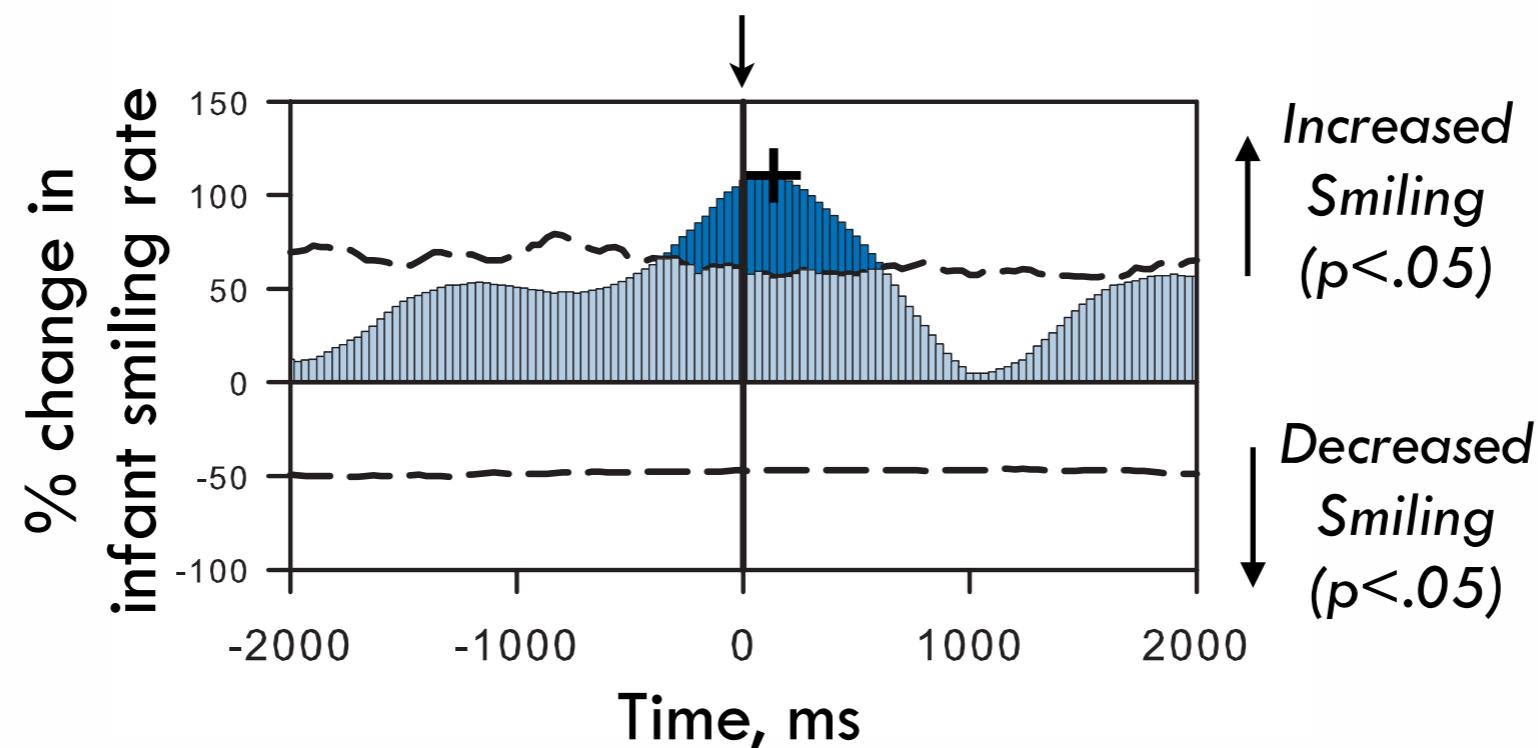
Moments When Caregiver Smiled



TD

Bootstrap Sample # 2

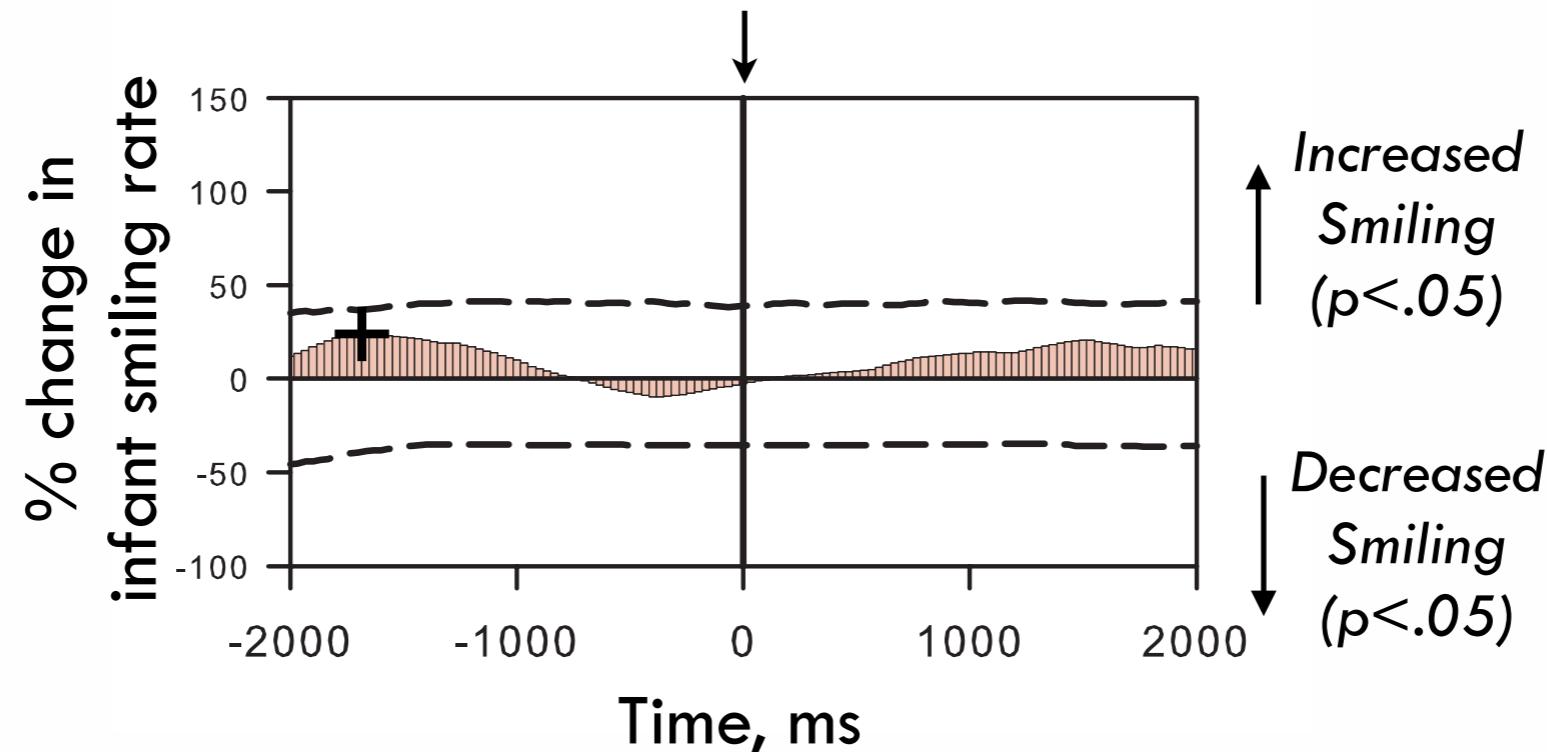
Moments When Caregiver Smiled



ASD

Bootstrap Sample # 2

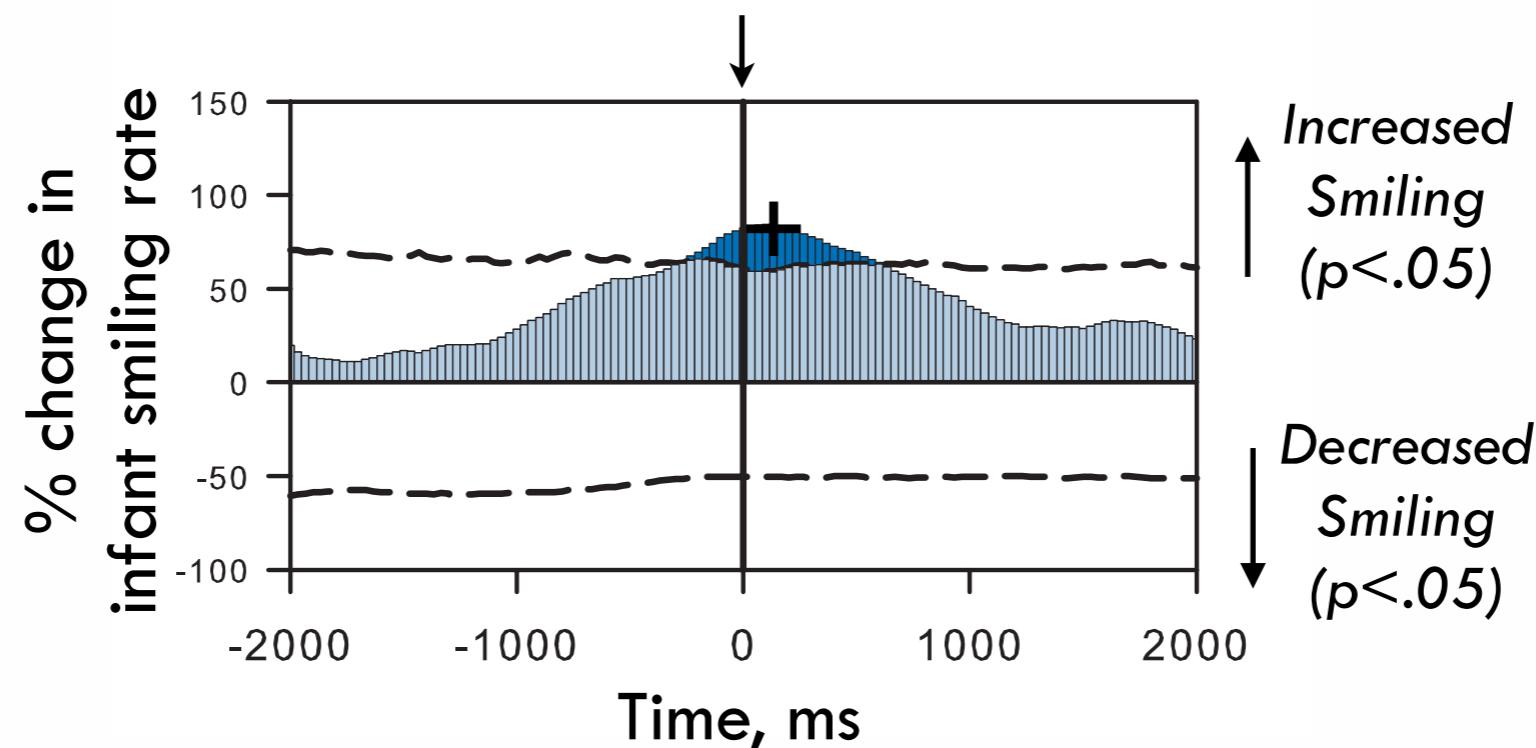
Moments When Caregiver Smiled



TD

Bootstrap Sample # 3

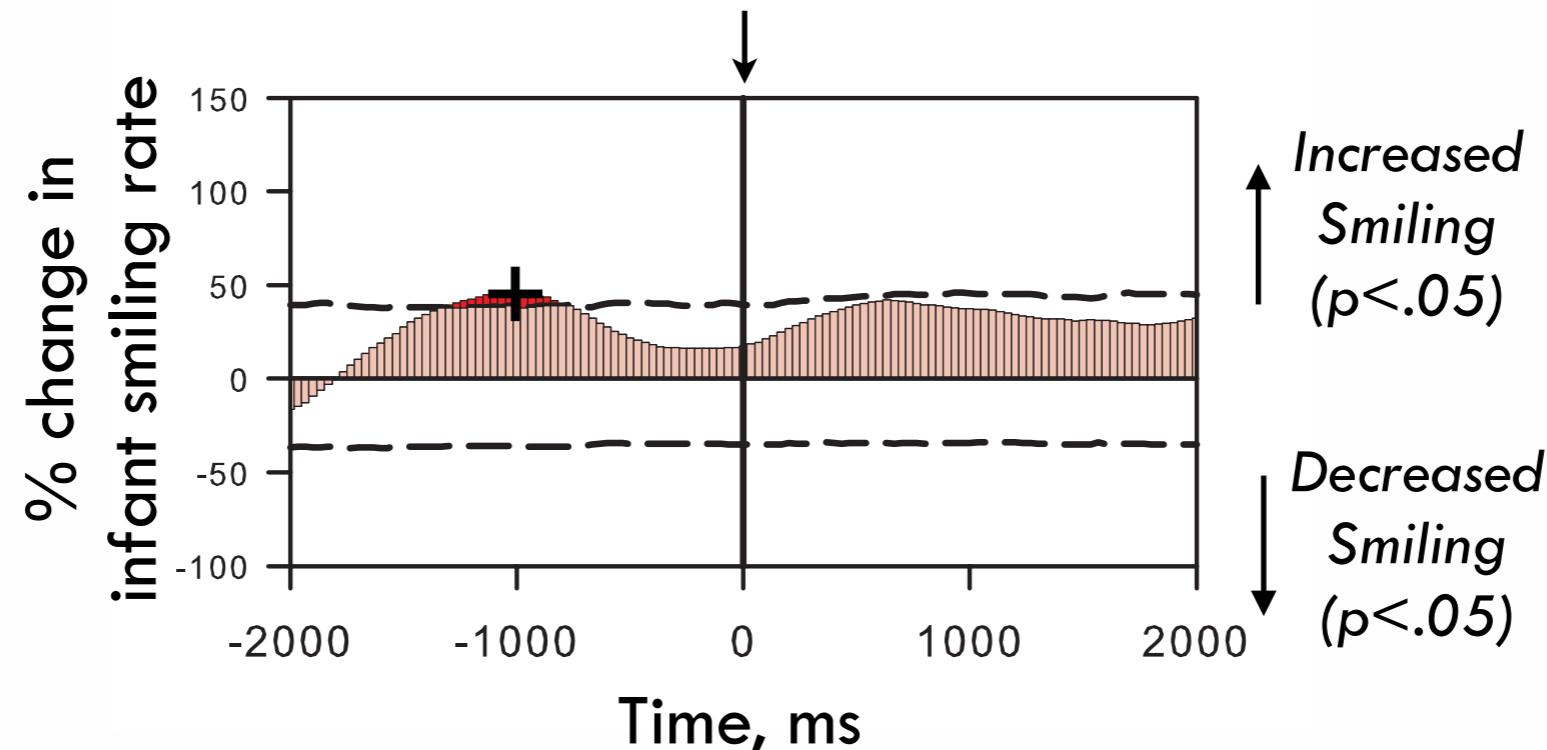
Moments When Caregiver Smiled



ASD

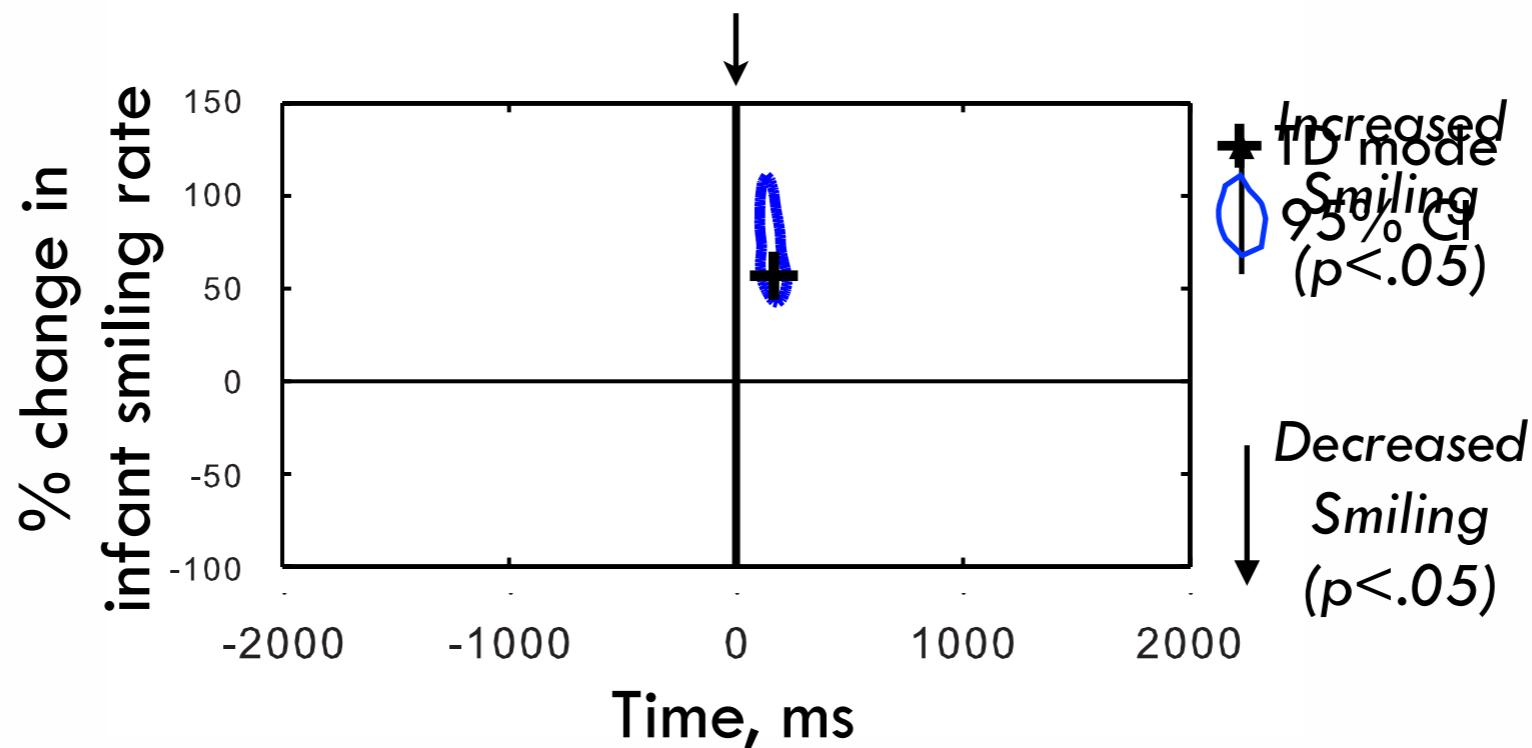
Bootstrap Sample # 3

Moments When Caregiver Smiled



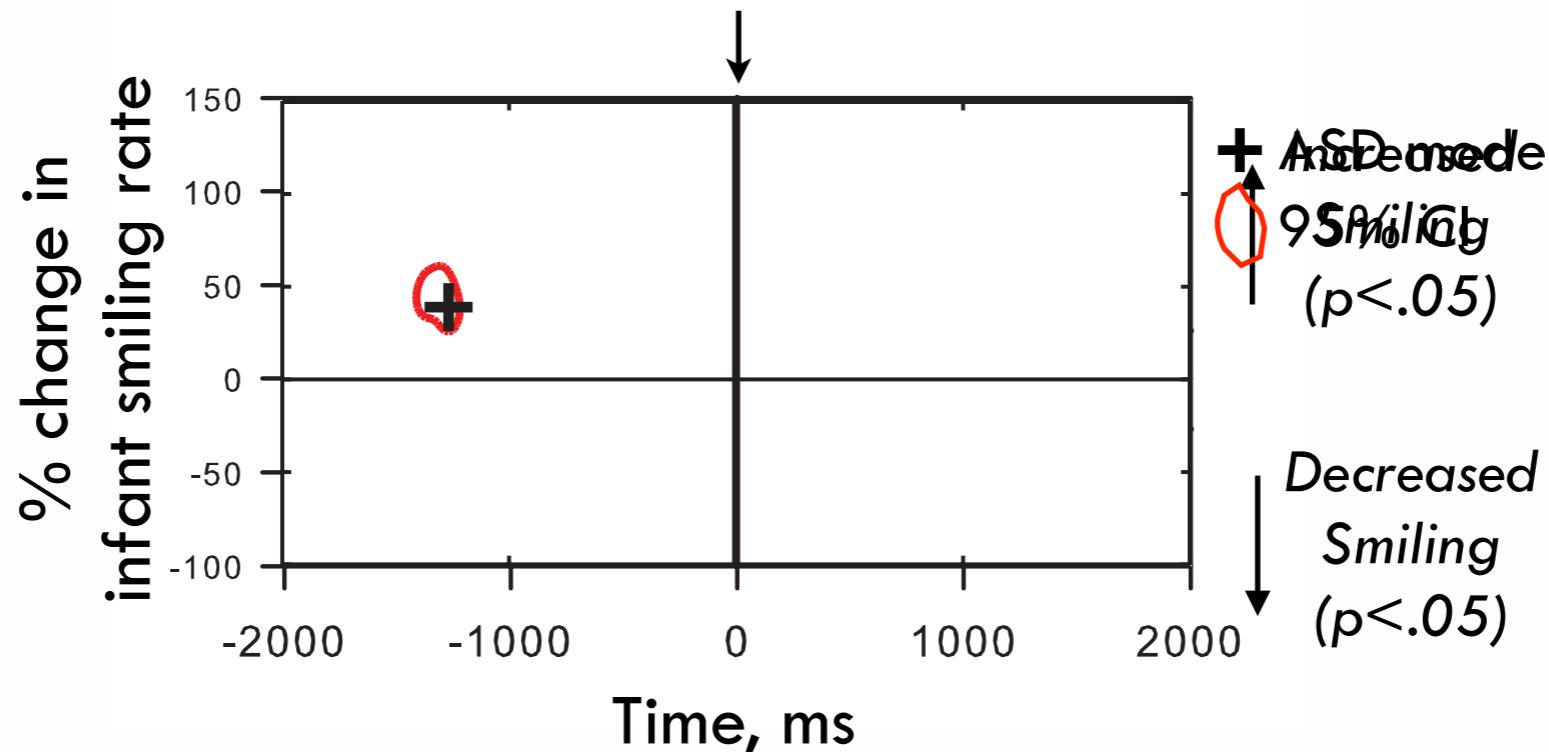
TD

Moments When Caregiver Smiled

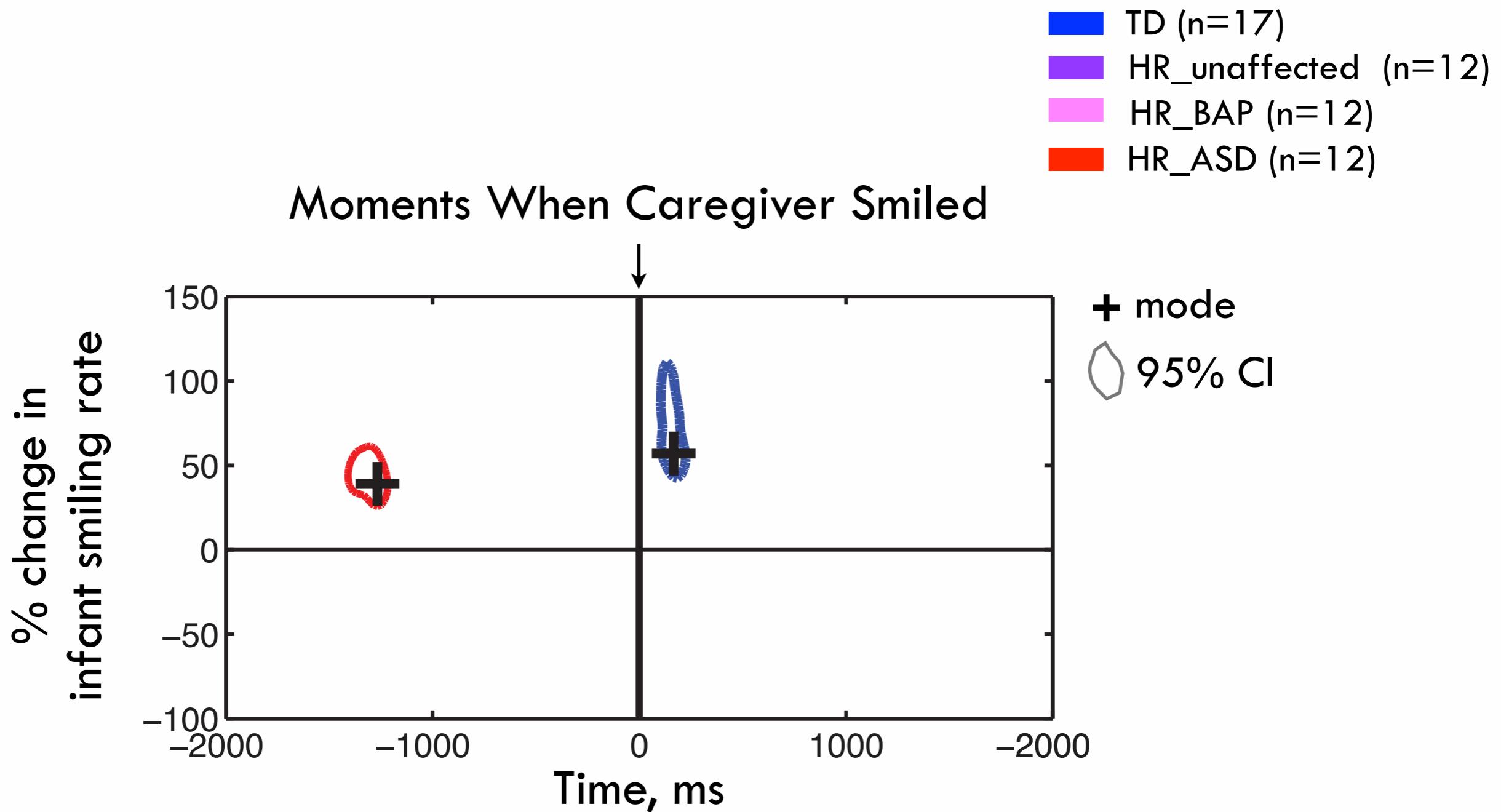


ASD

Moments When Caregiver Smiled

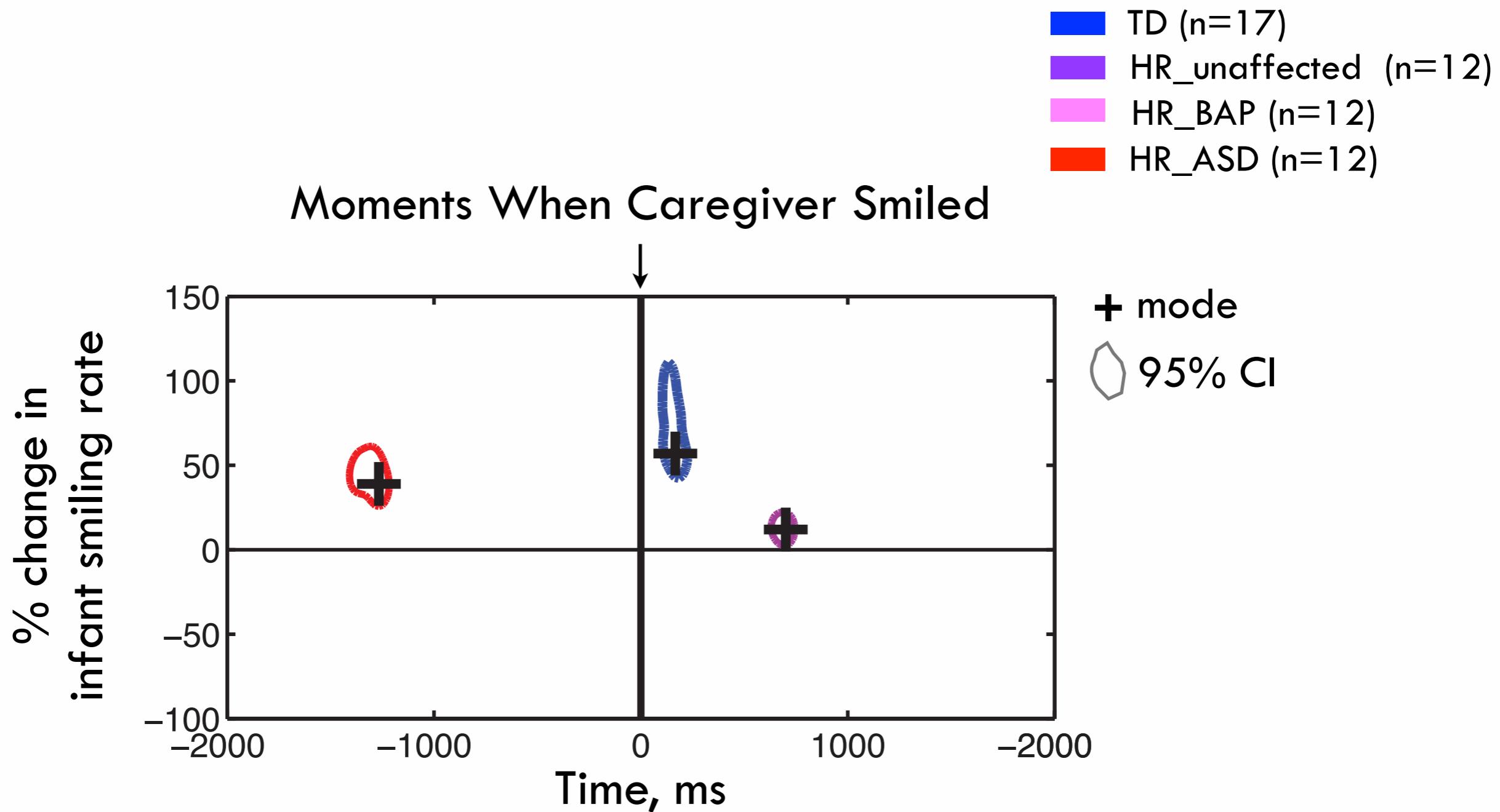


Gradations Across the Spectrum: HR-unaffected and BAP outcomes



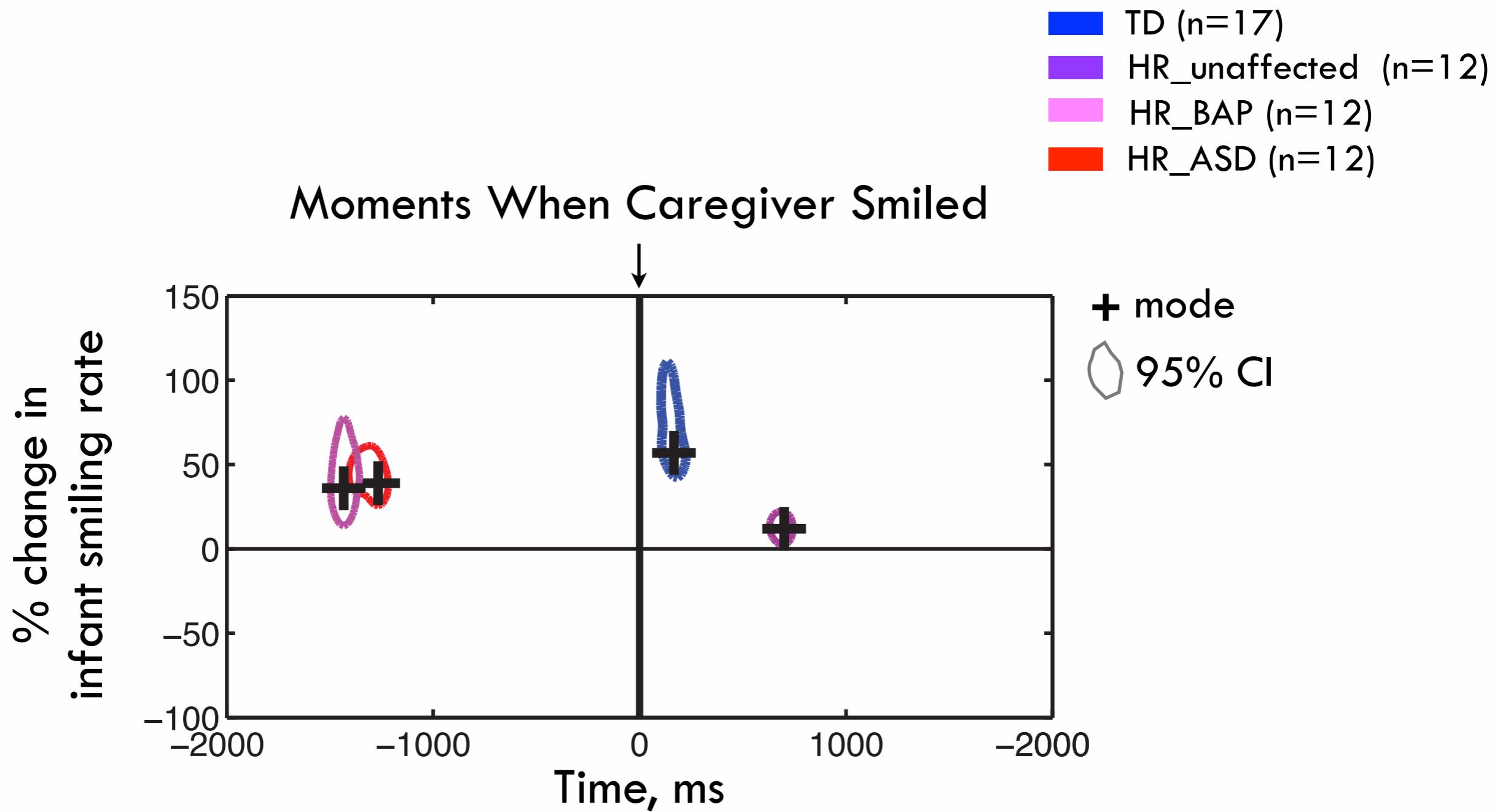
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Gradations Across the Spectrum: HR-unaffected and BAP outcomes



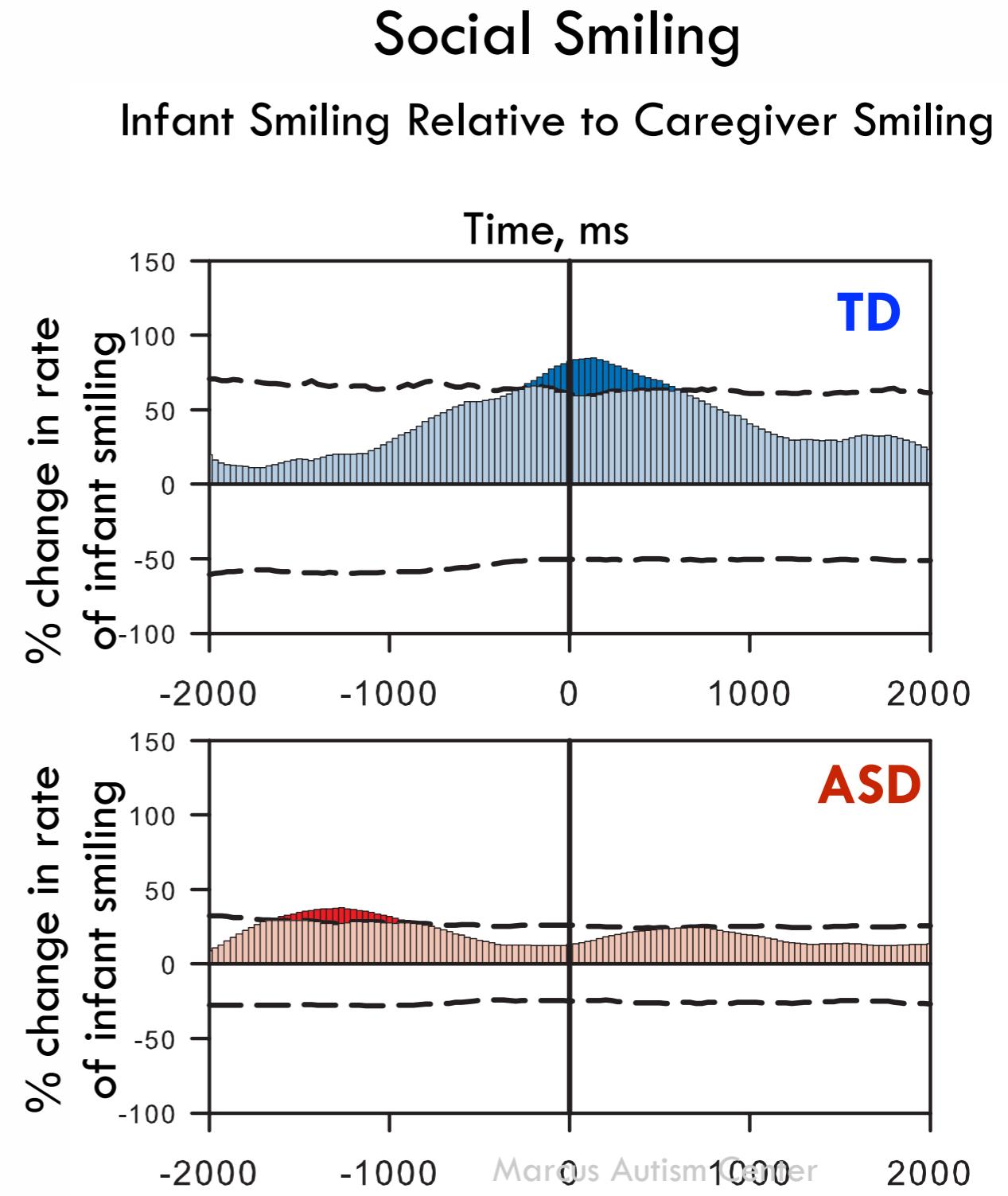
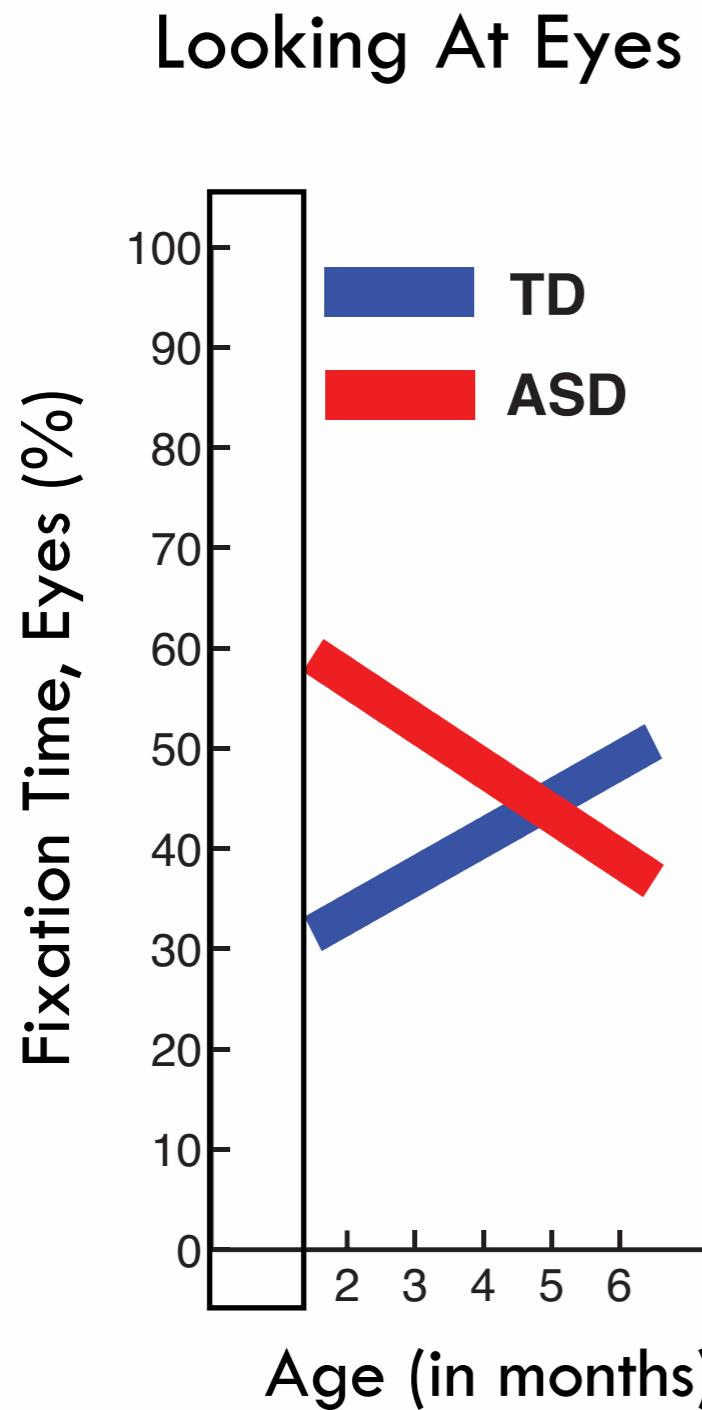
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Gradations Across the Spectrum: HR-unaffected and BAP outcomes

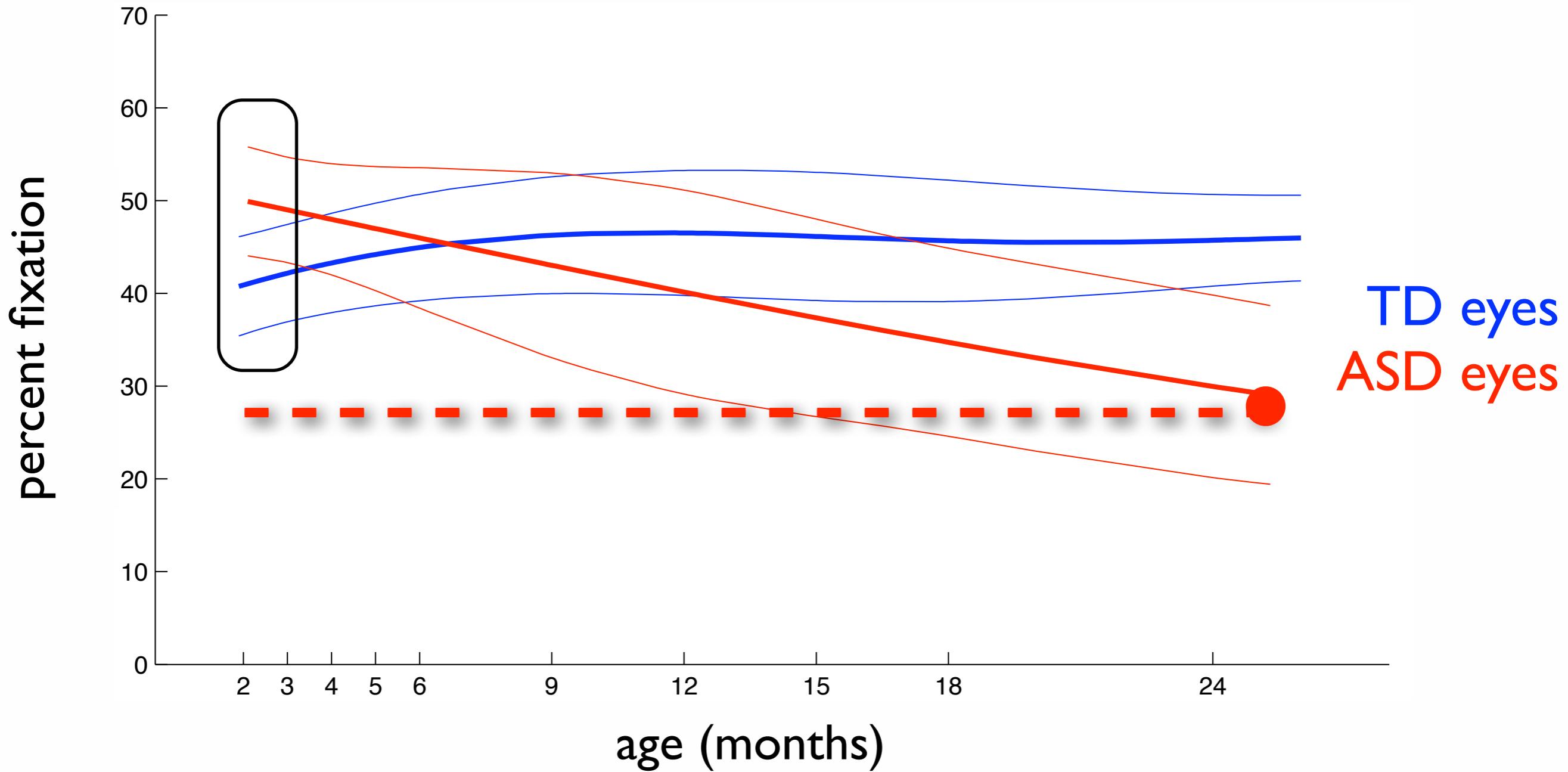


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Early Derailment of Social Processes in Autism



New Hypotheses



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Window of Dynamic Transition in Typical Infancy

Abilities Present Shortly After Birth



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



Subcortically mediated

Typical Transitions by ~2 months



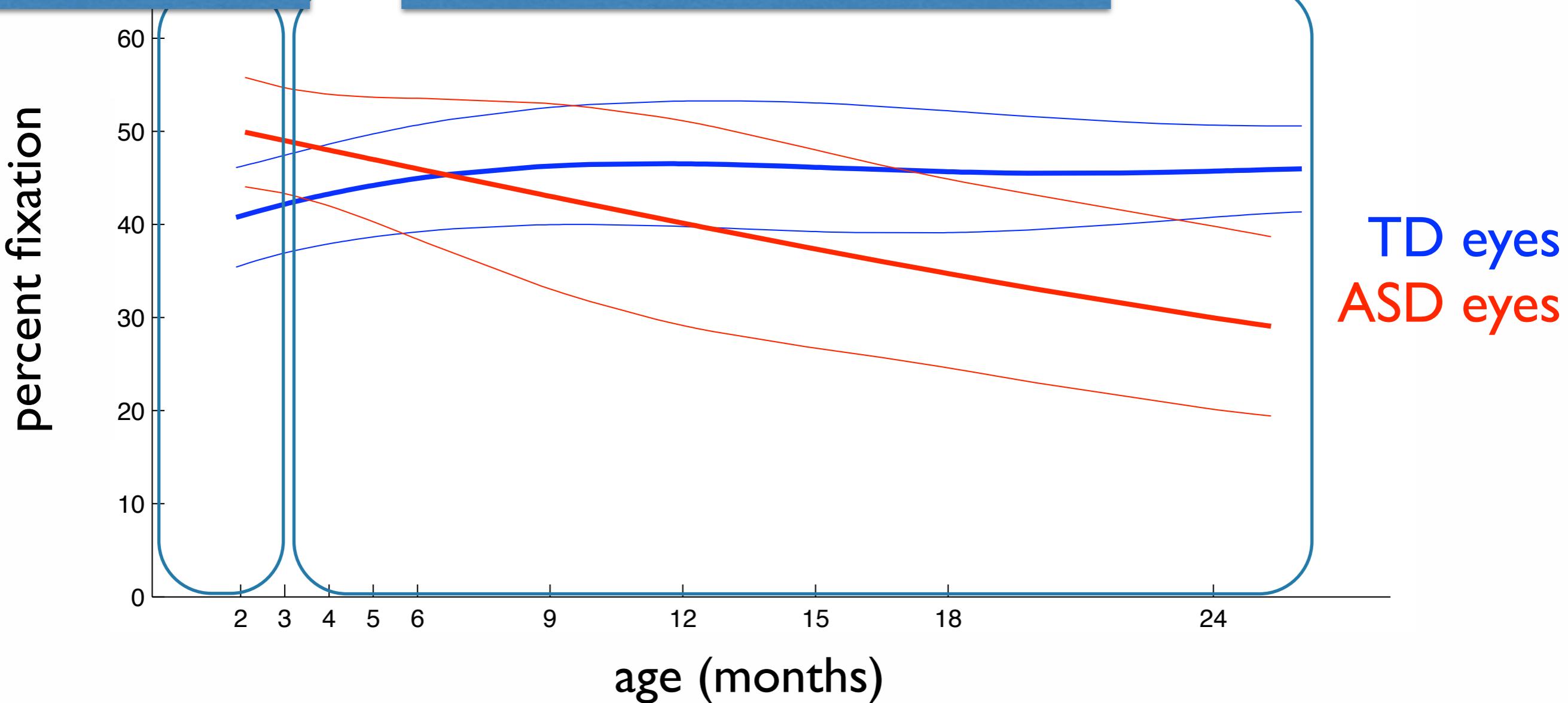
- Decline in reflex-like behavior (Johnson et al., 1991)
- Increased alertness & control over own movements (Wolff, 1987; Bronson, 1974)
- Active and intentional exploration (Rochat, 2001)
- Engagement in contingent social interaction
 - Increased looking to eyes (Haith et al., 1997; Jones & Klin, 2013)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

Cortically mediated

New Hypotheses

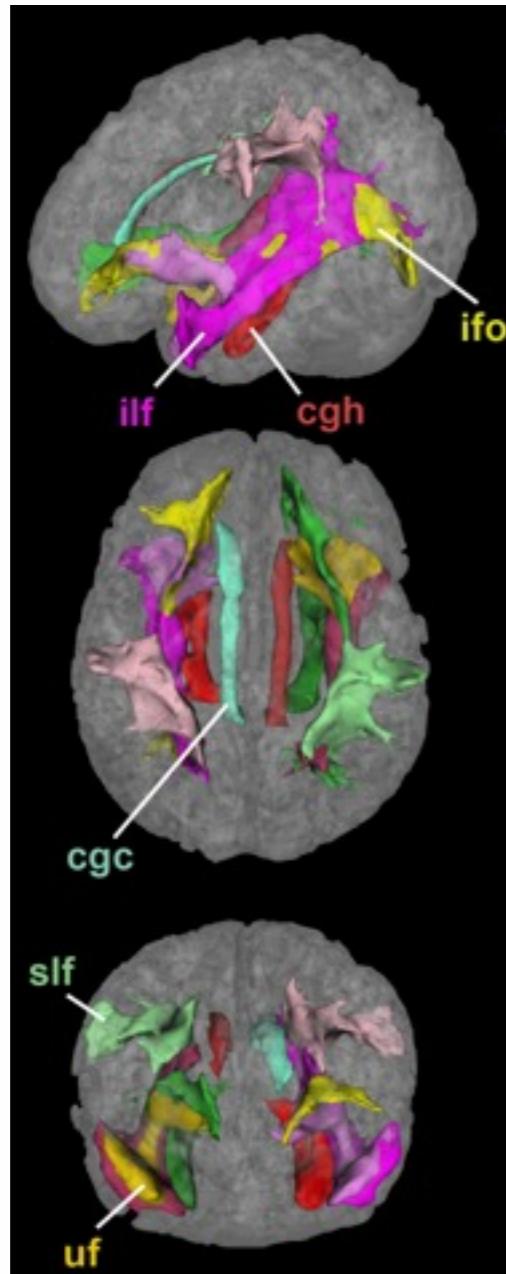
- ‘Reflex-like’ predispositions
- Subcortically mediated

- Active engagement in social interaction
- Cortically mediated

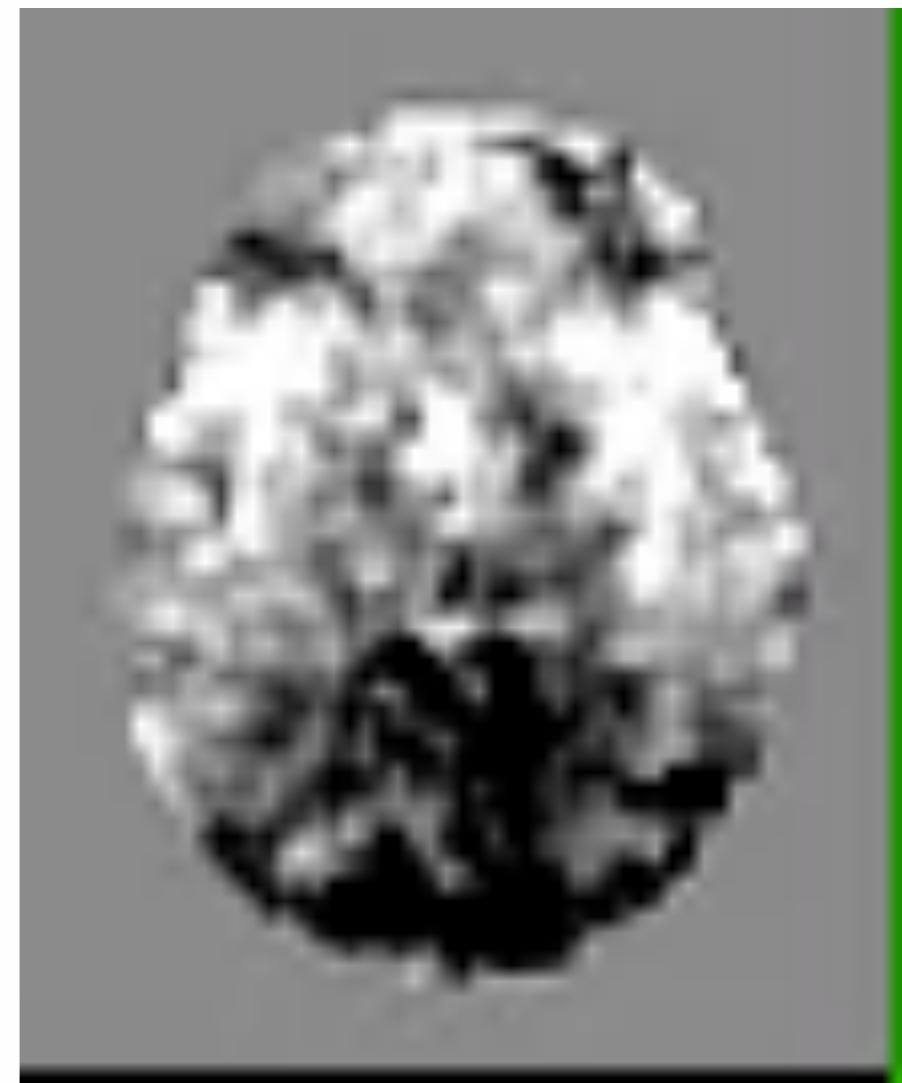


MRI Studies of Infants

Diffusion Tensor Imaging and Tractography



Resting-State Functional Connectivity

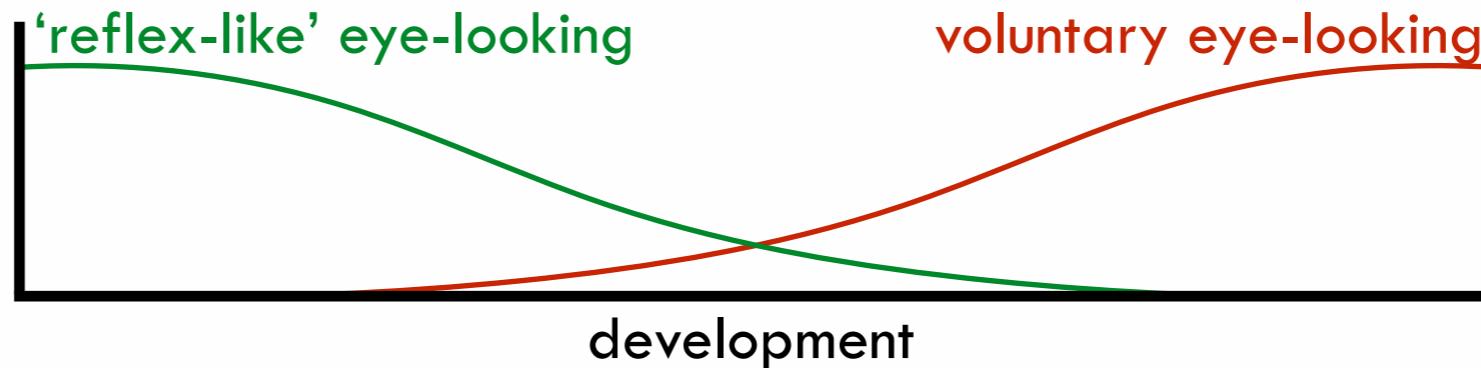


30-day-old infant

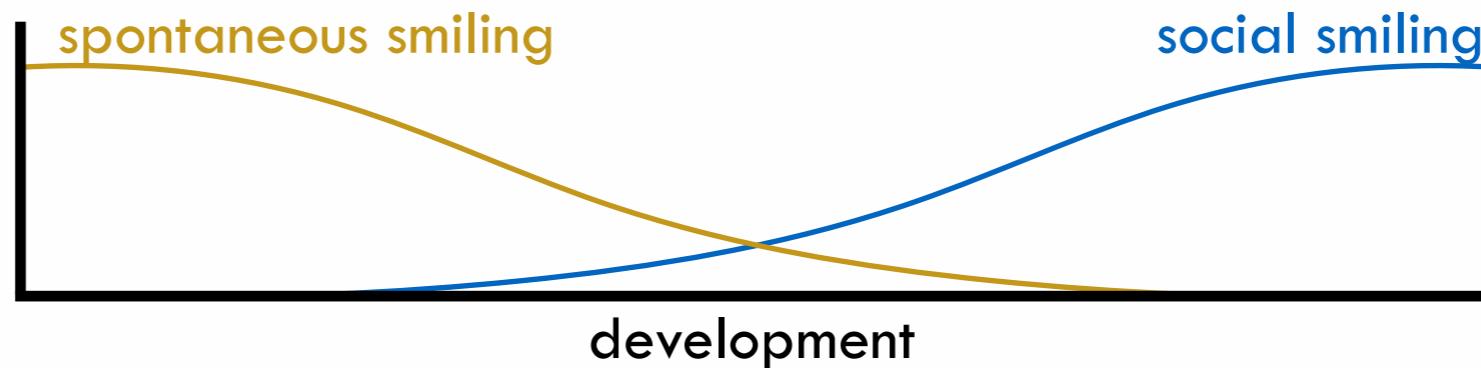
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Associated Changes in Brain and Behavior

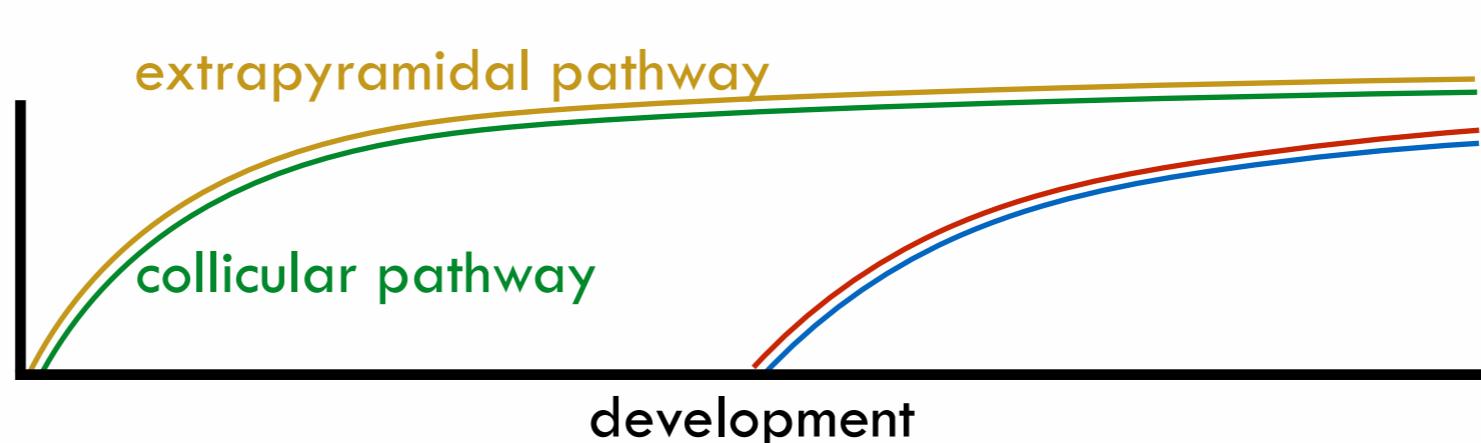
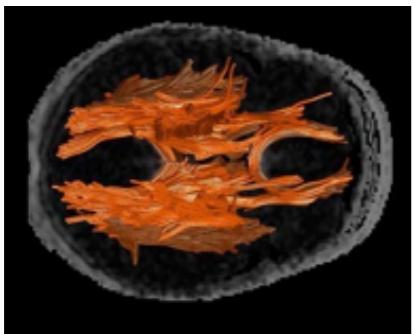
eye-looking



smiling



brain networks



FG, IOG, OFC,
STS, FEF

anterior temporal,
OFC, MPFC, ACC

Thank you

Pediatric Neuroimaging Core

Dr. Longchuan Li

Brittney Pearson

Joanna Beugnon

Carly Reineri

Mahmoud Zeydabadinezhad

Dr. Christa Payne

Social Neuroscience Core

Dr. Ami Klin

Dr. Warren Jones

Rachel Sandercock