Yale Child Study Center

FROM GENERATION TO GENERATION

Neural Signatures of Autism

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My Laboratory's Mission

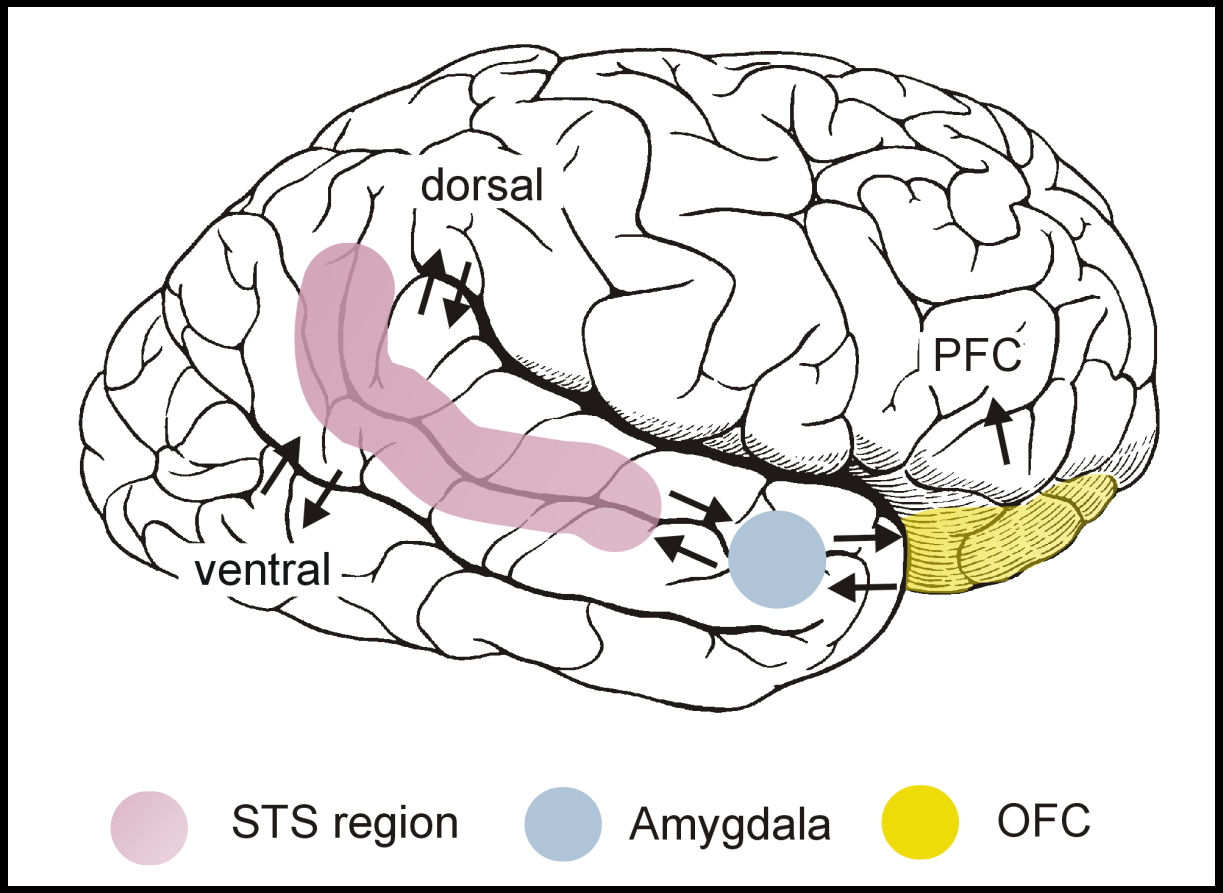
To employ the techniques of cognitive neuroscience (neuroimaging, imaging genomics, eye tracking, and virtual reality) to understand the brain basis of autism and thereby improve the diagnosis and treatment of this and related neurodevelopmental disorders.

Social Perception

The initial stages in the processing of biological motion cues that culminate in the accurate analysis of the psychological dispositions, motives, and intentions of other individuals.

The Fortune-Teller, George de La Tour
ca. 1625

The Social Brain



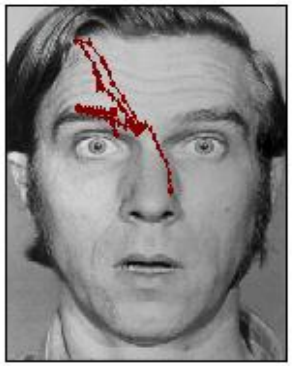
From Allison et al. (2000) *Trends in Cognitive Sciences*

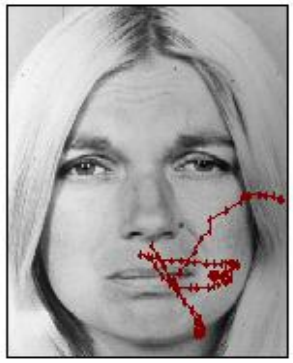
Autism Spectrum Disorder

- Qualitative impairments in social interaction
  - Impairment in eye contact and social reciprocity
- Qualitative deficits in communication
  - Delay in or lack of spoken language
- Restricted, repetitive, and stereotyped patterns of behavior
  - Persistent preoccupations with parts of objects
  - Self-stimulatory behavior

Autism

Typically Developing





Pelphrey et al. (2002)
Journal of Autism and Developmental Disorders

Outline

I. Social perception in the human brain and its disruption in autism

II. Insights from the developing social brain

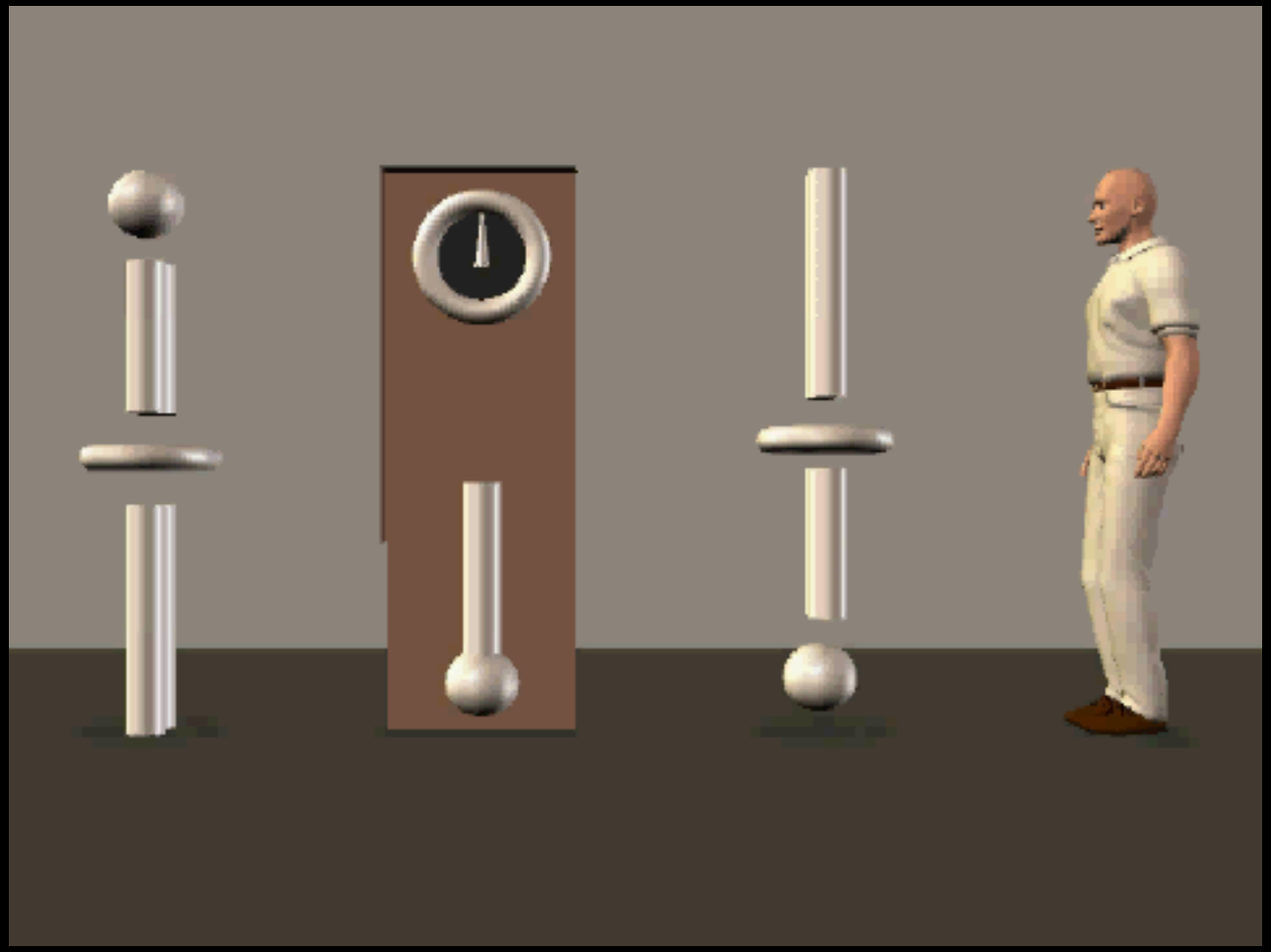
III. Recent directions

I. Social Perception in the human brain and its disruption in autism

A critical component of social perception is the detection and recognition of other dynamic agents in the environment.

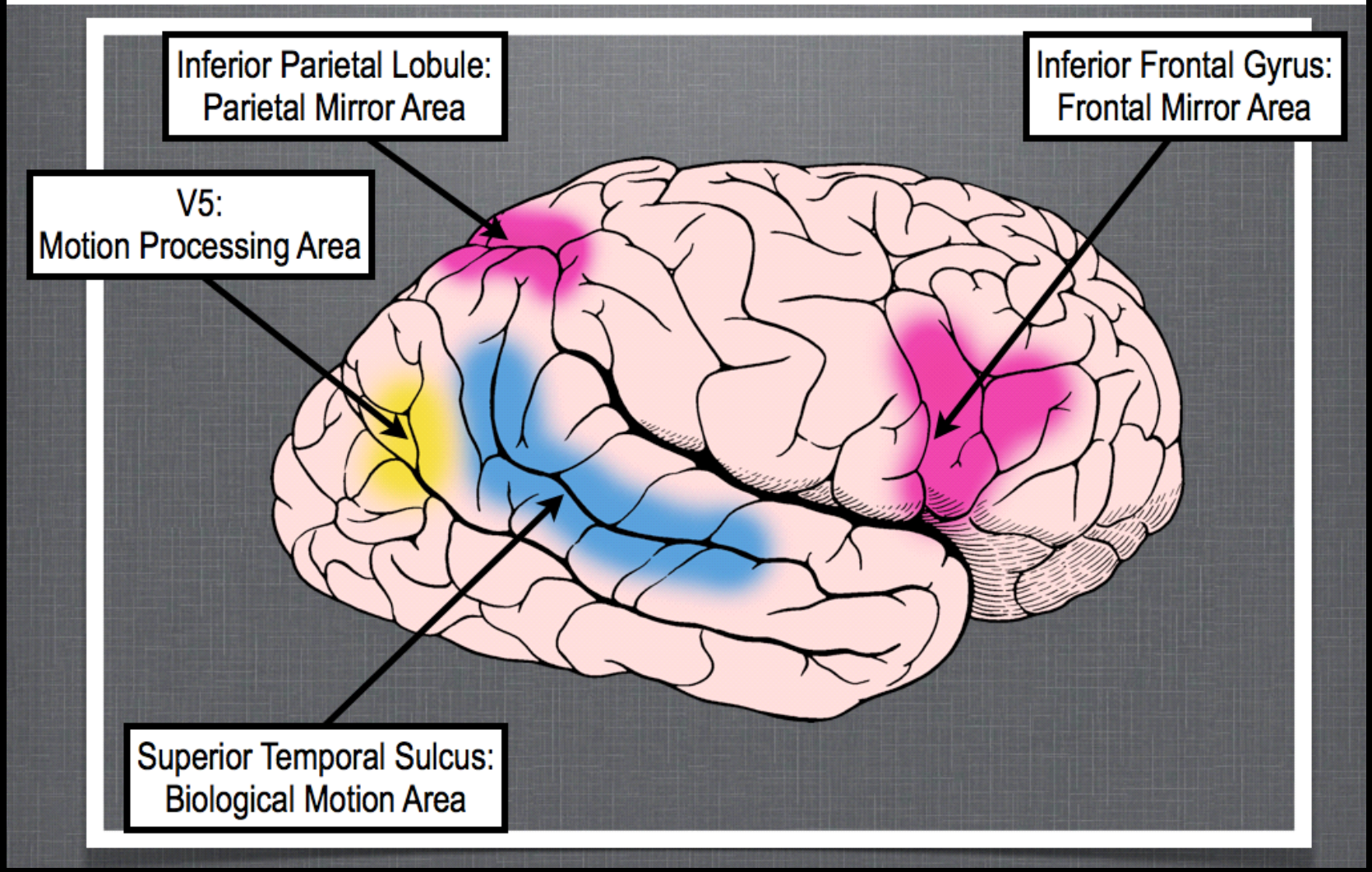
What brain mechanisms support recognition of biological motion?

Borofsky, *Walking To The Sky*

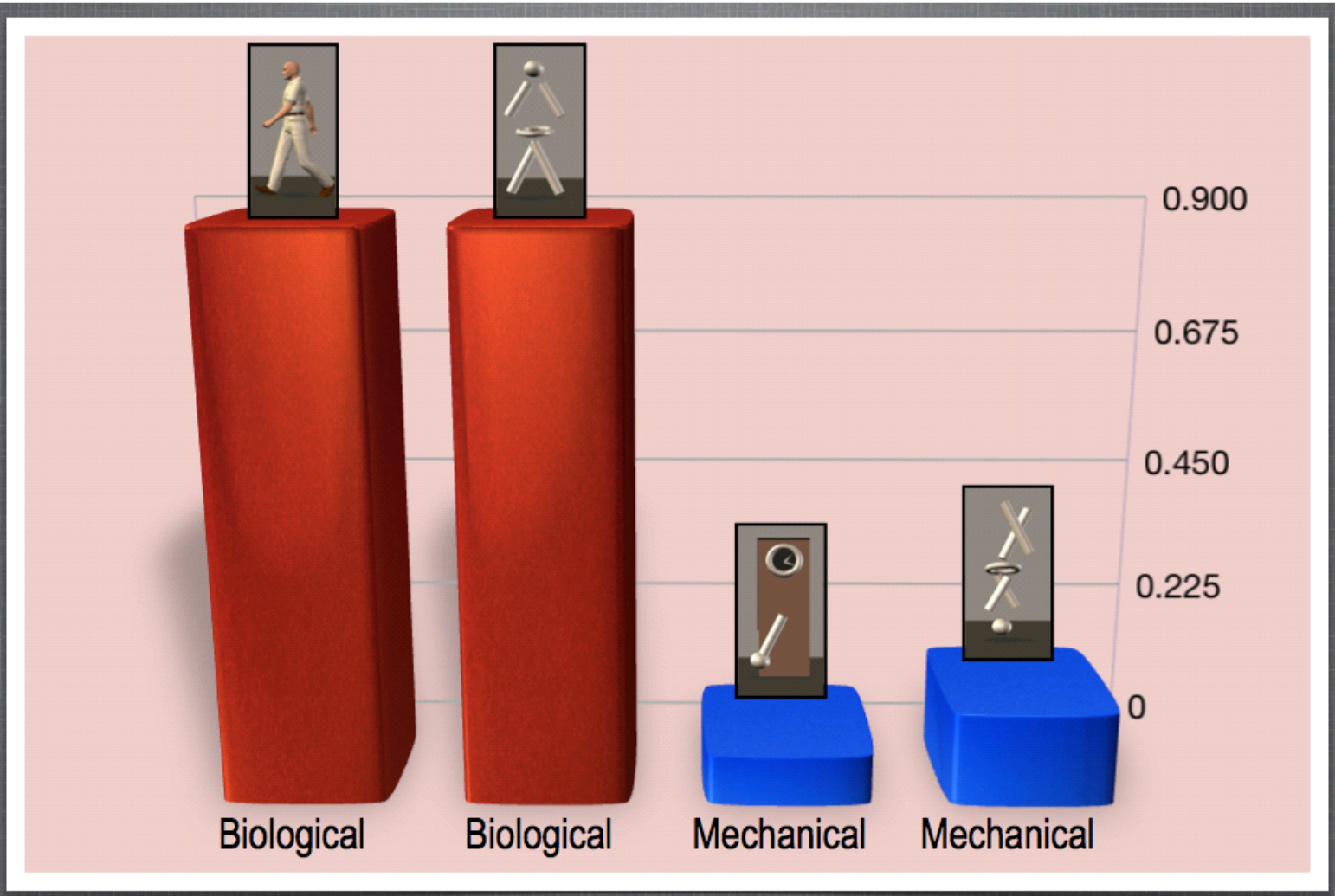


Pelphrey et al. (2003) *Journal of Neuroscience*

There is regional localization of areas involved in social perception.

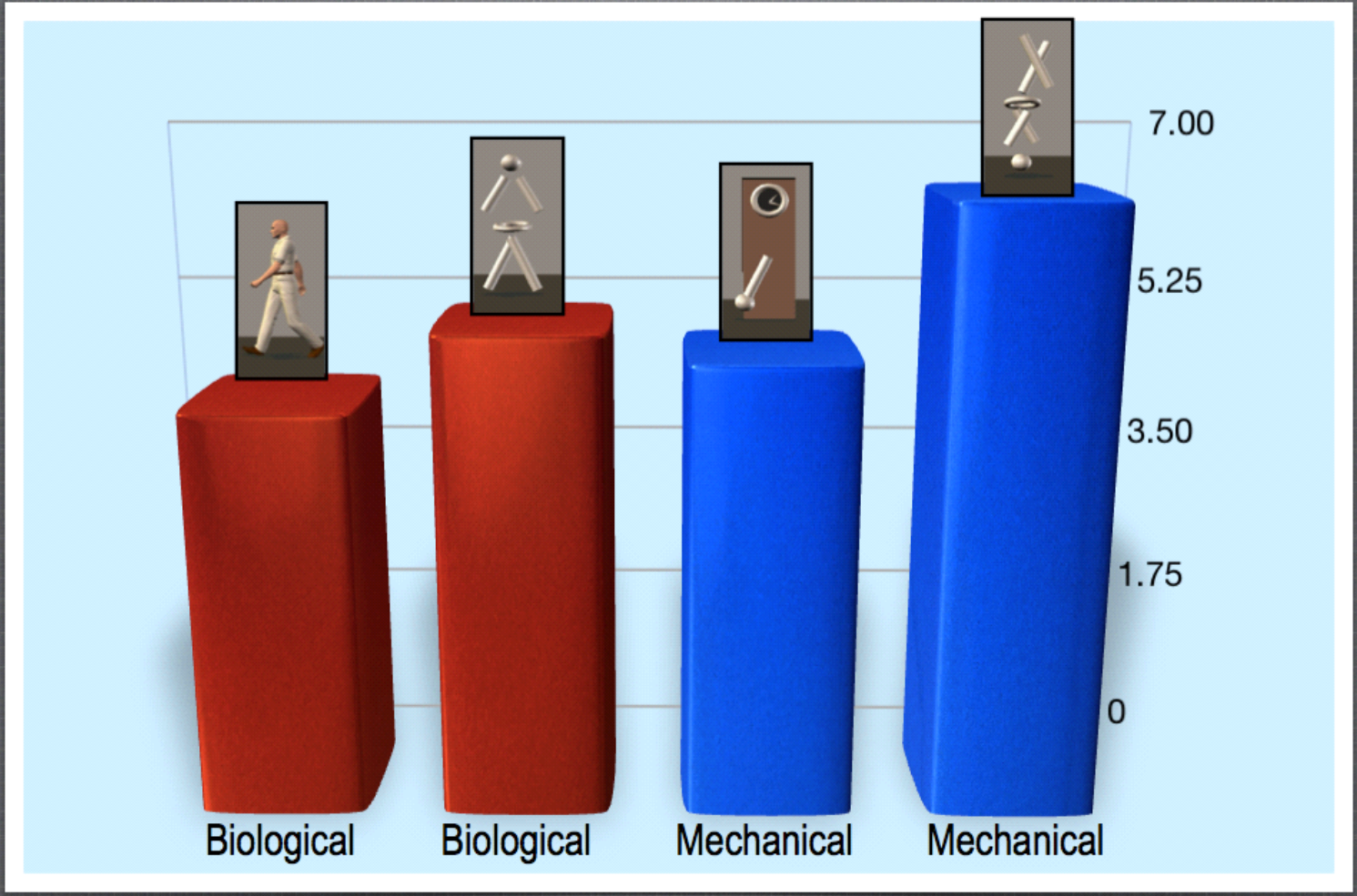


The biological motion area responds only to biological motion.



Pelphrey et al. (2003) *Journal of Neuroscience*

The motion processing area responds to all motion.



Pelphrey et al. (2003) *Journal of Neuroscience*

Does the posterior STS region derive higher-level, mentalistic descriptions from motion for use in action interpretation and other inferences?

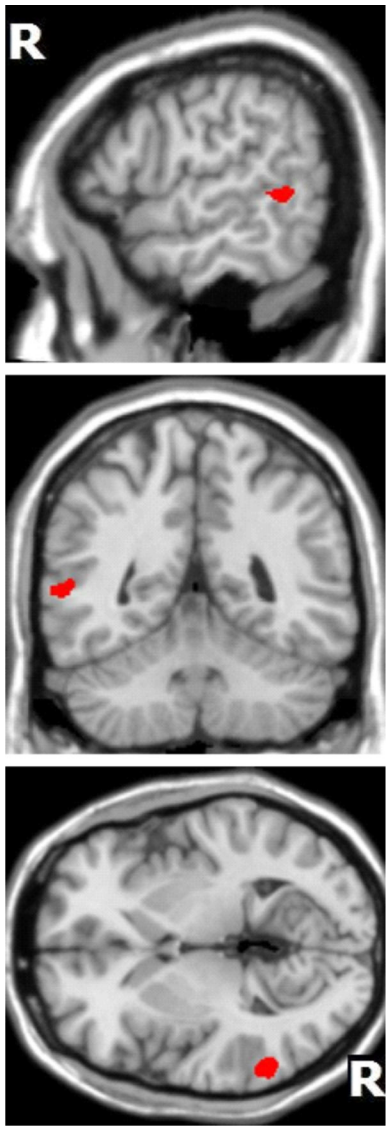
George de La Tour ‘The Fortune-Teller’ detail, ca. 1625

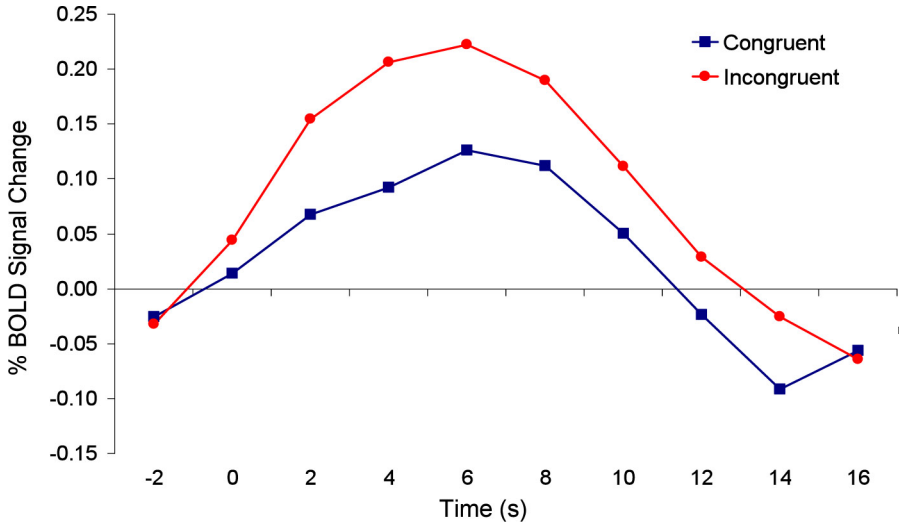
Positive Congruent

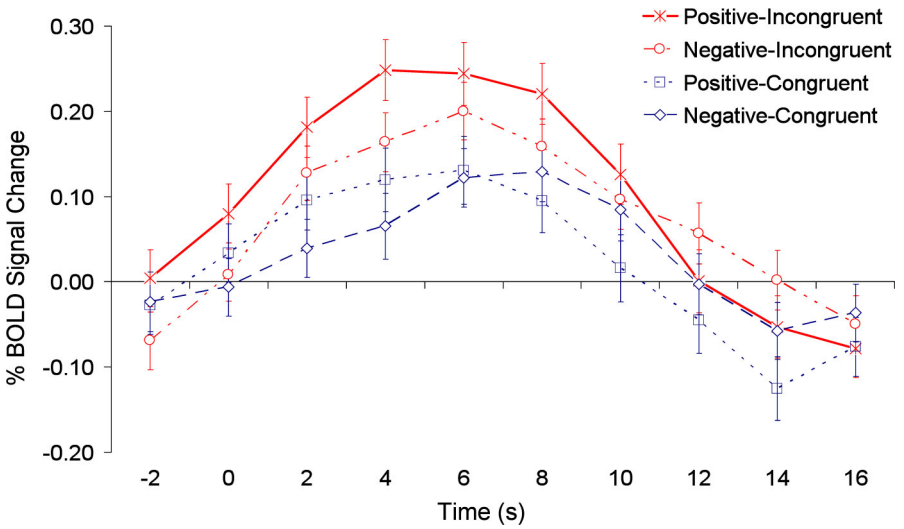
Positive Incongruent

Negative Congruent

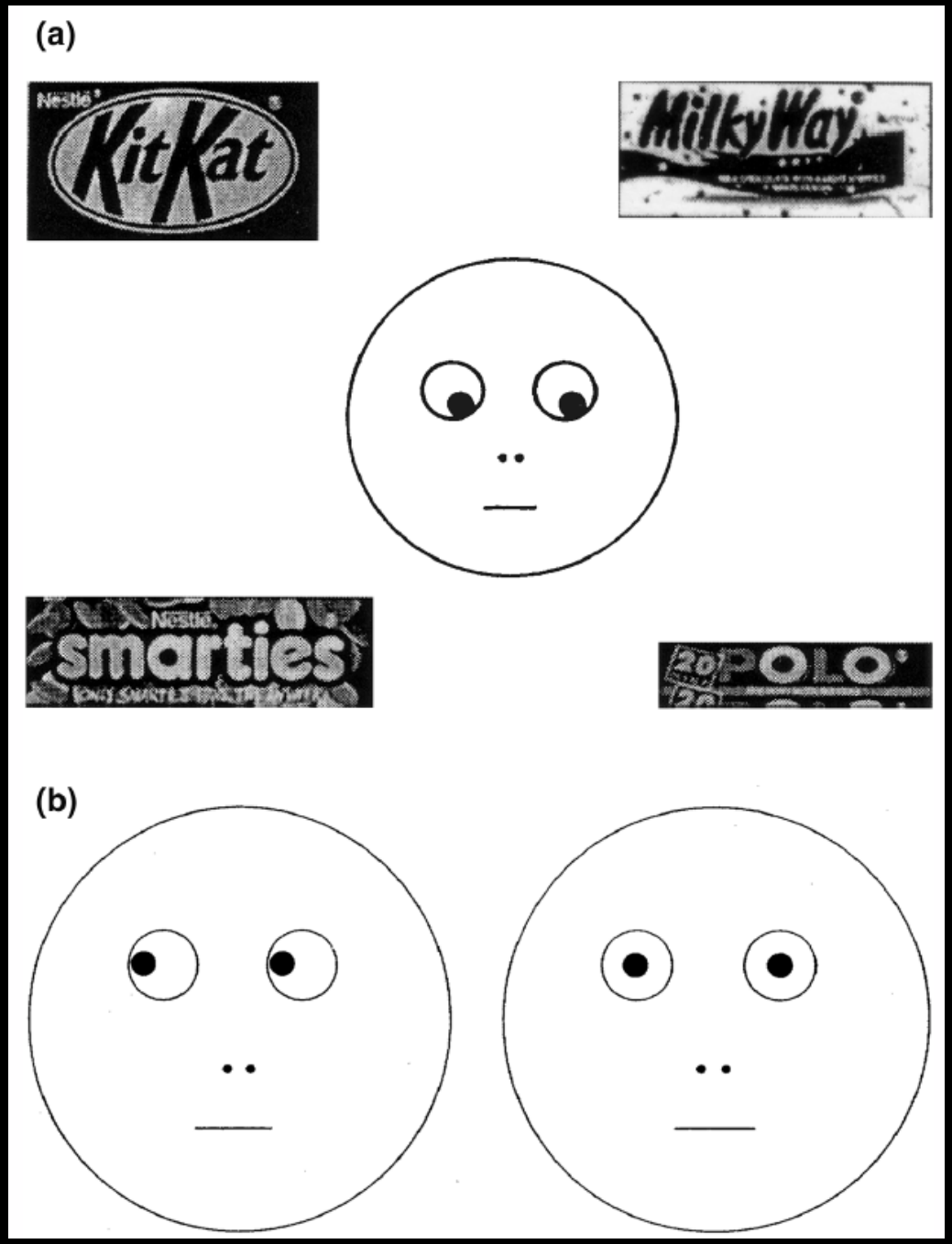
Negative Incongruent







Vander Wyk et al. (2009) *Psychological Science*



From Baron-Cohen (1995)

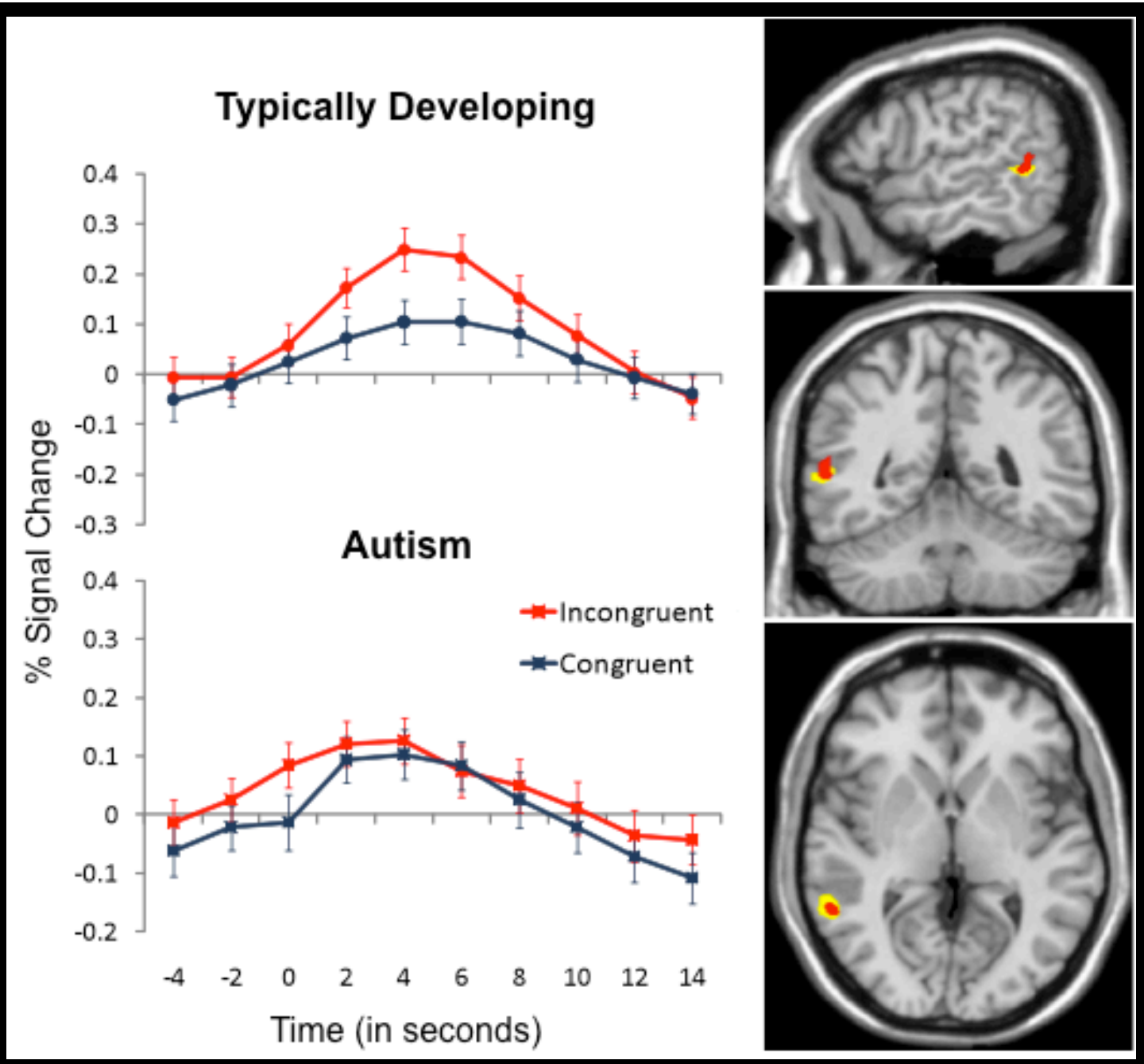
Given the natural history of eye-gaze processing deficits in autism, might dysfunction of the STS region be involved?

Positive Congruent

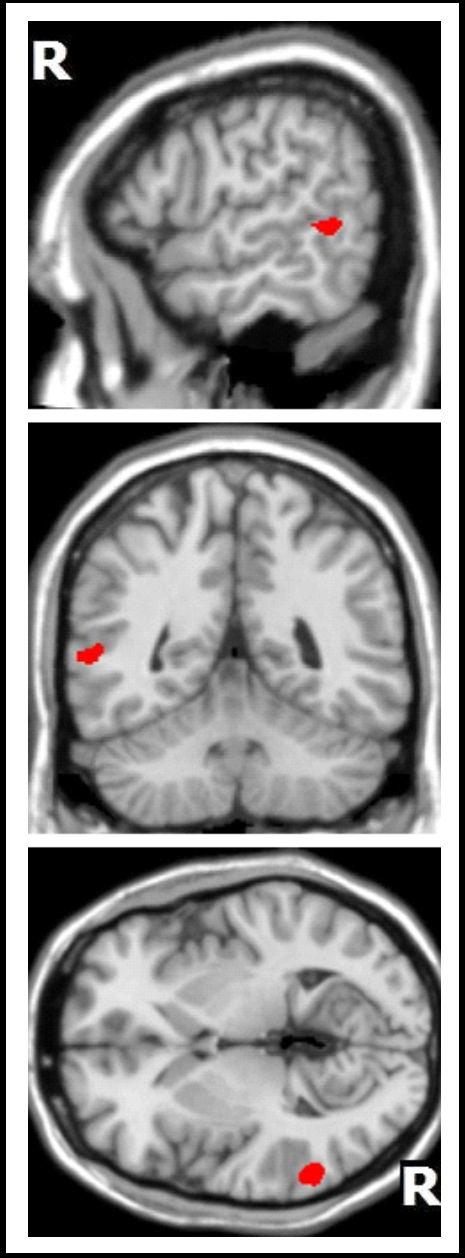
Positive Incongruent

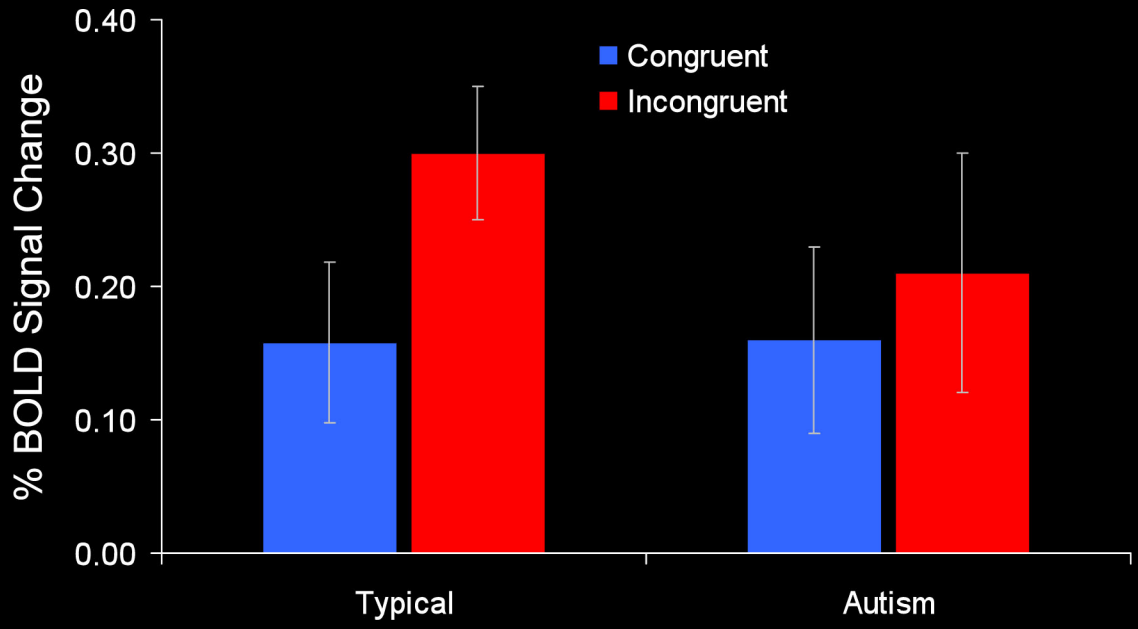
Negative Congruent

Negative Incongruent



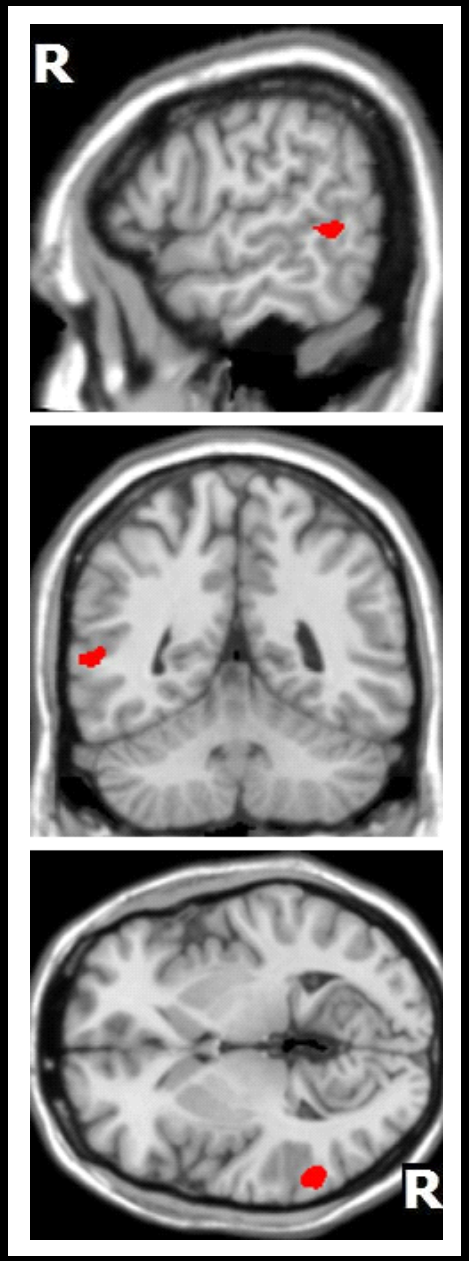
Pelphrey et al. (in press) *JCPP*

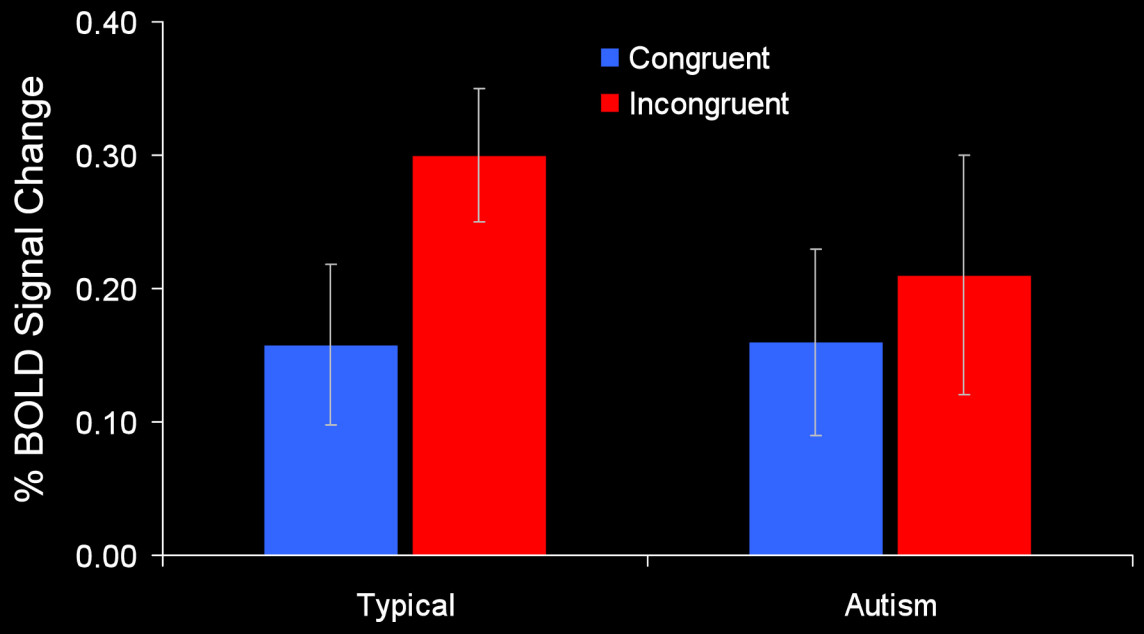


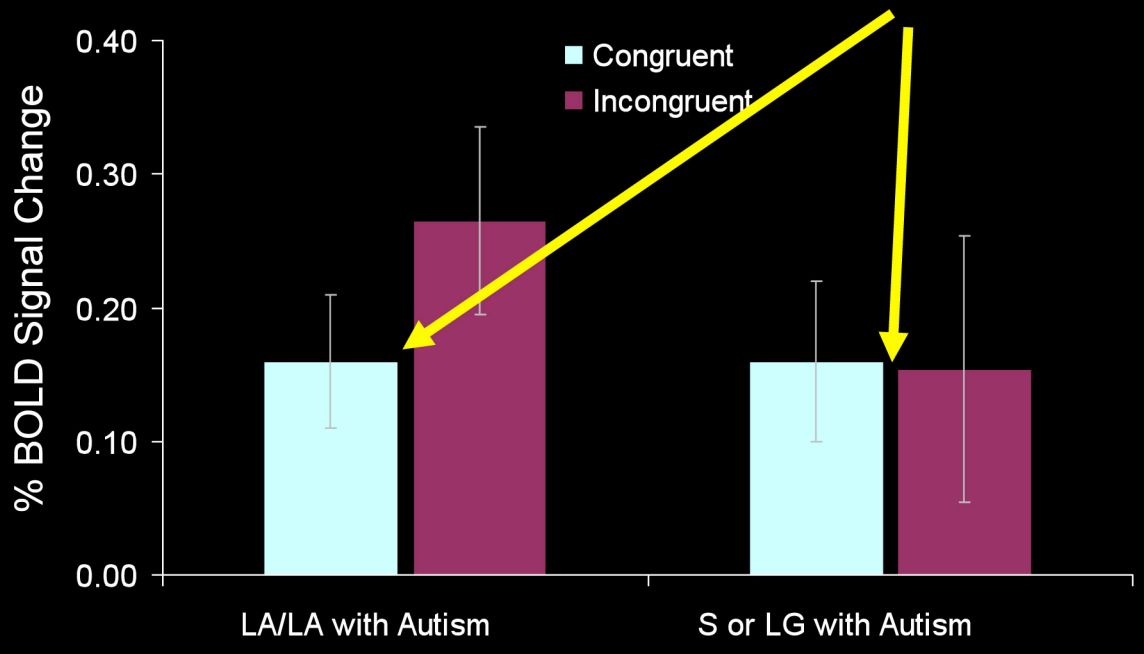


Pelphrey et al. (in press) *JCPP*

How might we account for the heterogeneity in the imaging data from the STS?


R
R


0.40
0.30
0.20
0.10
0.00
% BOLD Signal Change
Congruent
Incongruent
Typical
Autism


0.40
0.30
0.20
0.10
0.00
% BOLD Signal Change
Congruent
Incongruent
LA/LA with Autism
S or LG with Autism

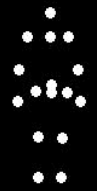
II. Insights from the developing social brain

Behavioral training for fMRI

Does the STS respond selectively to biological motion in children with autism?

Biological Motion Processing

- Toddlers with ASD show abnormal preferential attention to biological motion.
  - Klin et al., 2009
- Adults with ASD exhibit dysfunction within the right posterior superior temporal sulcus (pSTS).
  - Freitag et al., 2008
  - Pelphrey et al., 2005



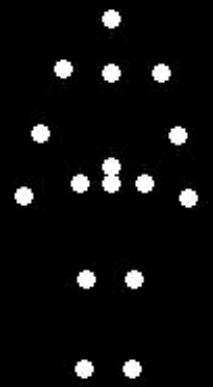
Participant Characteristics

	TD	US	ASD
Number of Subjects:	25	25	25
Mean Age in Years:	10.9	11.3	11.8
Age Range:	4 - 17	6 - 16	4 - 17
Differential Ability Scale-II:			
Overall (SD)	116.0 (16.7)	114.2 (7.7)	100.2 (19.7)
Amount of Movement:	0.9 (0.7)	1.4 (0.9)	1.1 (0.6)
Social Responsiveness Scale:			
Raw scores	24.2 (14.2)	18.3 (14.5)	98.8 (23.9)
T-scores	46.3 (6.7)	43.9 (7.5)	83.0 (13.1)
Vineland Adaptive Behavior Scales:			
Communication	102.5 (15.8)	102.0 (12.9)	78.3 (10.5)
Daily Living	93.1 (10.4)	93.6 (10.9)	78.5 (11.0)

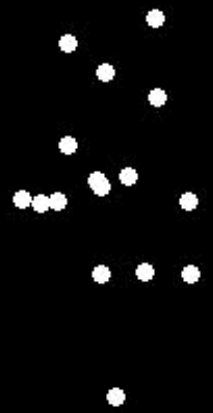
Neural Signatures of ASD

- State markers are defined as regions of dysfunction in children with ASD relative to US and TD children.
- Trait markers are defined as regions of activity reflecting shared dysfunction in US and children with ASD.
- Compensatory mechanisms are defined as enhanced differential activity unique to US relative to TD and ASD.

Biological

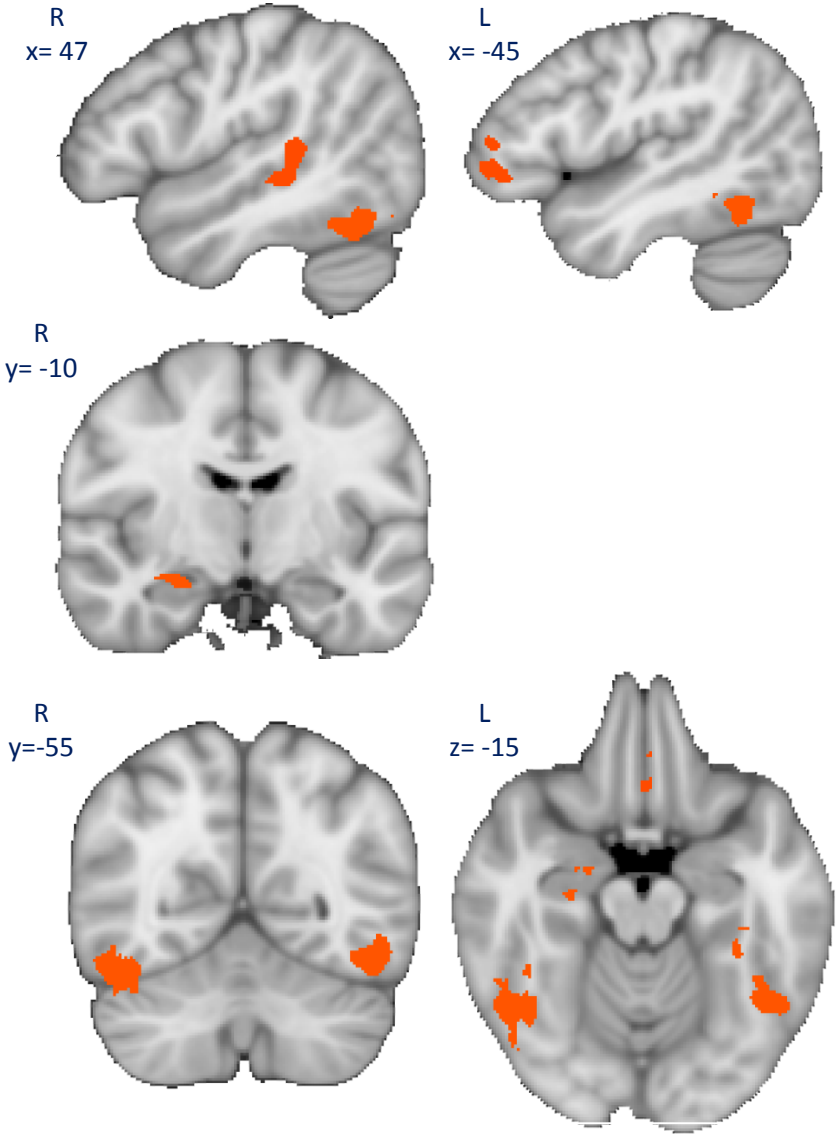


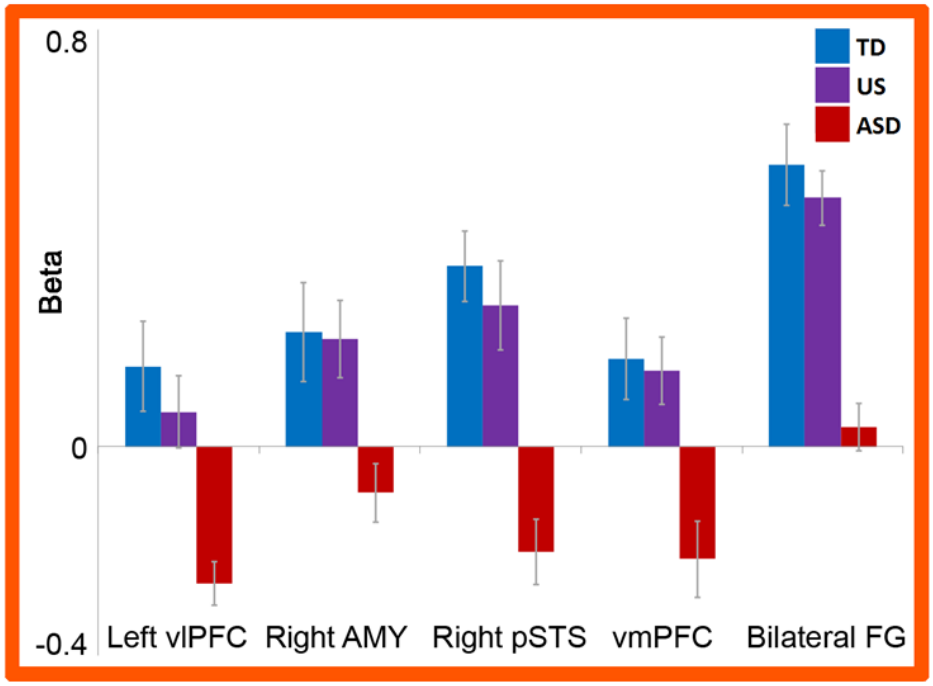
Scrambled



Kaiser et al. (In Press) *PNAS*

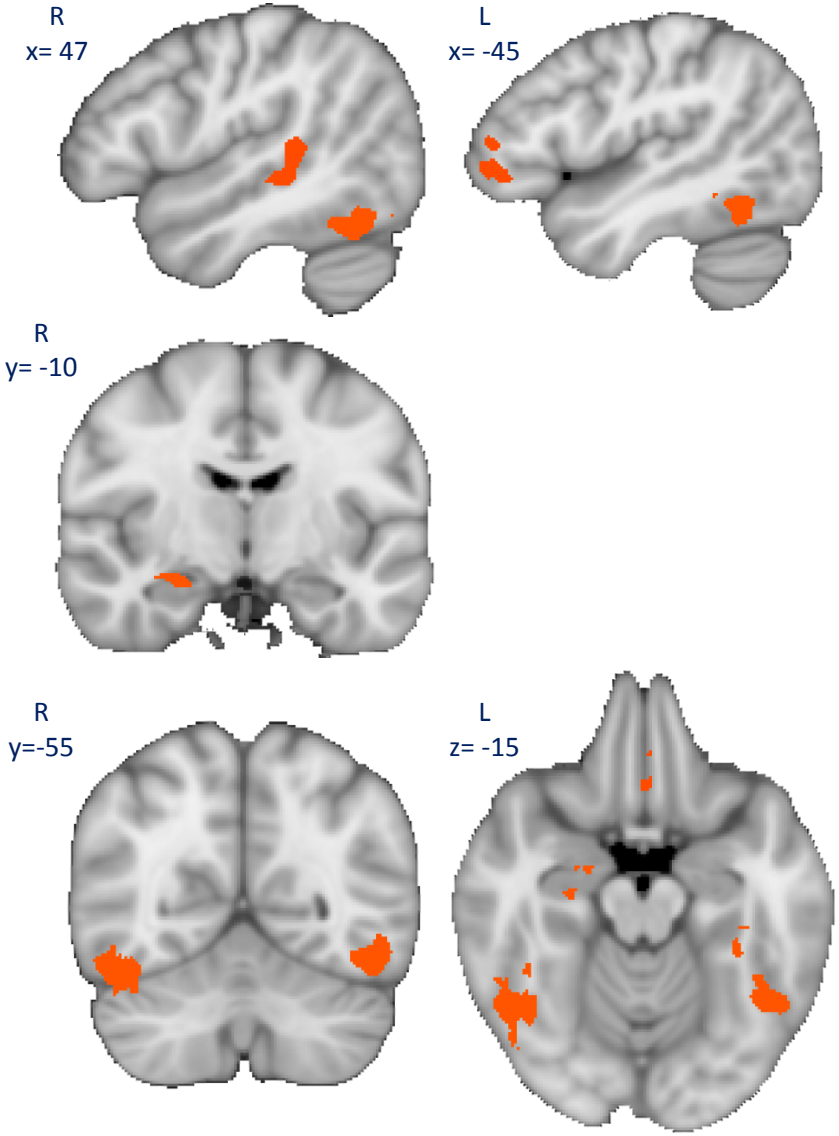
State Activity: TD>ASD and US>ASD

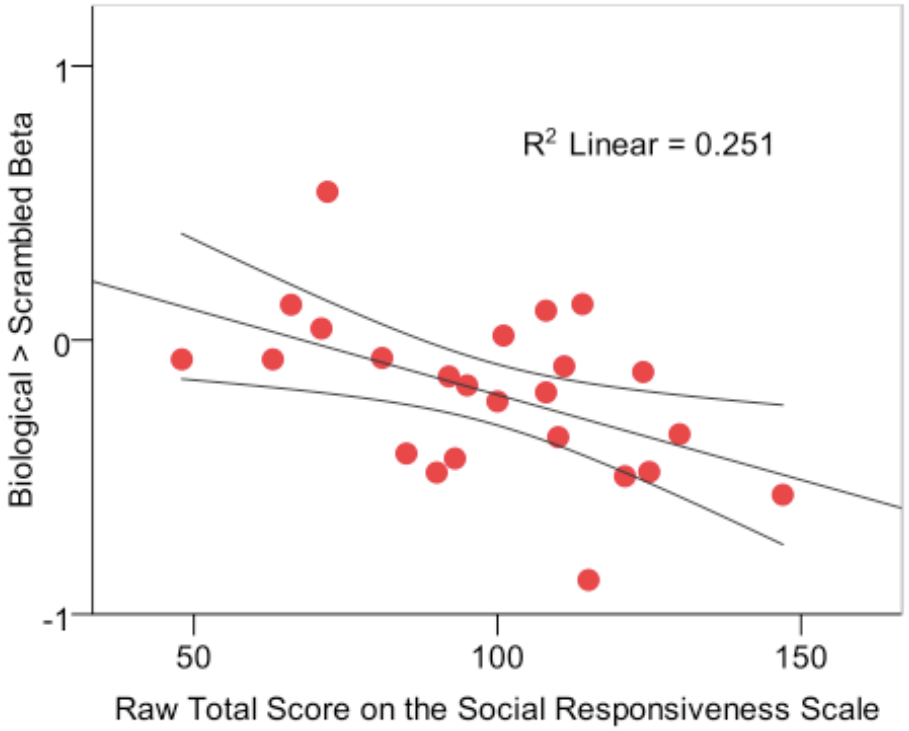




Kaiser et al. (In Press) *PNAS*

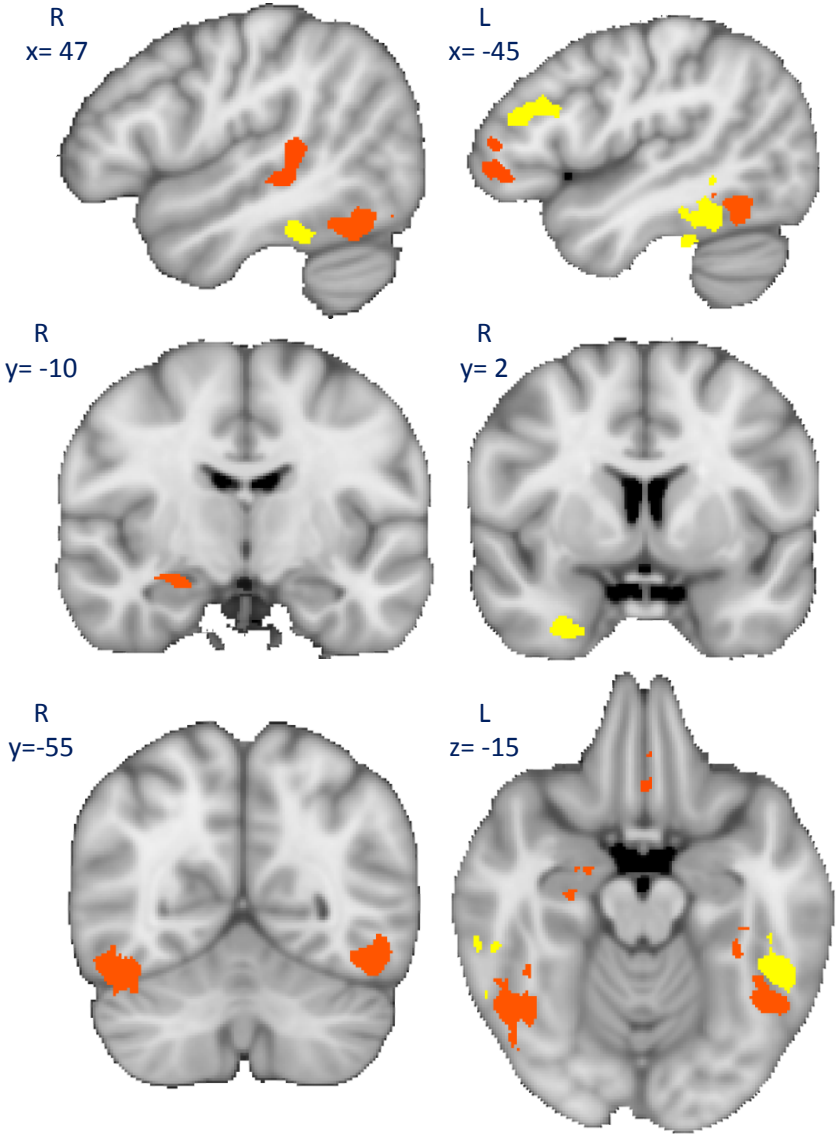
Behavioral Correlations

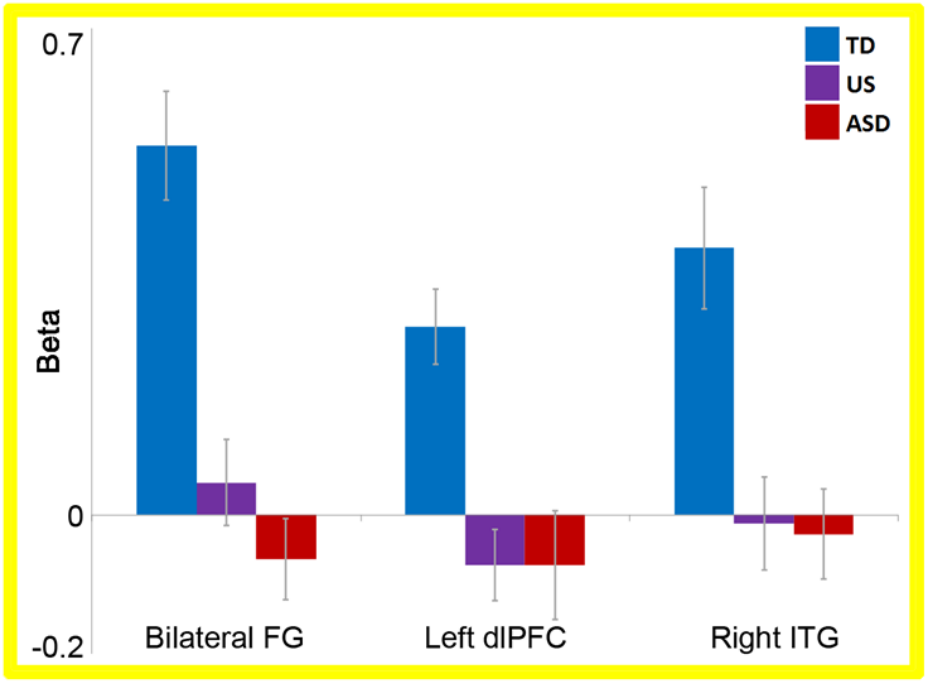




Kaiser et al. (In Press) *PNAS*

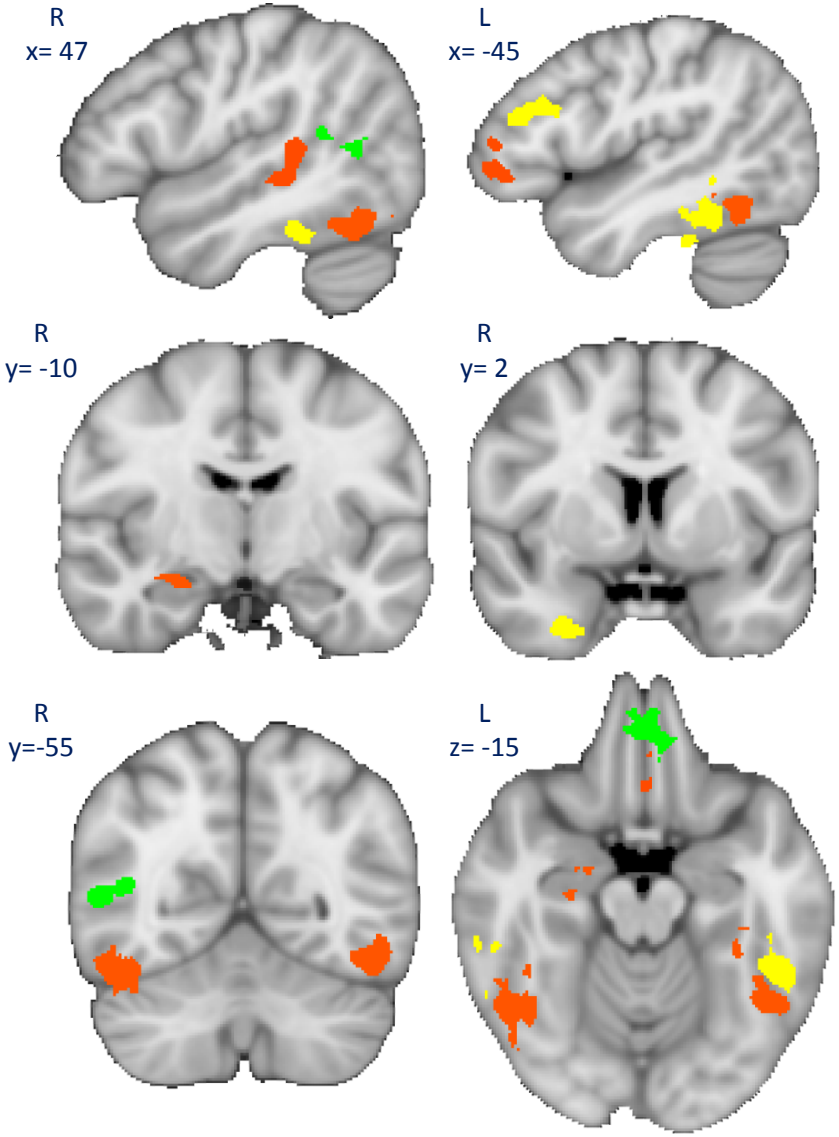
Trait Activity: TD>ASD and TD>US

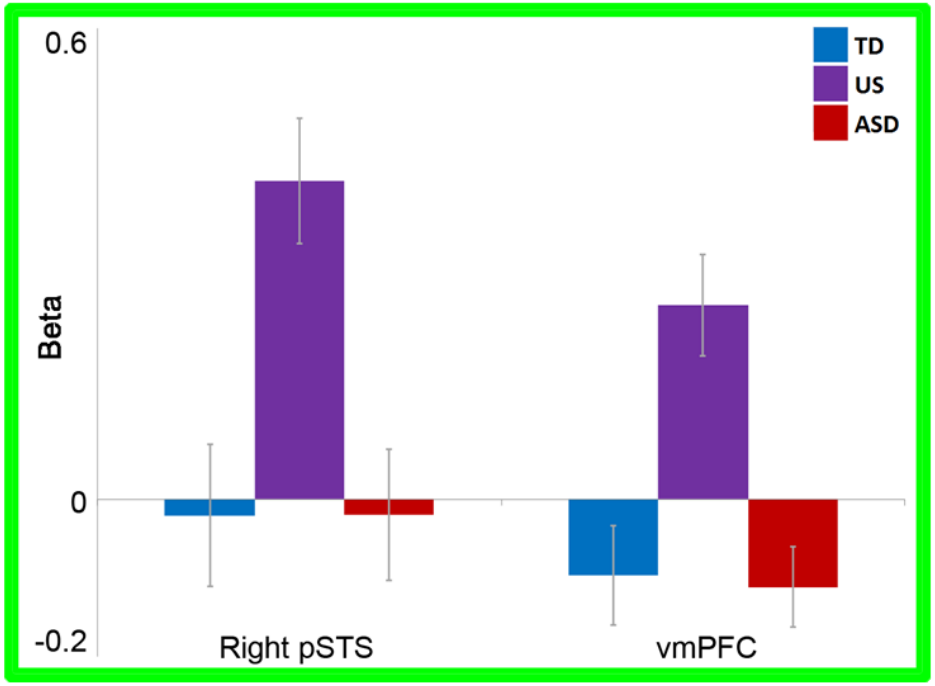




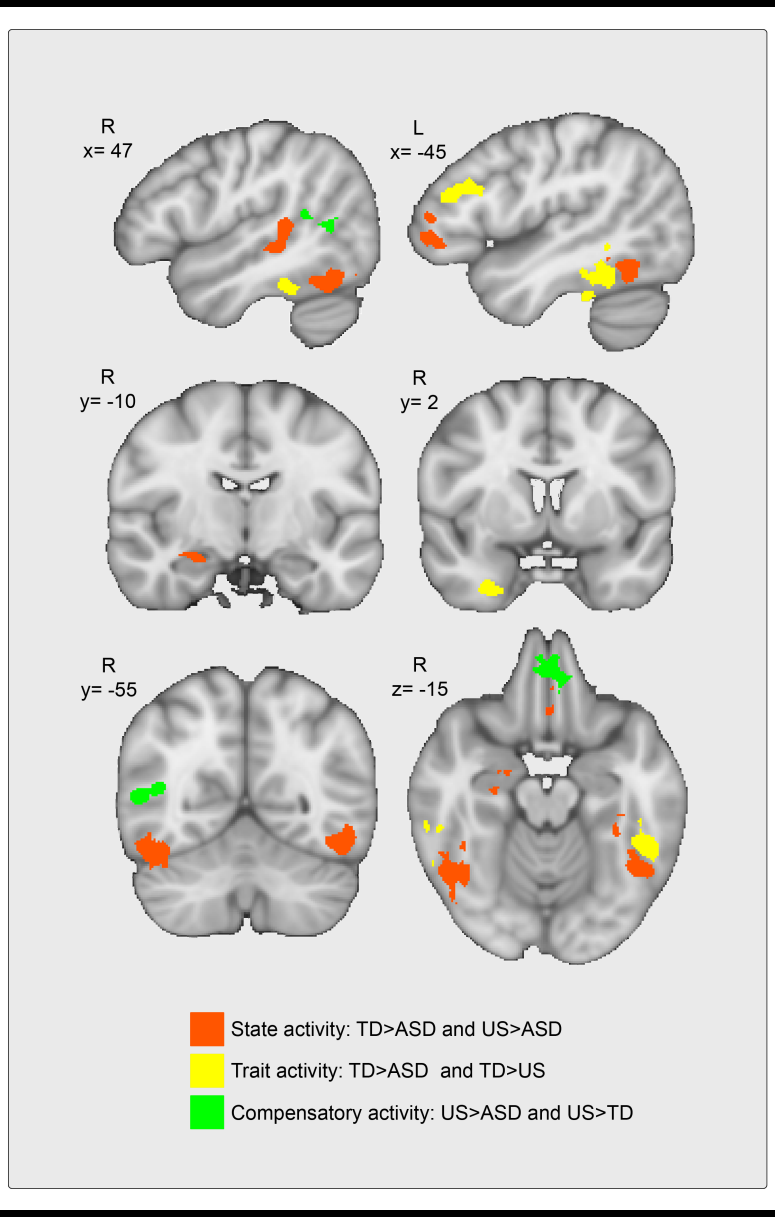
Kaiser et al. (In Press) *PNAS*

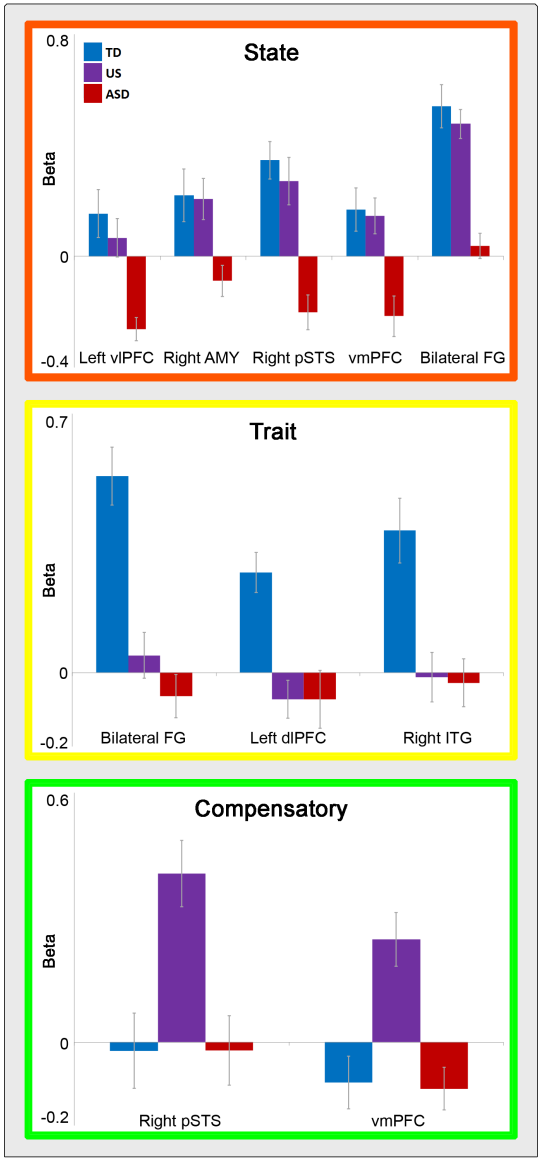
Compensatory Activity: US>TD and US>ASD





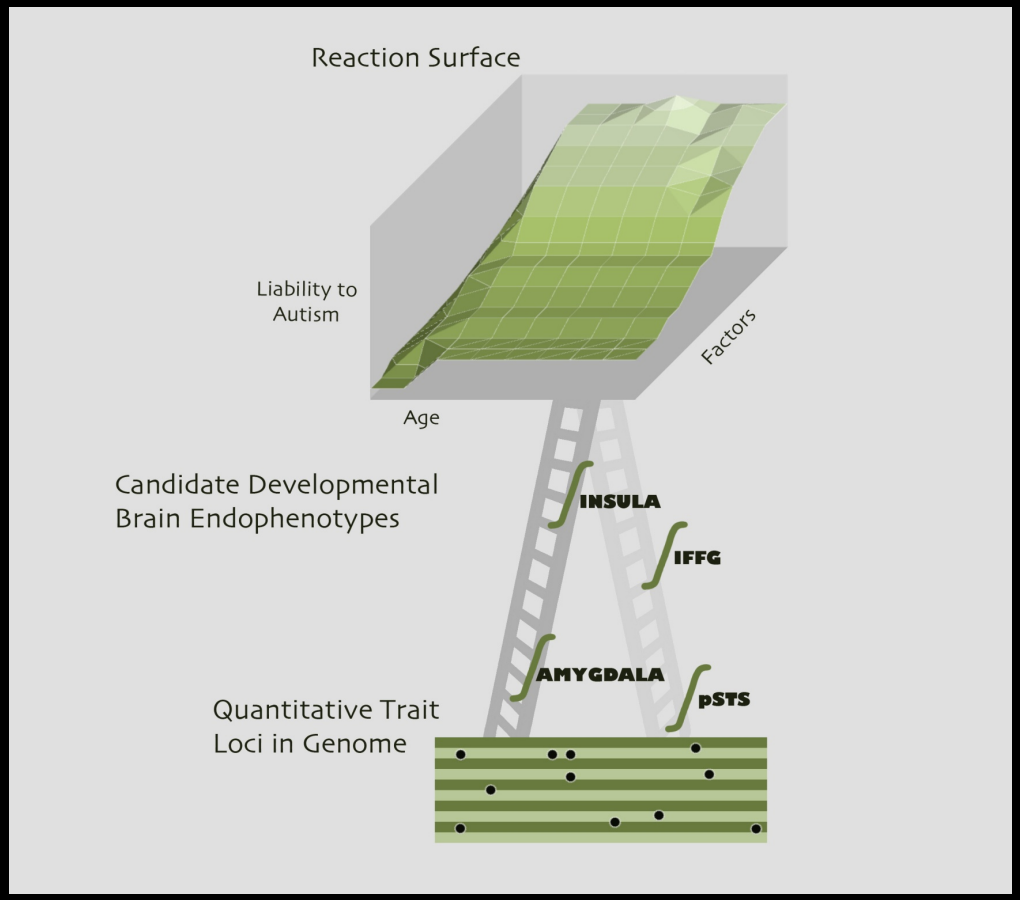
Kaiser et al. (In Press) *PNAS*





Kaiser et al. (In Press) *PNAS*

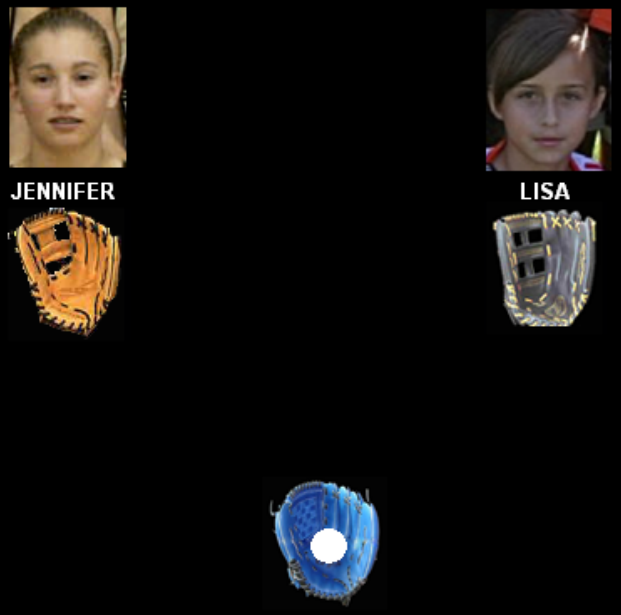
1. Identifying brain mechanisms underlying the moderating effects of common polymorphisms.
2. Whole-genome analyses using the functional brain phenotype as a quantitative trait.
3. Using the brain phenotype to select maximally divergent sibling pairs for selective whole-exome analysis.



Development of brain mechanisms for processing social exclusion

Photo Credit: Neil Harris

Social Exclusion: Cyberball

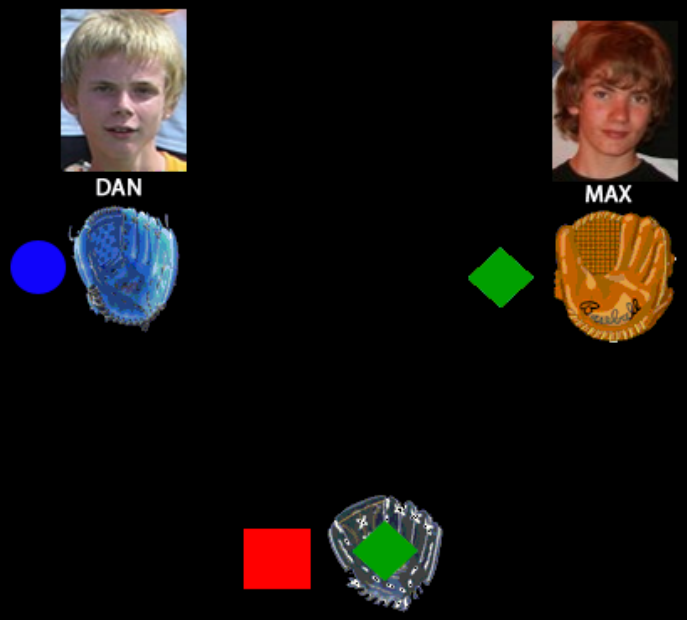


Fair Play	Exclusion	Fair Play	Exclusion	Fair Play	Exclusion	Fair Play	Exclusion	Fair Play	Exclusion

Each block = 30 seconds (12 throws)

Bolling et al. (In Press) *NeuroImage*

Rule Violation: Cybershape



Fair Play	Rule Violation	Fair Play	Rule Violation	Fair Play	Rule Violation	Fair Play	Rule Violation	Fair Play	Rule Violation

Each block = 30 seconds (12 throws)

Bolling et al. (In Press) *NeuroImage*

In Adults: Two Dissociable brain networks
for social exclusion and rule violation

Social Exclusion > Fair Play

Areas in warm colors were more active in exclusion.

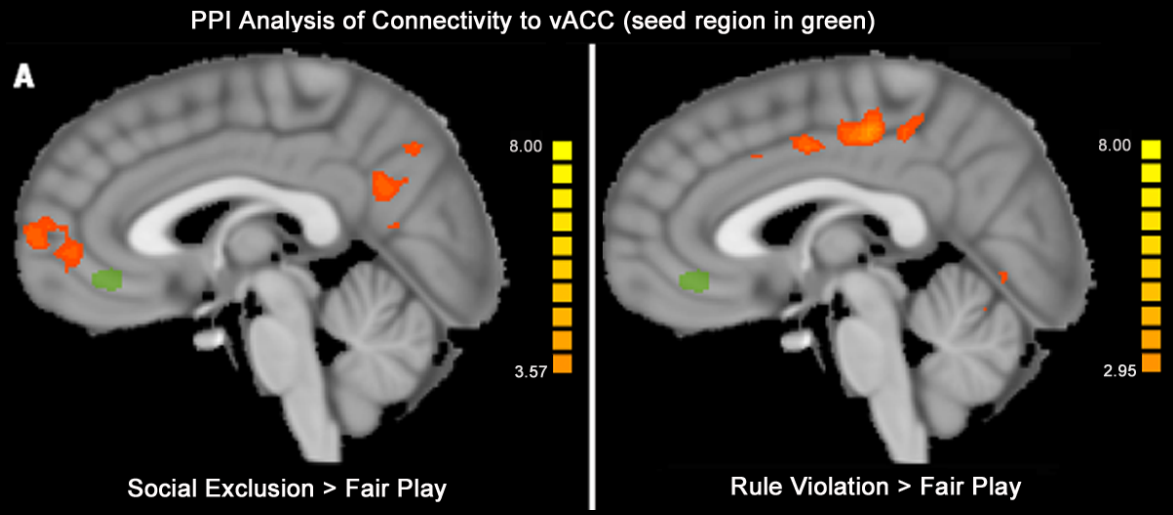
Rule Violation > Fair Play

Areas in warm colors were more active in rule violation.

Bolling et al. (In Press) *NeuroImage*

Two Dissociable brain networks

Connectivity Analyses



Above: Psychophysiological Interaction (PPI) analysis. Seed region is functionally defined from activity in social exclusion > fair play full brain contrast.

Bolling et al. (In Press) *NeuroImage*

Self-Report Measures

10 questions given in the scanner after each game:

Cyberball examples:

"I felt rejected"

"I felt unsure of myself"

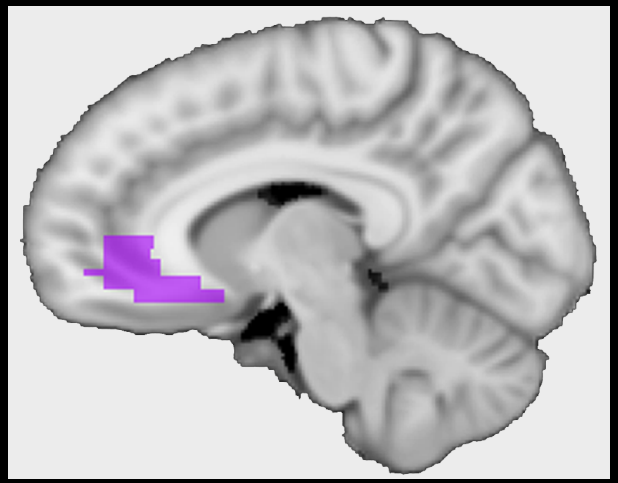
Cybershape examples:

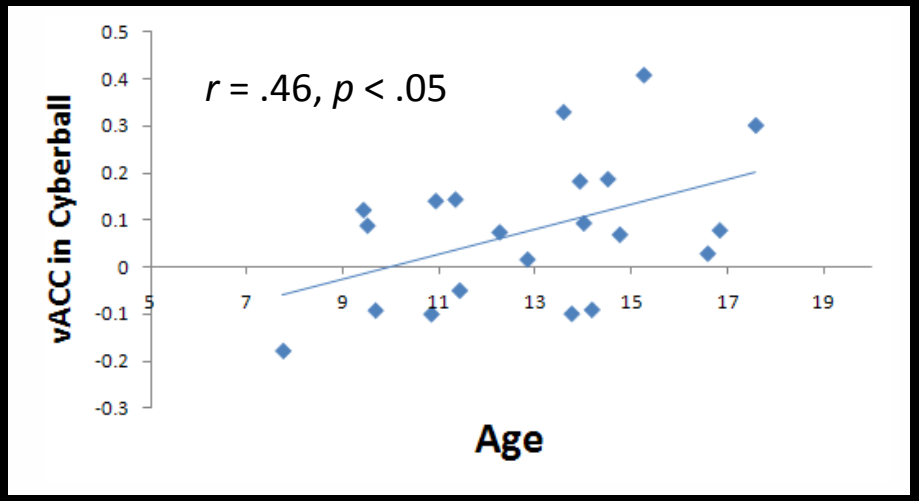
"I was annoyed when players didn't follow the rules"

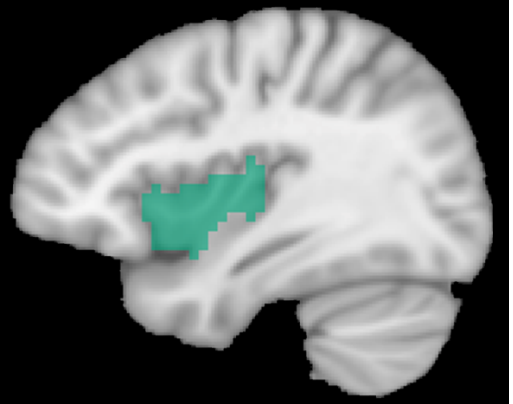
"I felt upset when something unexpected happened in the game"

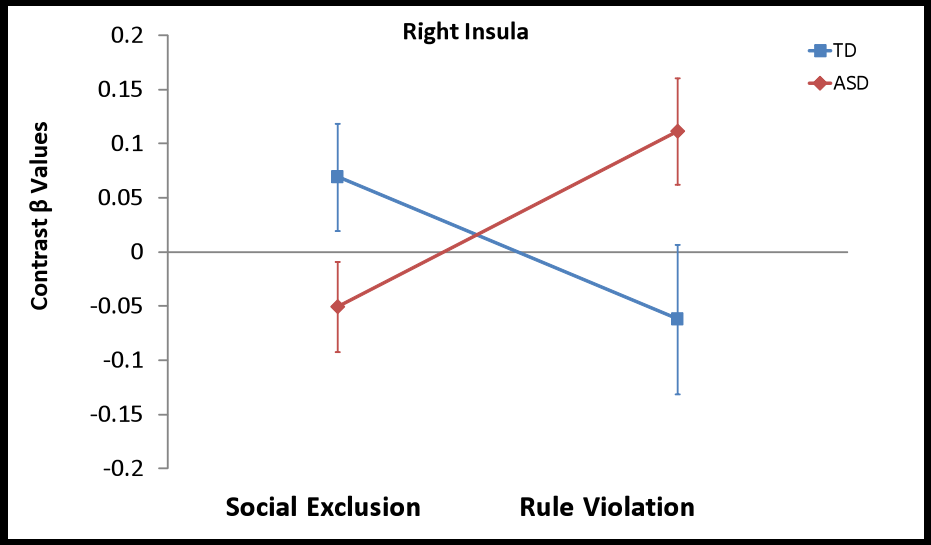
Age Correlations: Typical Children

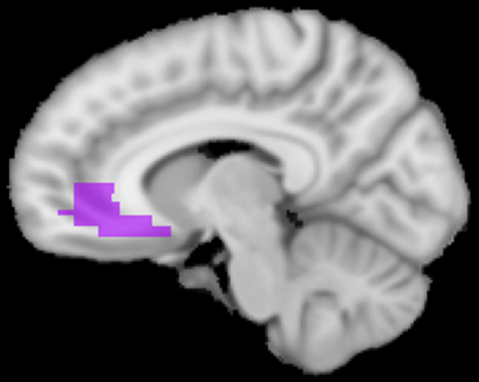
Structural vACC

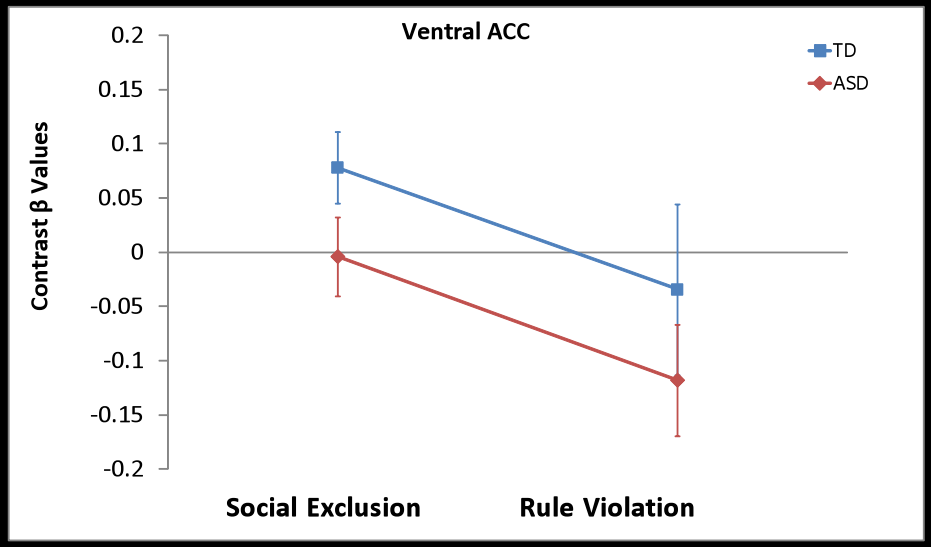







Right Insula
Contrast β Values
0.2
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2
TD
ASD
Social Exclusion
Rule Violation




Ventral ACC
Contrast β Values
0.2
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2
TD
ASD
Social Exclusion
Rule Violation

III. Recent directions

Linking brain phenotype, genes, and behavior in the longitudinal study of infants at high risk for developing autism

Yale Infant Siblings Project

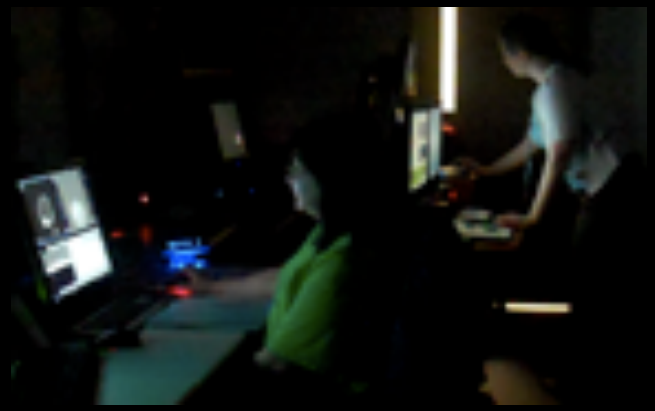
- An intensive and comprehensive infant siblings project; involving several hundred babies seen from the earliest weeks of life, regularly (every few months) into childhood.
- As a clinical research center, the intention is to follow the children throughout their lives.










TOM Trio

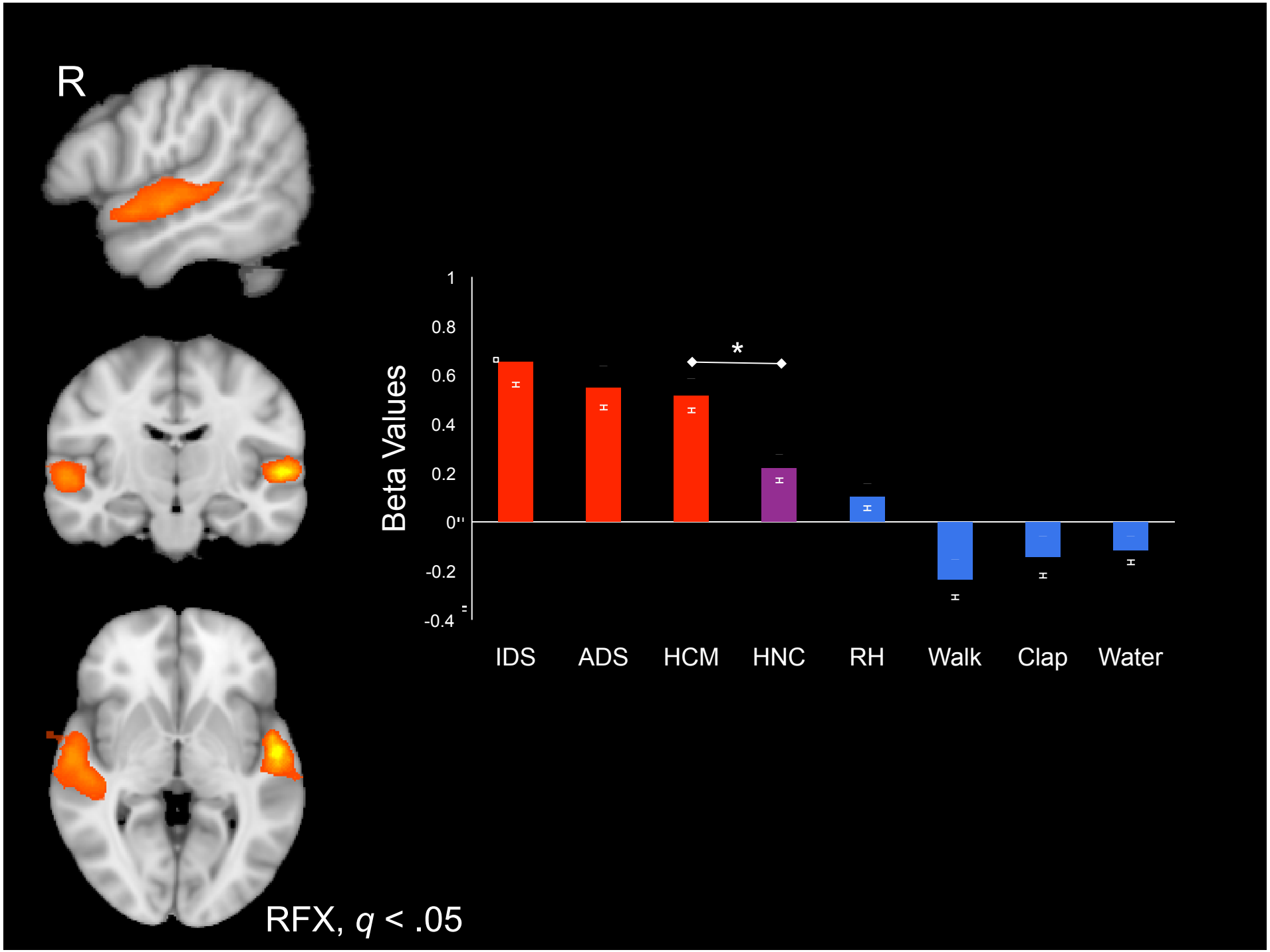
The STS is sensitive to communicative versus non-communicative sounds

Communicative Sounds

- Infant-directed speech
- Adult-directed speech
- Human communicative vocalizations (e.g., laughter)

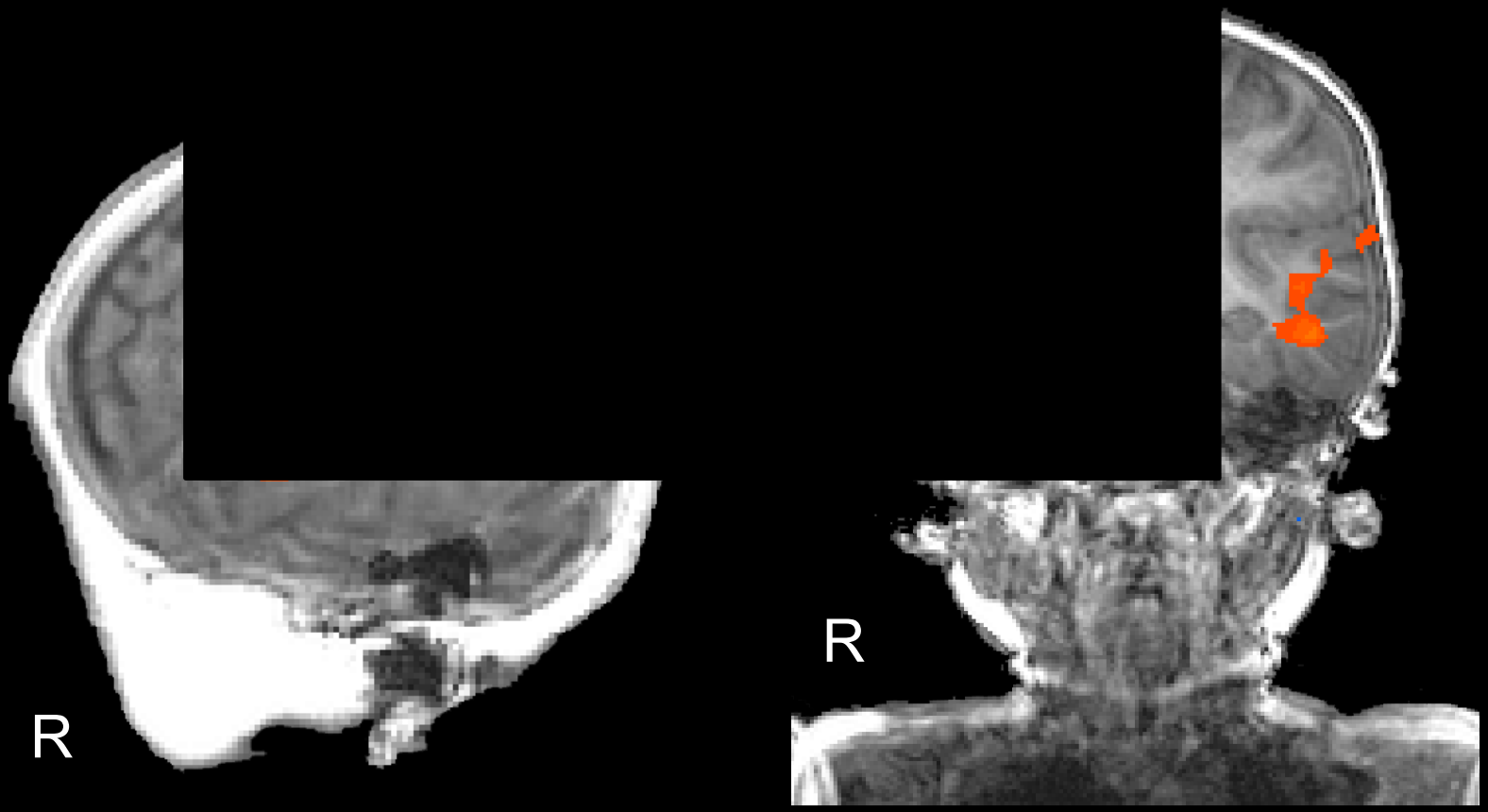
Non-Communicative Sounds

- Human non-communicative vocalizations (e.g., coughs)
- Walking
- Clapping
- Water
- Rhesus calls


R
Beta Values
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
*
IDS
ADS
HCM
HNC
RH
Walk
Clap
Water
RFX, q < .05

Responses to Communicative Intent in the Infant Brain

Communicative vs. Non-communicative



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Jessica Cantlon
Roger Jou
Benjamin Deen
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Abha Gupta
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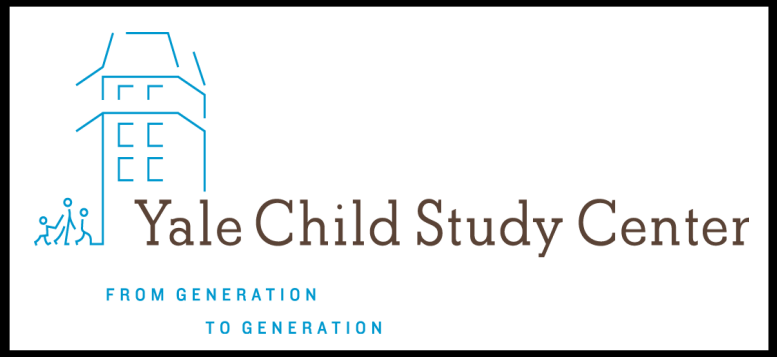
Mike Crowley

The children and families who participate in our research.



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