Autism and the Brain

Dustin Moraczewski

Developmental Social Cognitive Neuroscience Lab

University of Maryland Autism Research Consortium

2.25.2017

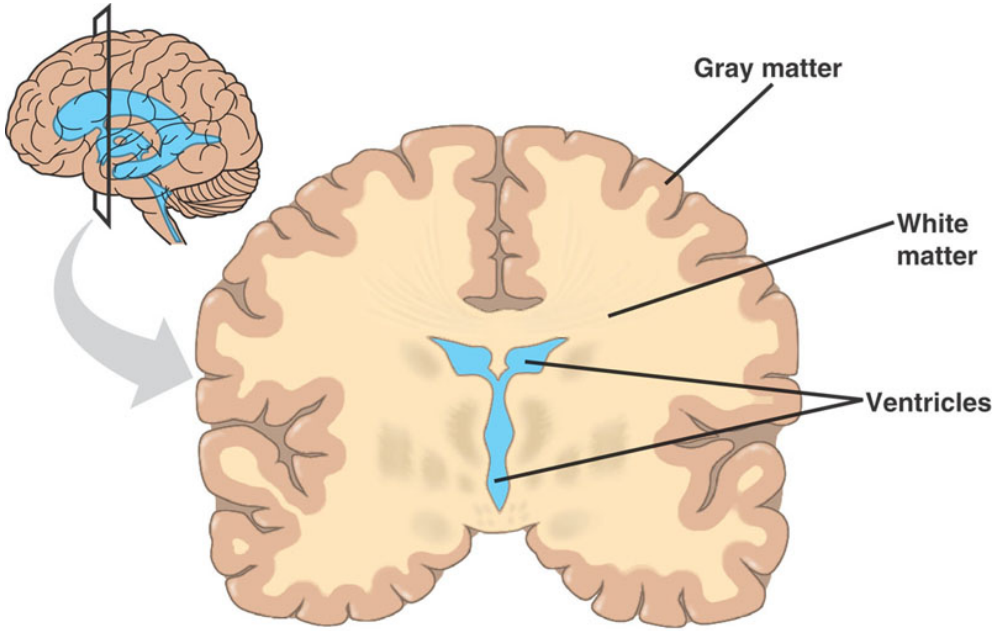
About me…

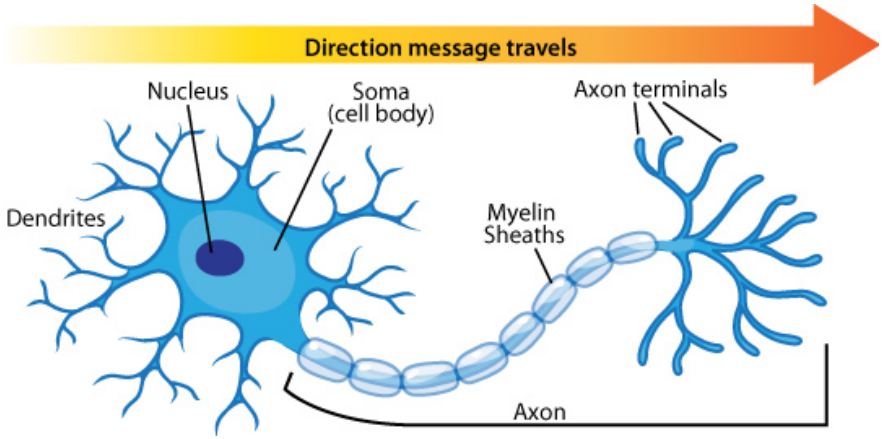
- 3rd year graduate student
  - Neuroscience and Cognitive Science Program
  - Dr. Elizabeth Redcay's Developmental Social Cognitive Neuroscience Lab
  - Research interest:
    - How brain networks develop to support naturalistic social processing using fMRI in typically developing children and those with ASD

About me…

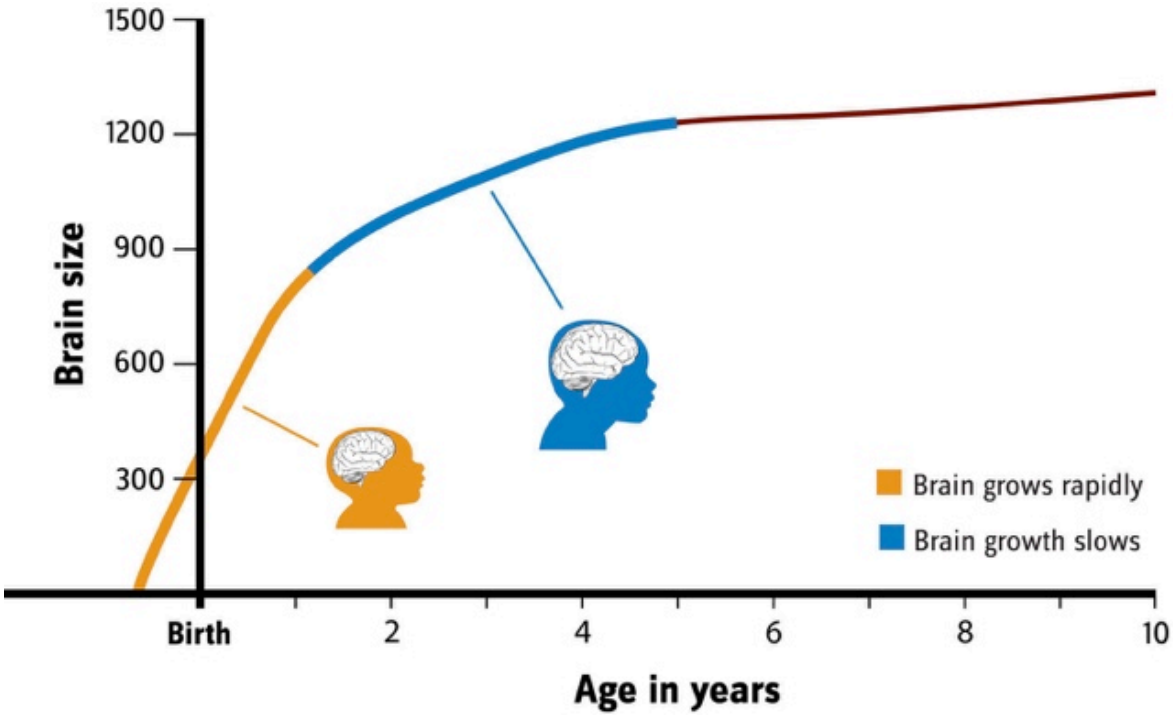
- Prior to graduate school:
  - Behavior therapist for foster children with ASD in Miami and Broward counties for the Devereaux Foundation
  - One-on-one behavioral therapist
  - Group home manager for Autism Services Center in Huntington, WV
  - One-on-one direct support staff at Autism Services Center
  - Bachelor's in psychology and music from Marshall University

Overview of brain anatomy





How does the brain develop?



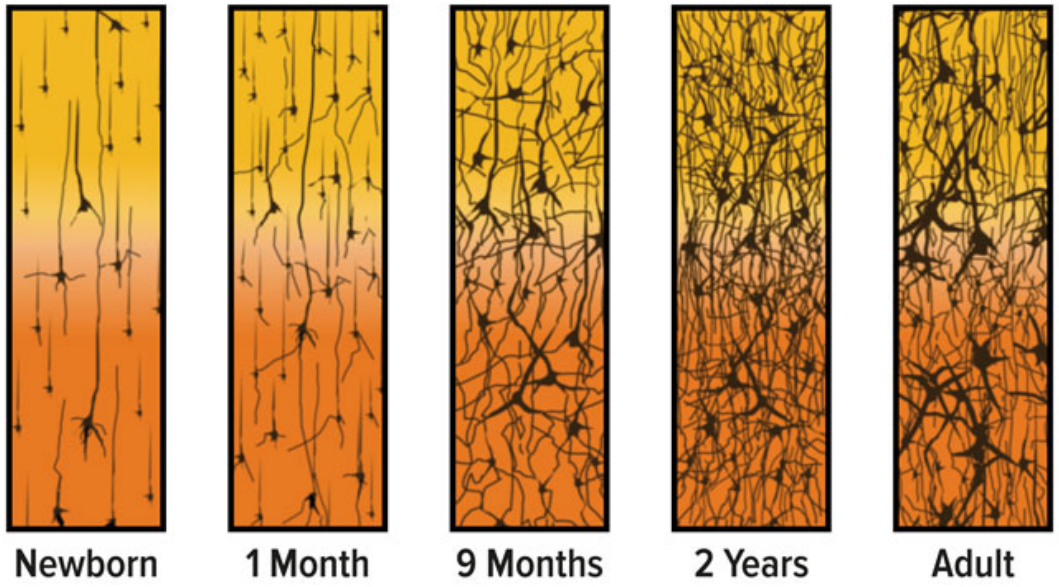
However…

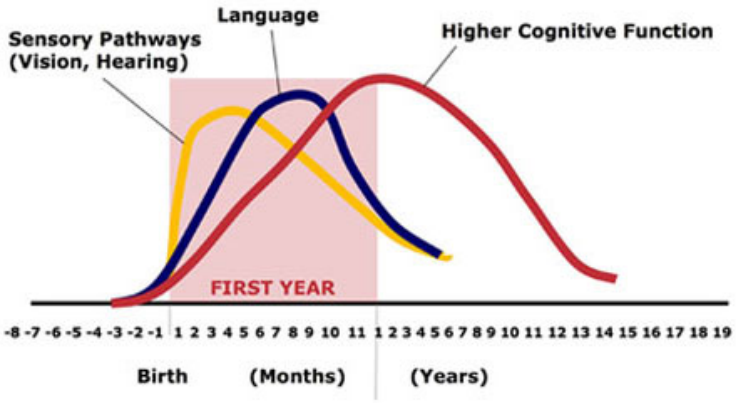
Almost all neurons are in place before birth!

(Rakic, 1995)

Image from Smithsonian National Museum of Natural History

How does the brain develop?

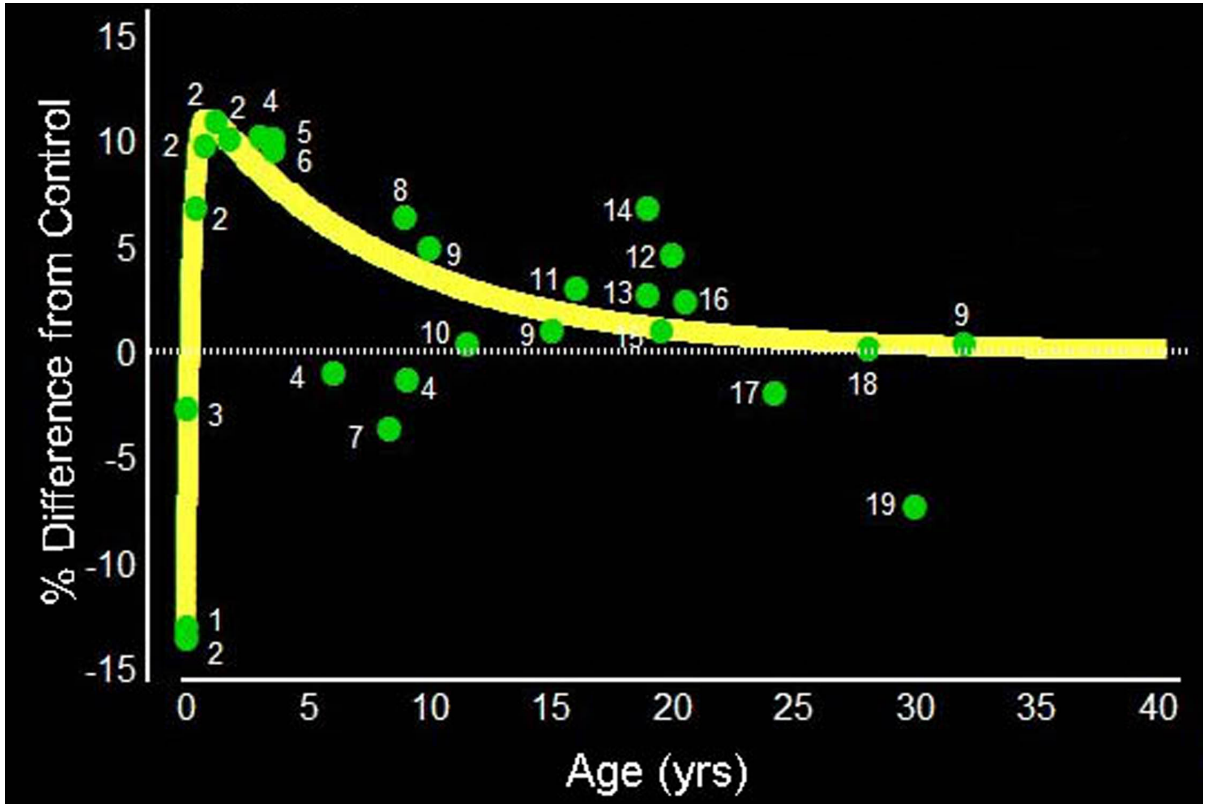




Images from the Center for the Developing Child at Harvard University

Brain size and ASD

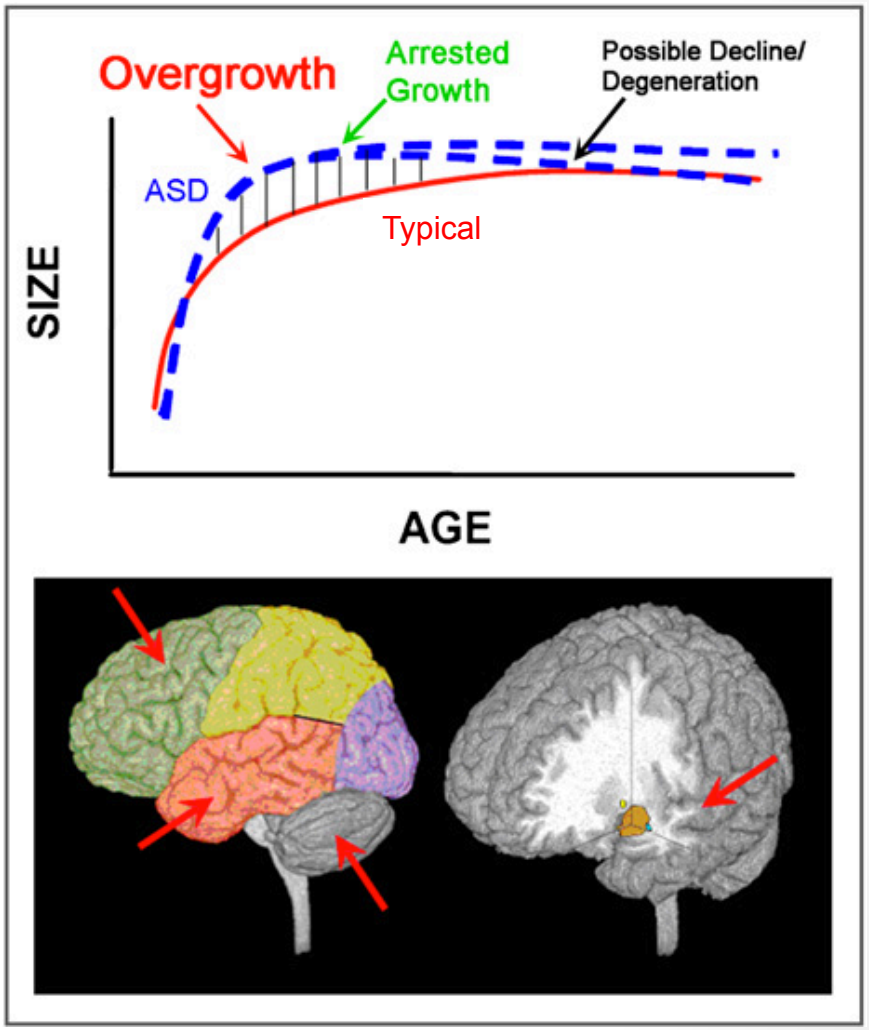
Meta-analysis of head circumference and MRI studies comparing typically developing individuals to ASD



Redcay & Courchesne, 2005

Brain overgrowth in ASD

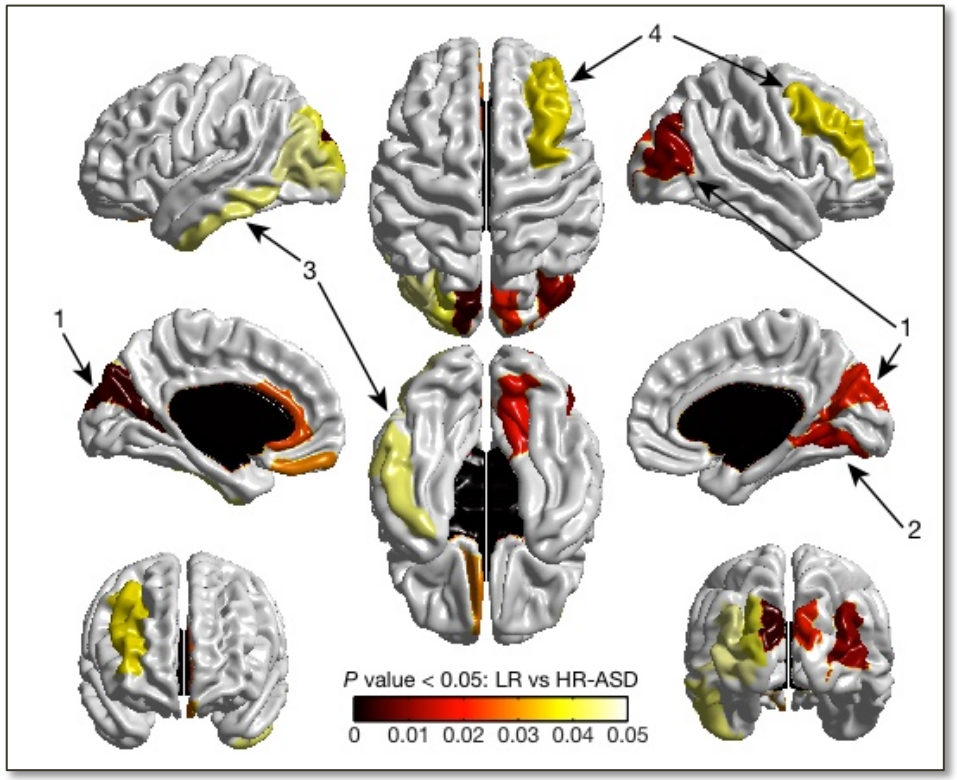
- Frontal lobe
  - social, executive functioning, language
- Temporal lobe
  - social, language
- Cerebellum
  - attention, movement
- Amygdala
  - social, emotion, novelty



Courchesne et al., 2007

(very) Recent work

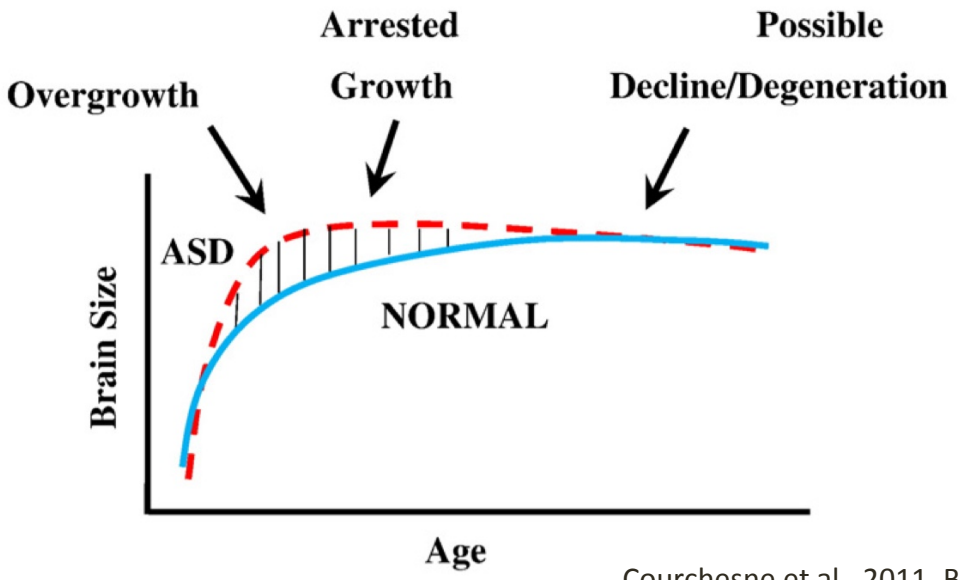
- Hyper-expansion of the brain surface between 6-12 months preceded brain overgrowth in 12-14 months in **15 infants** who would later be diagnosed with ASD.
- Brain overgrowth was linked to severity of social deficits



Hazlett et al., 2017

What could it mean?

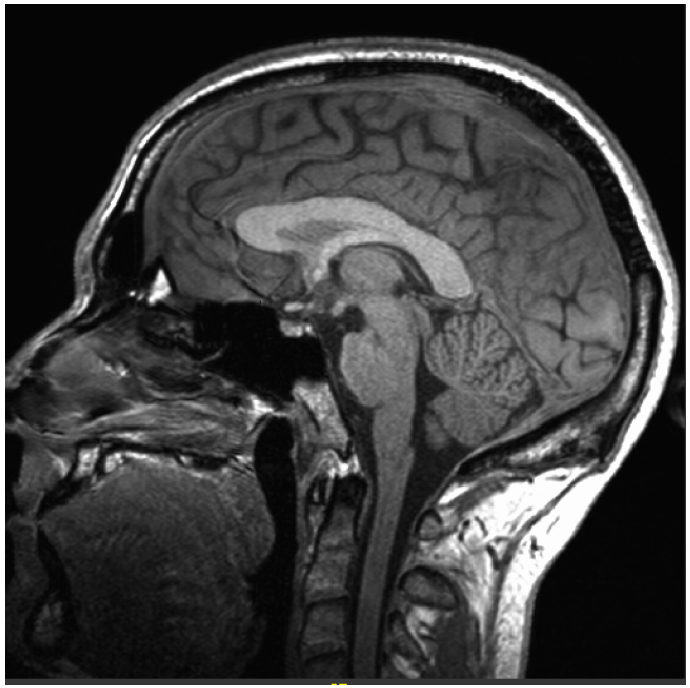
- Greater number of neurons
  - Evidence of this in prefrontal cortex (Courchesne et al., 2011. JAMA.)
- Greater connections between neurons (more noisy)
- Atypical experience-dependent pruning
- Altered local (short range) and global (long range) connections



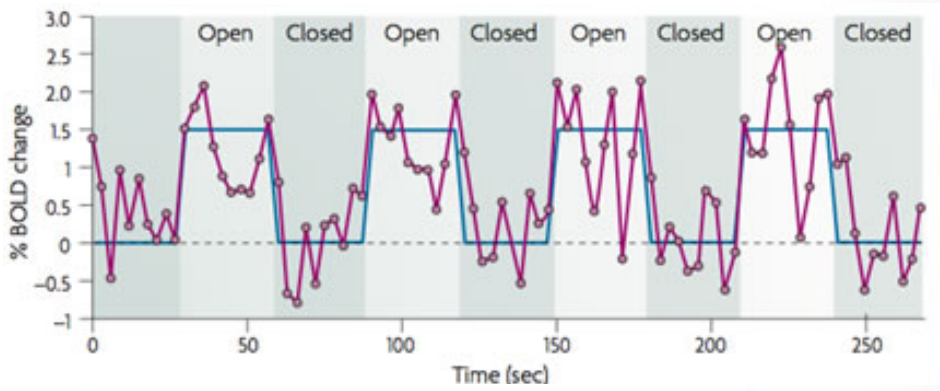
Courchesne et al., 2011. Brain Research.

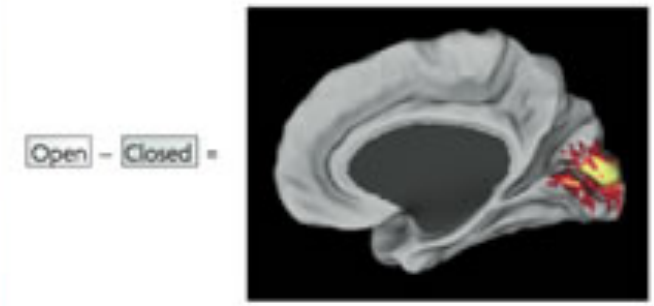
Structural vs functional MRI

Structural



Functional





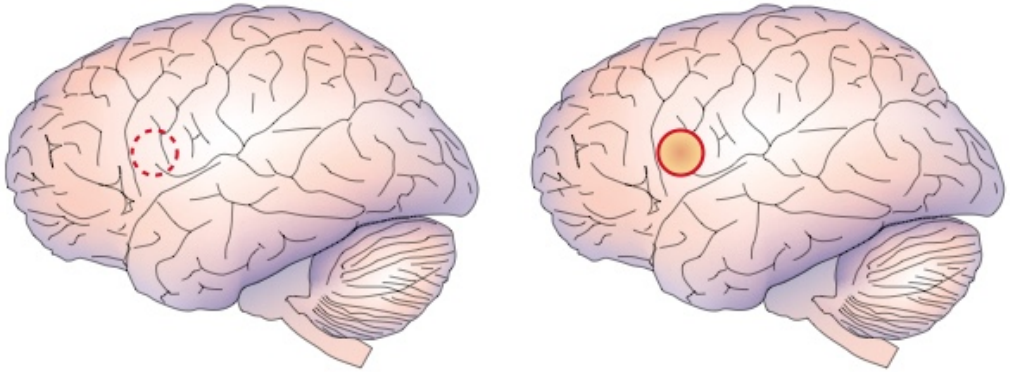
Fox & Raichle, 2007

- Whole brain size
- Cortical thickness (processing)

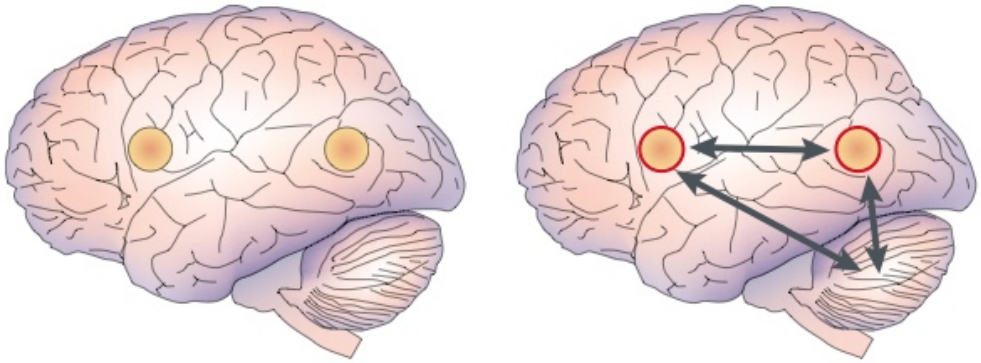
- Changes in blood flow across time
- Greater blood flow → more brain activity

How should we think of functional differences in ASD?

- Maturation, localization, and the lesion model



- Interactive specialization to understand atypical development
(Johnson, 2002)



Images from Johnson, 2001

ASD as a disorder of brain connectivity

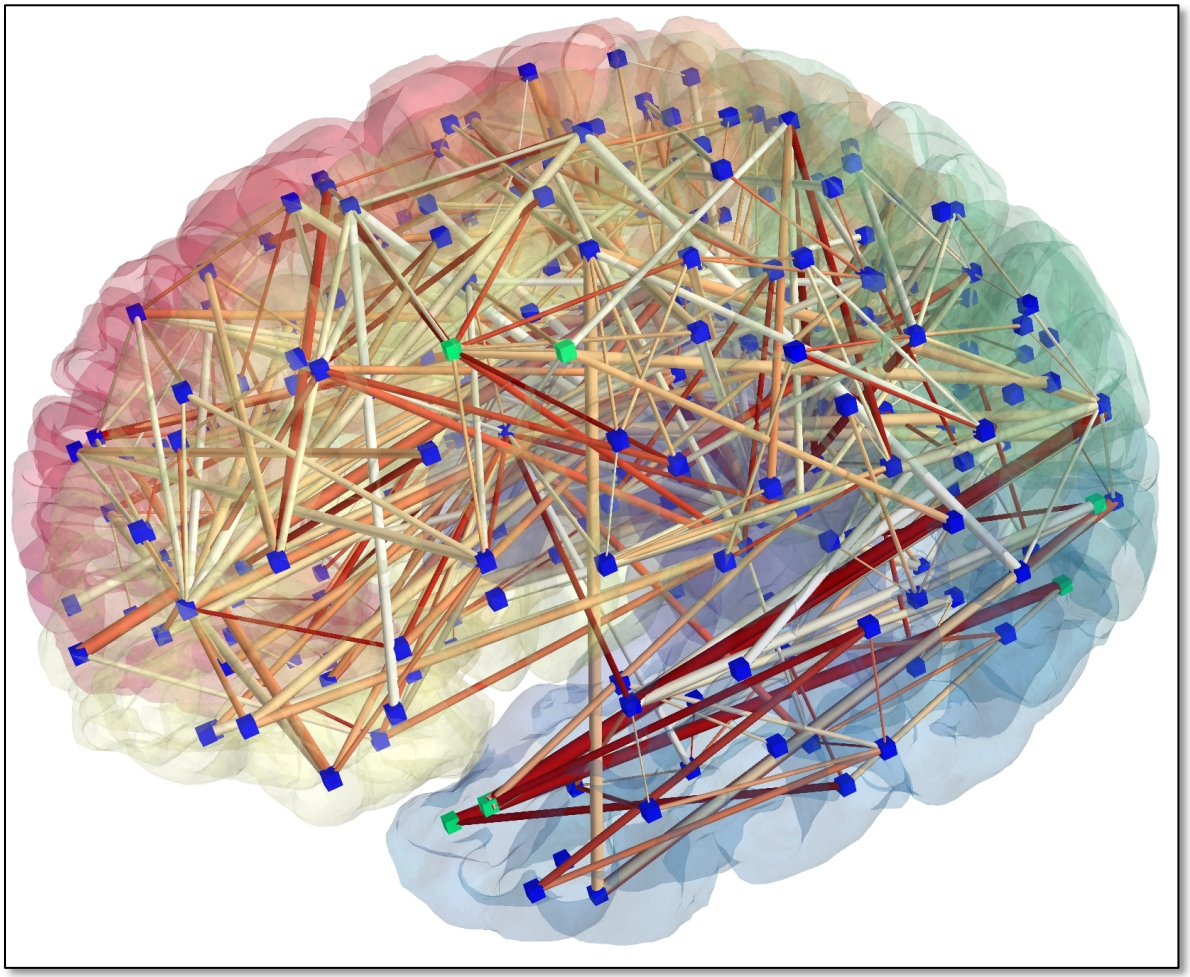


Image from The Connectome Mapper (www.cmtk.org)

Functional connectivity

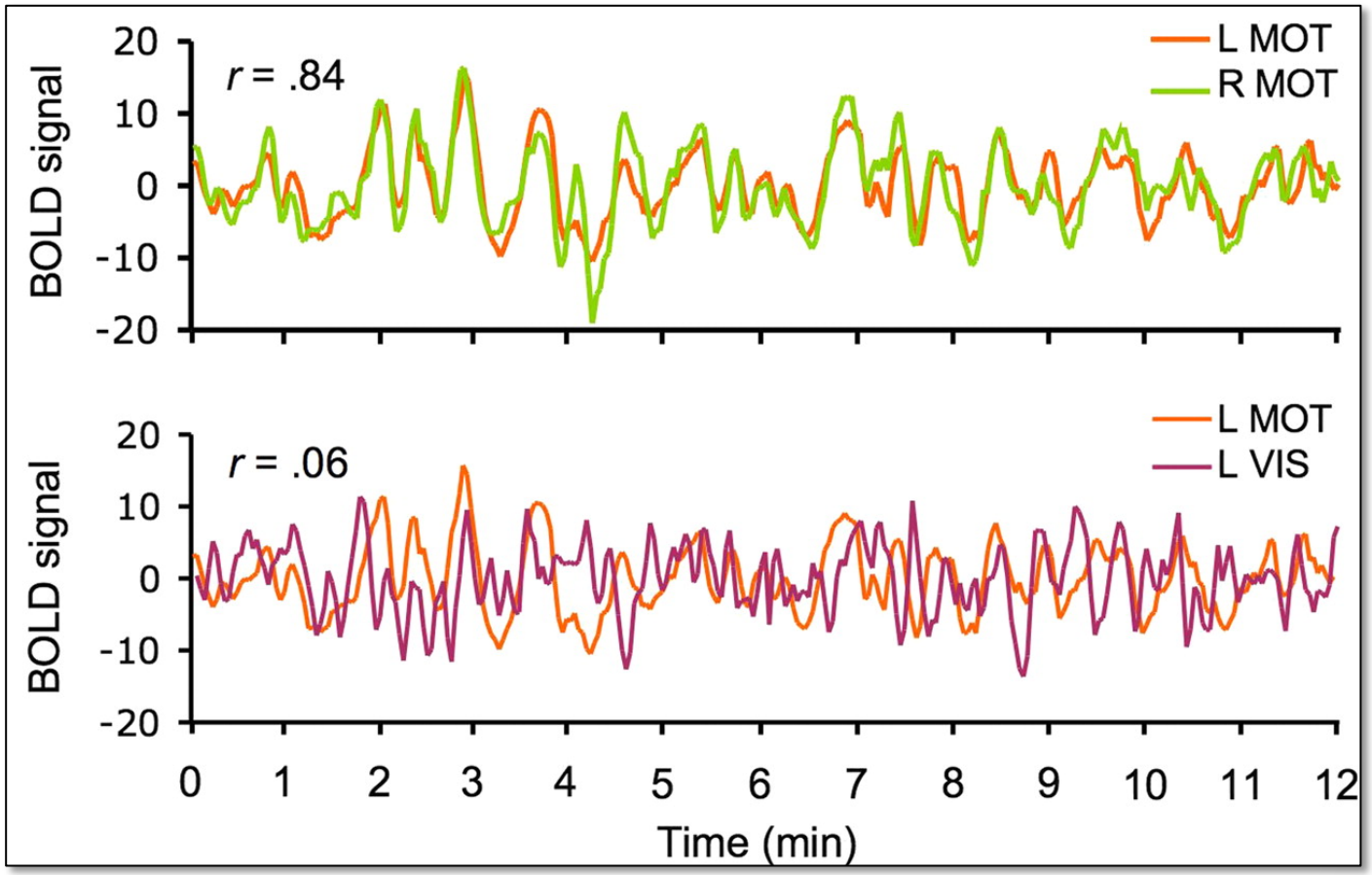
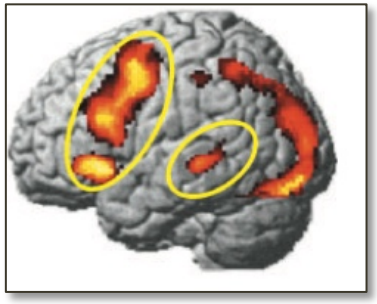
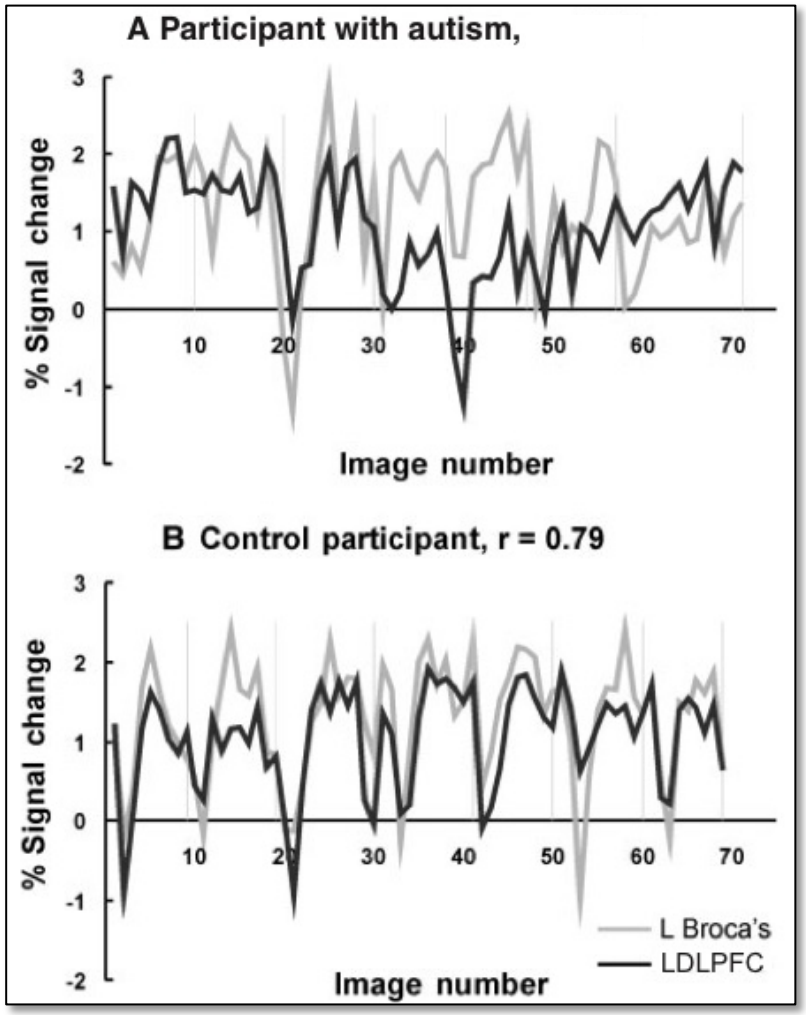
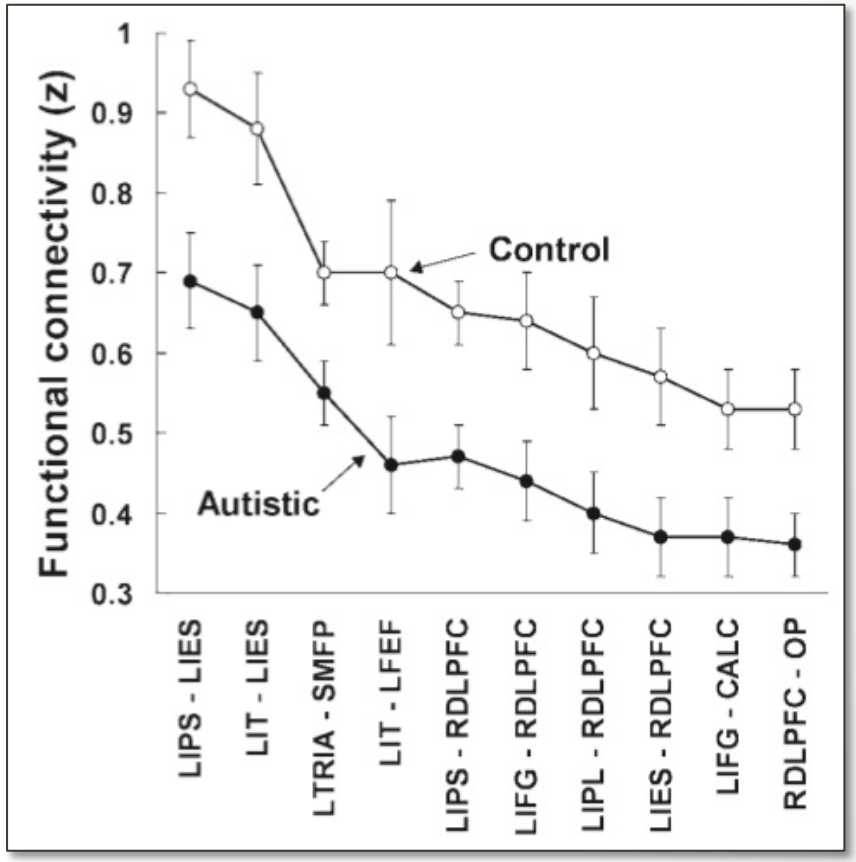


Image Van Dijk et al., 2010

Hypo-connectivity

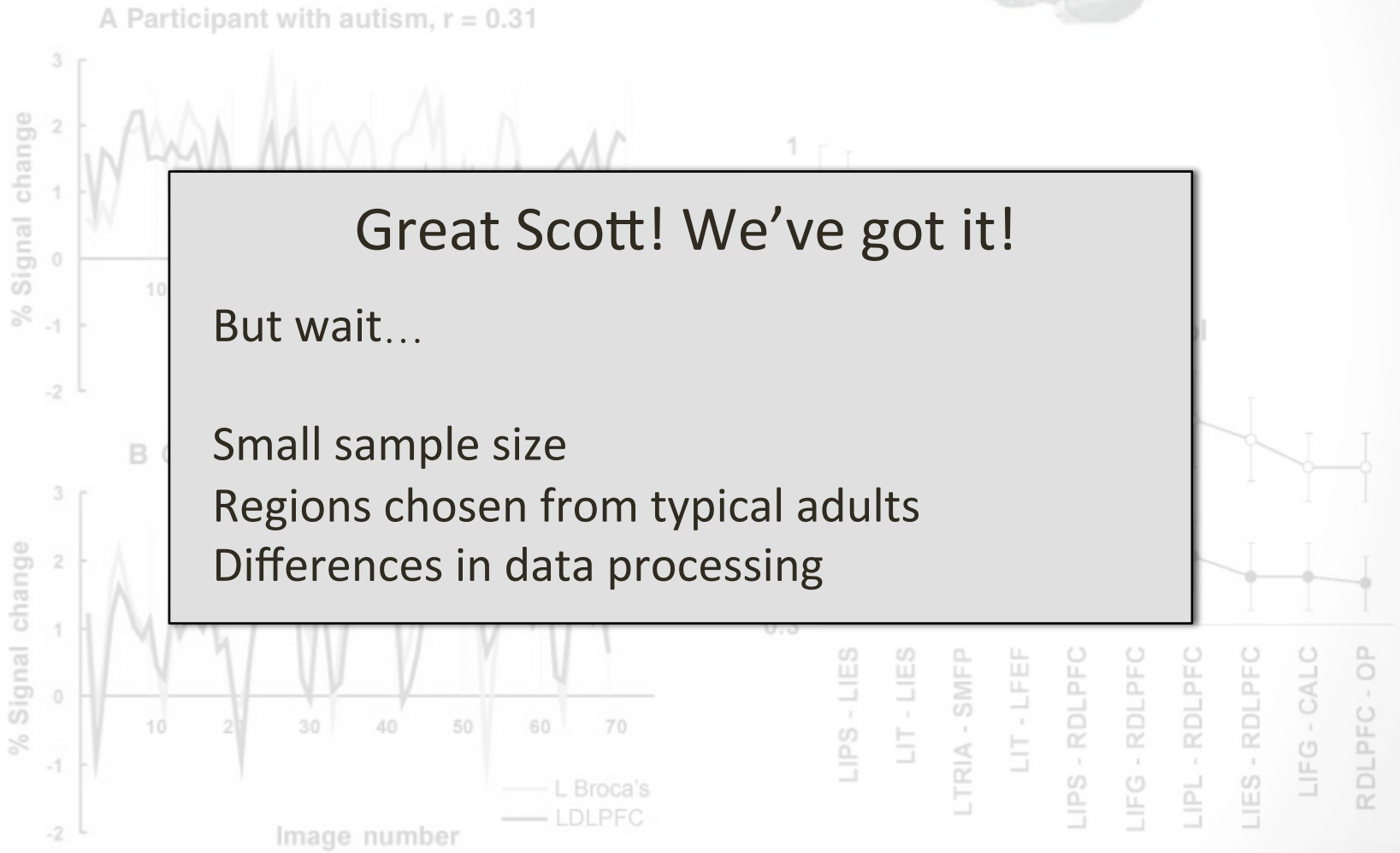






Just et al., 2004

Hypo-connectivity

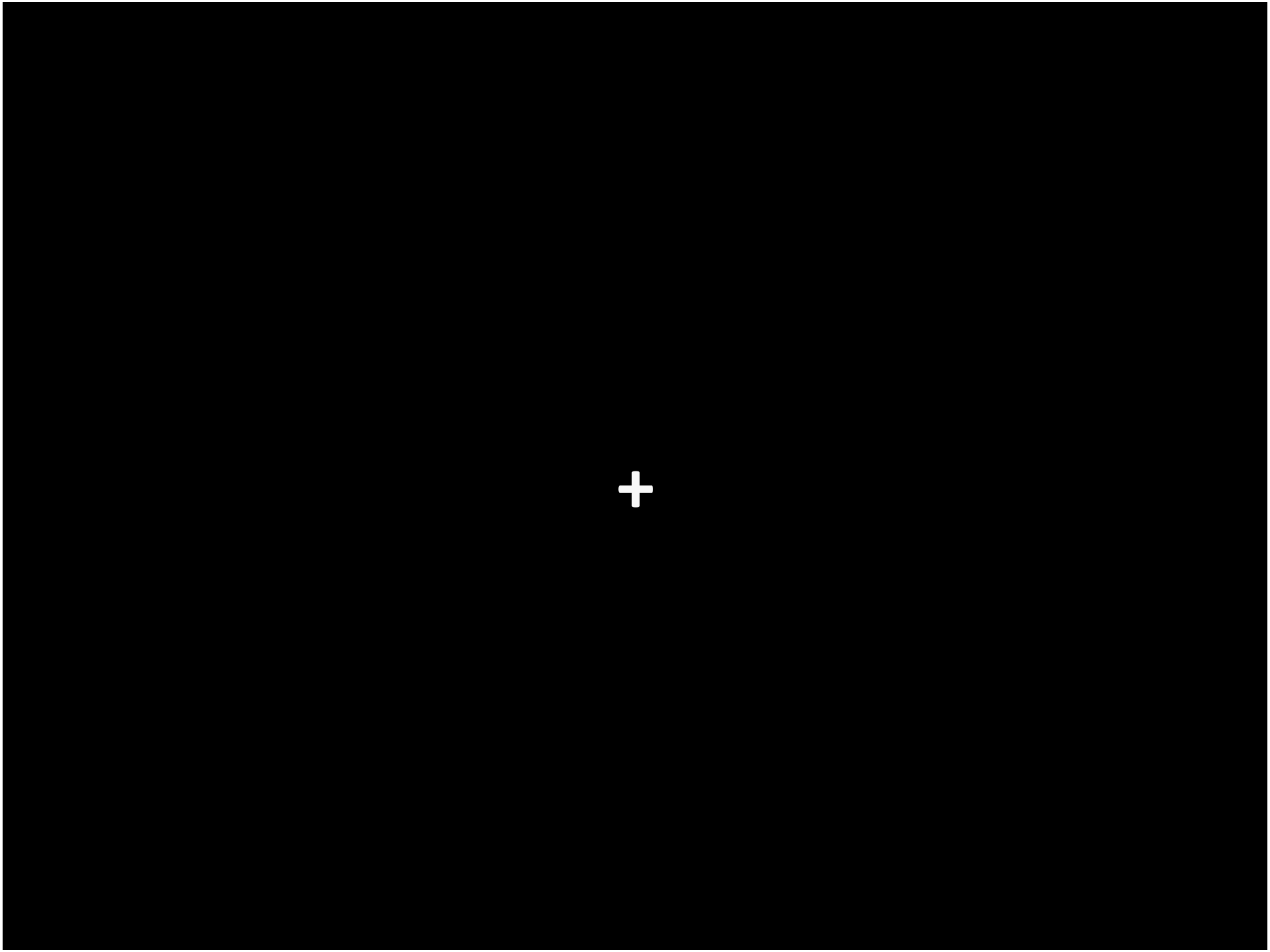


Great Scott! We've got it!

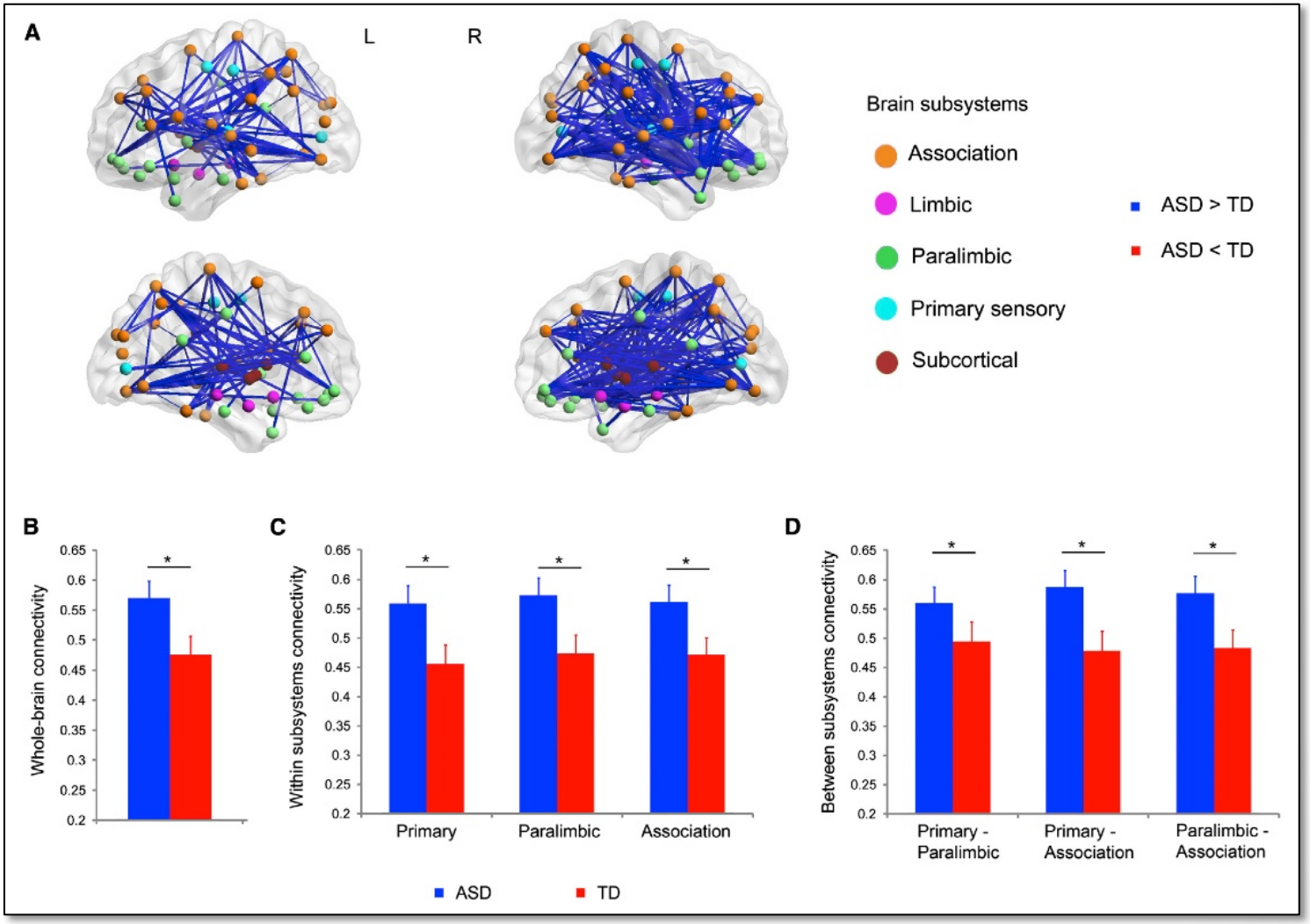
But wait…

Small sample size
Regions chosen from typical adults
Differences in data processing

Just et al., 2004

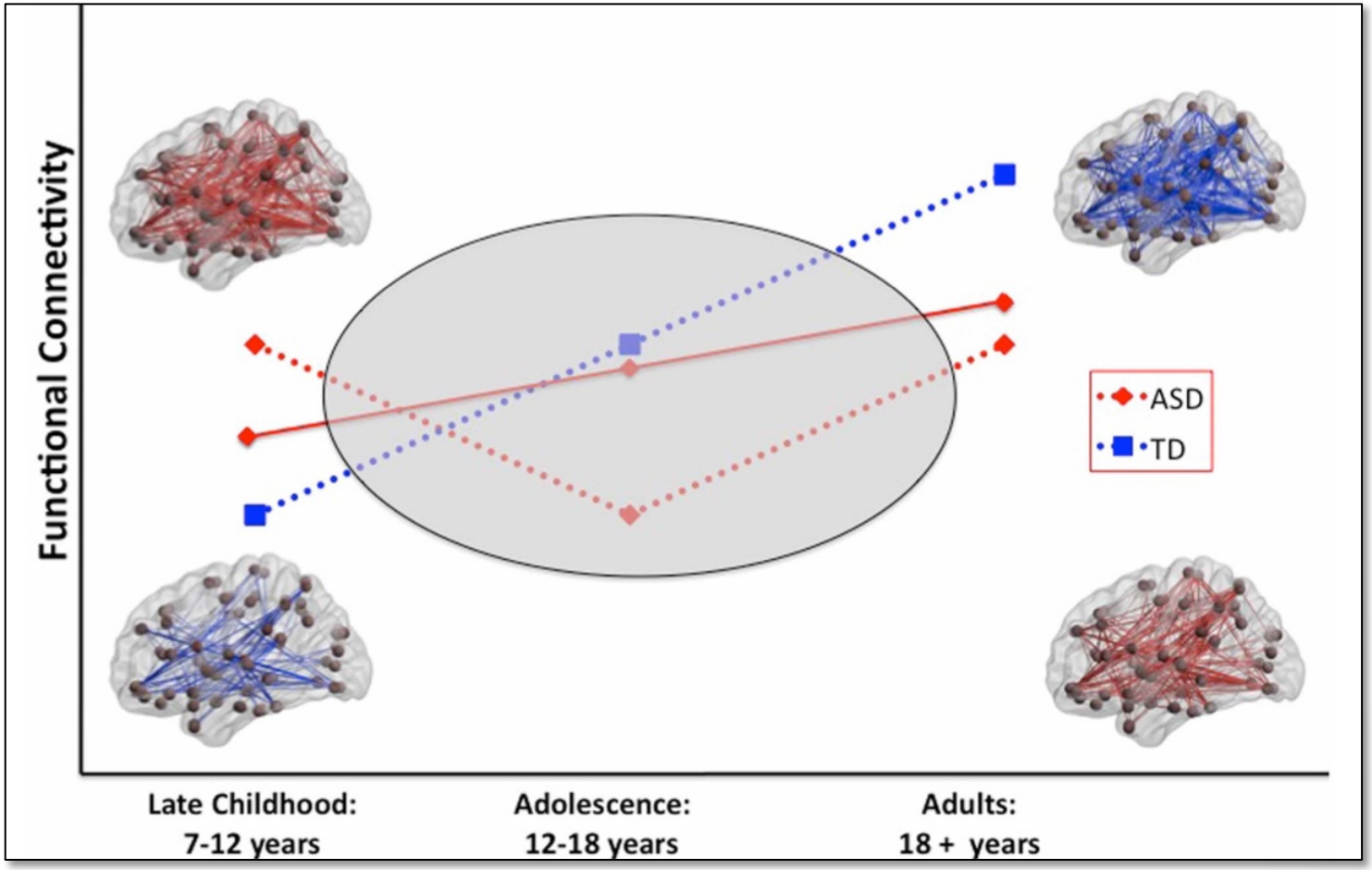


Hyper-connectivity hypothesis



Supekar et al., 2013

Hypo- or hyper-connectivity? Make up your mind!



Uddin et al., 2013

We need more data!

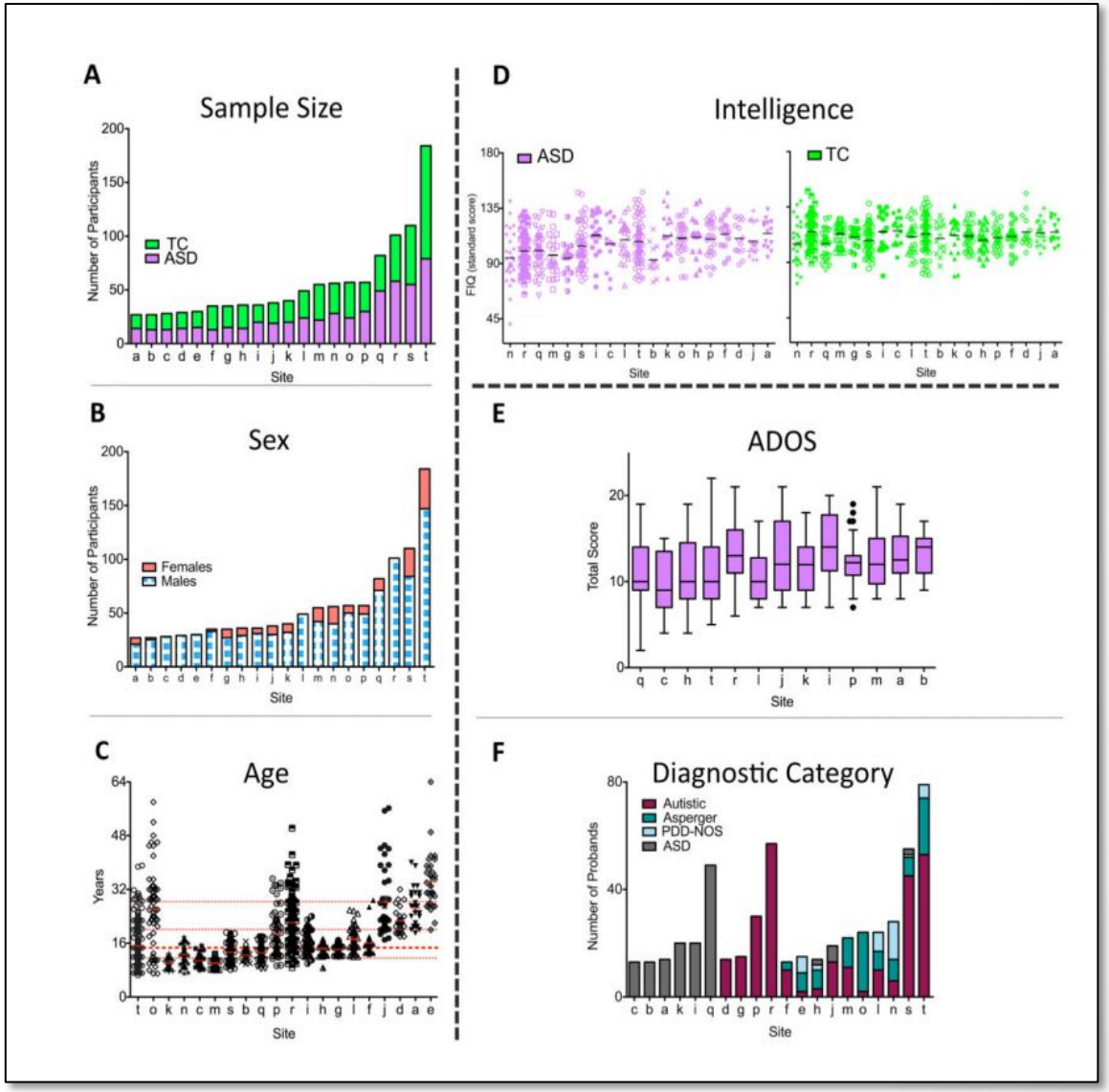
Autism
Brain
Imaging
Database
Exchange

Sample size: 1112

573 ASD 539 NT
984 M 218 F

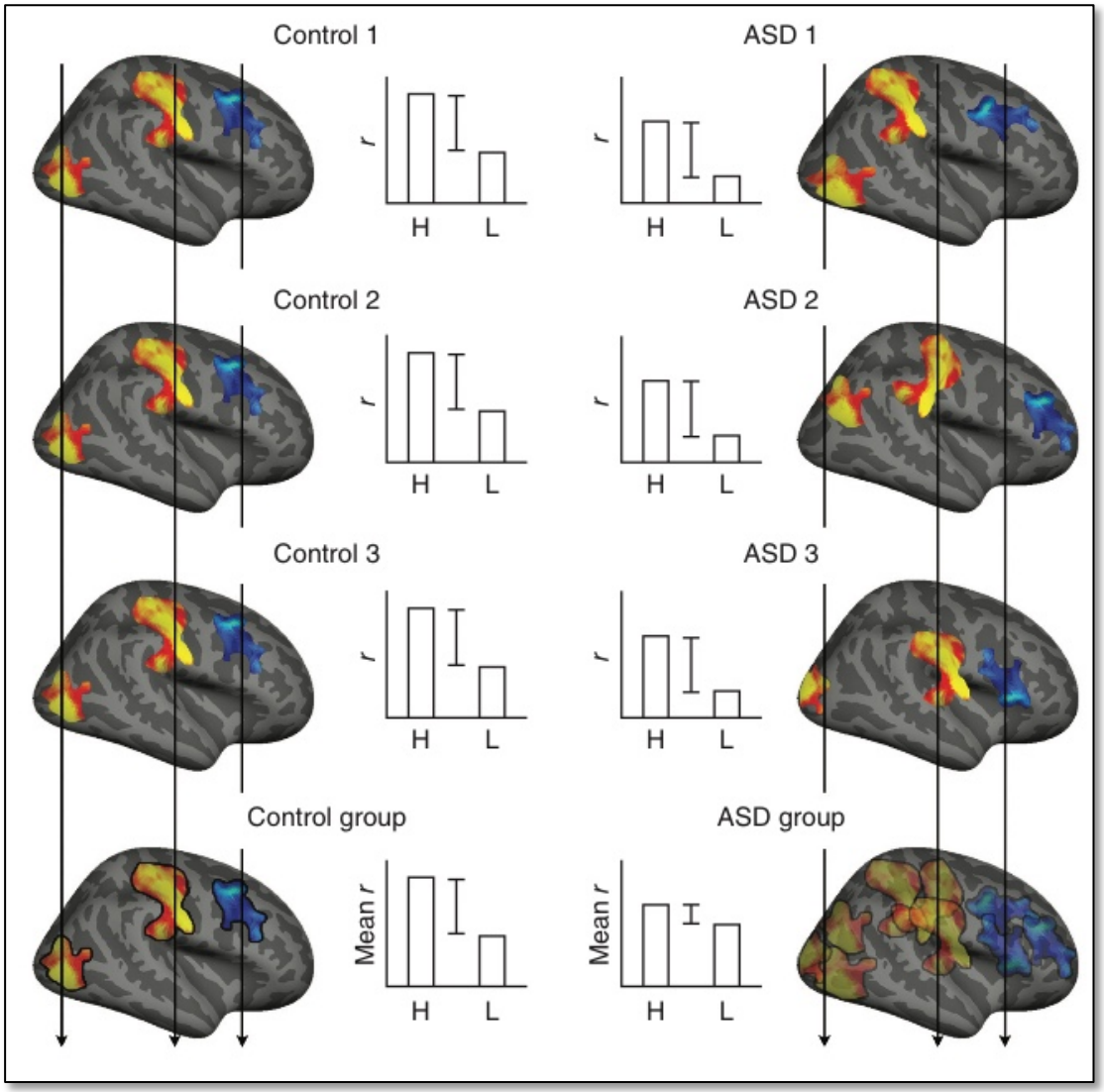
Age range 7-64 years
Mean age ~17 years

17 sites



Di Martino et al., 2014

The idiosyncratic brain



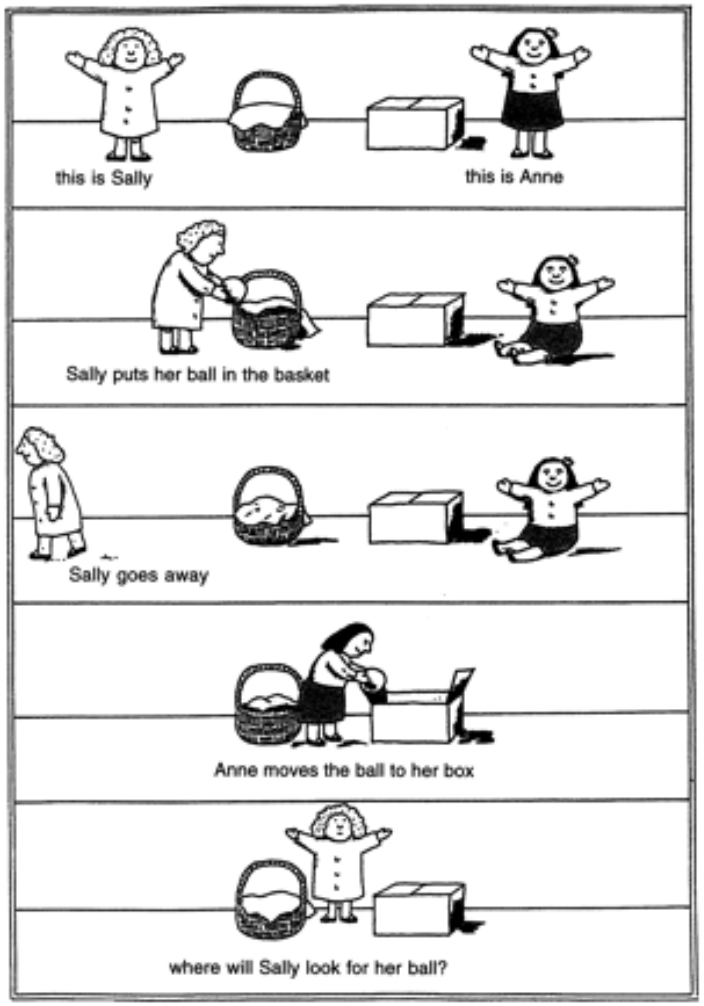
Hahamy et al., 2015

Functional connectivity summary

- There are differences in connectivity in ASD compared to neurotypical individuals
  - Reports of hypo- and hyper-connectivity
    - Possible age-related progression from hyper to hypo
  - Many studies relate atypical connectivity to symptom severity

- ASD may be characterized by more idiosyncratic connectivity patterns
  - Examining group averages could distort the results

Theory of mind and ASD



Belief

"The morning of high school dance Sarah placed her high heel shoes under her dress and then went shopping. That afternoon, her sister borrowed the shoes and later put them under Sarah's bed."

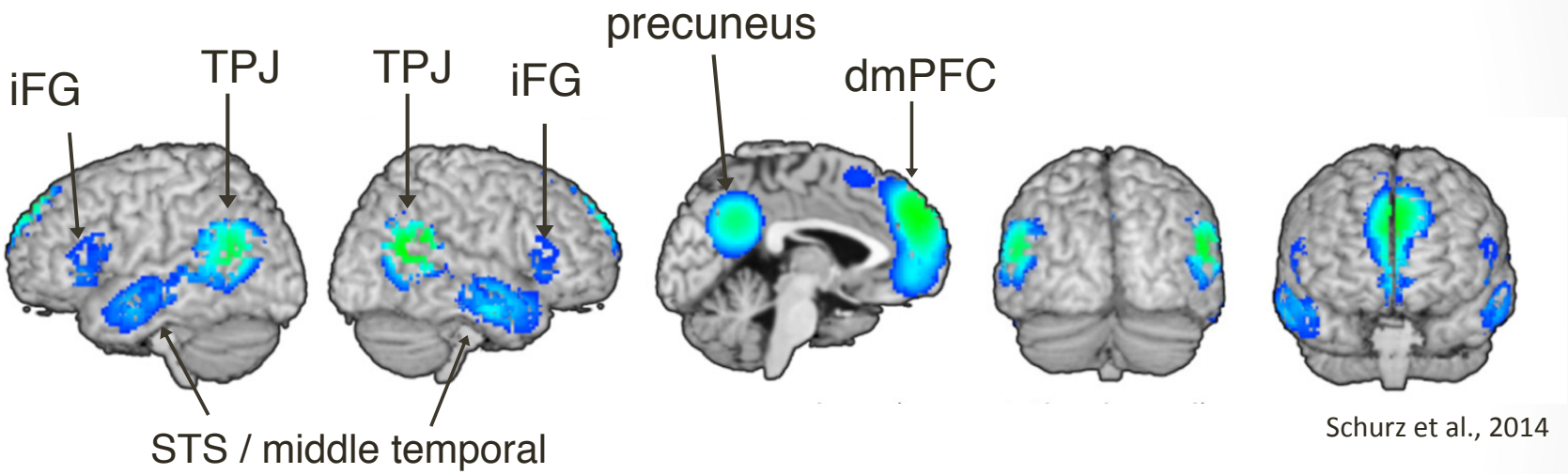
T/F: Sarah gets ready assuming her shoes are under her dress.

Photo

"The traffic camera snapped an image of the black car as it sped through the stoplight. Soon after, the car was painted red and the license plates were changed."

T/F: According to the traffic camera, the car is black.

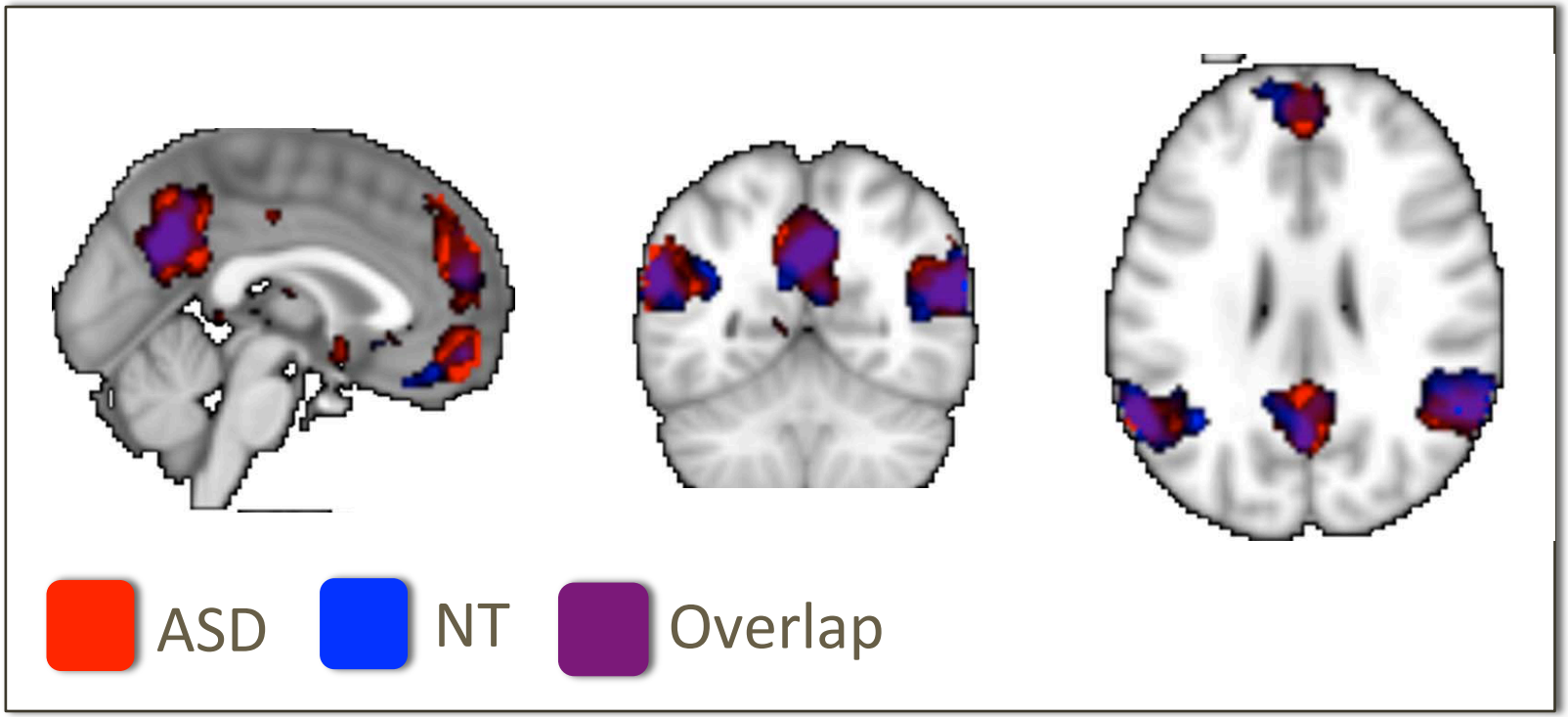
Theory of mind and the brain



Schurz et al., 2014

dmPFC	- dorsal medial prefrontal cortex
iFG	- inferior frontal gyrus
STS	- superior temporal sulcus
TPJ	- temporo-parietal junction

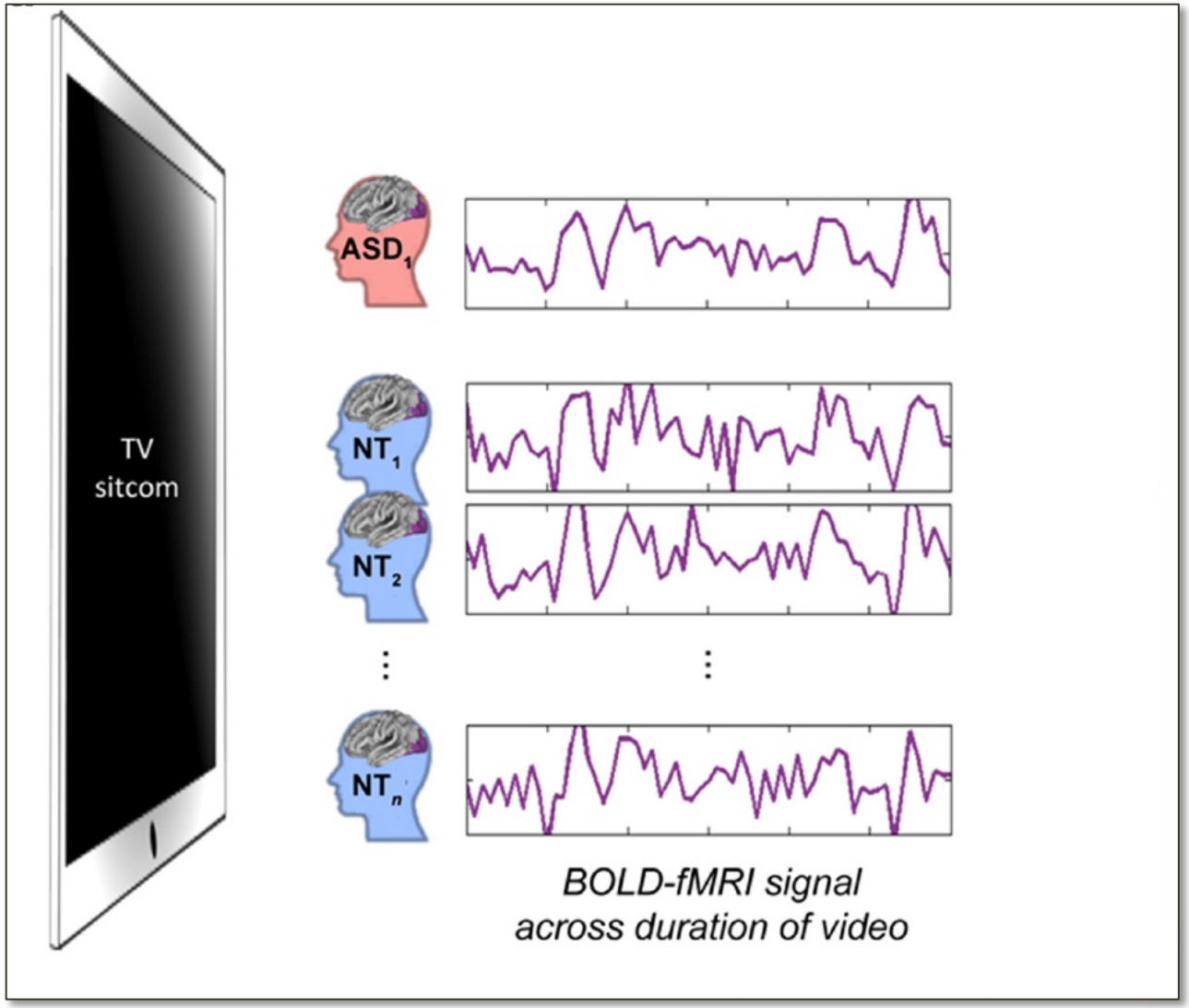
Theory of Mind and ASD



No difference between ASD and neurotypical adults

Dufour et al., 2013

Naturalistic viewing

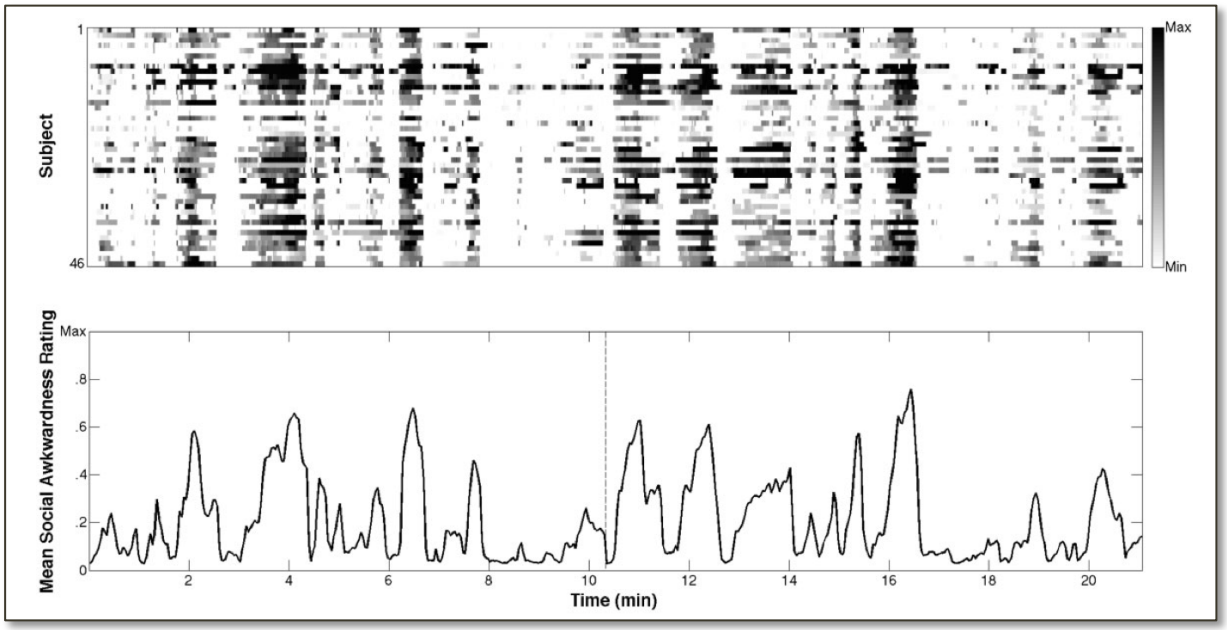


Byrge et al., 2015

Awkward naturalistic viewing

Byrge et al., 2015
Pantelis, et al., 2015

Neural response to social awkwardness



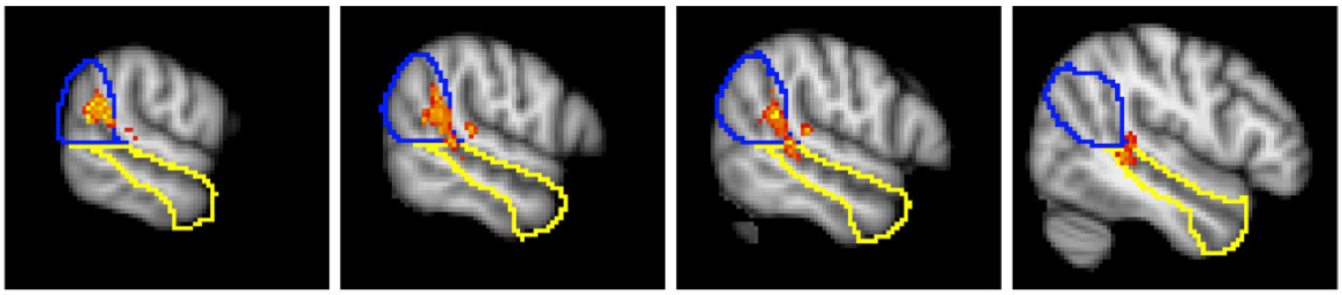
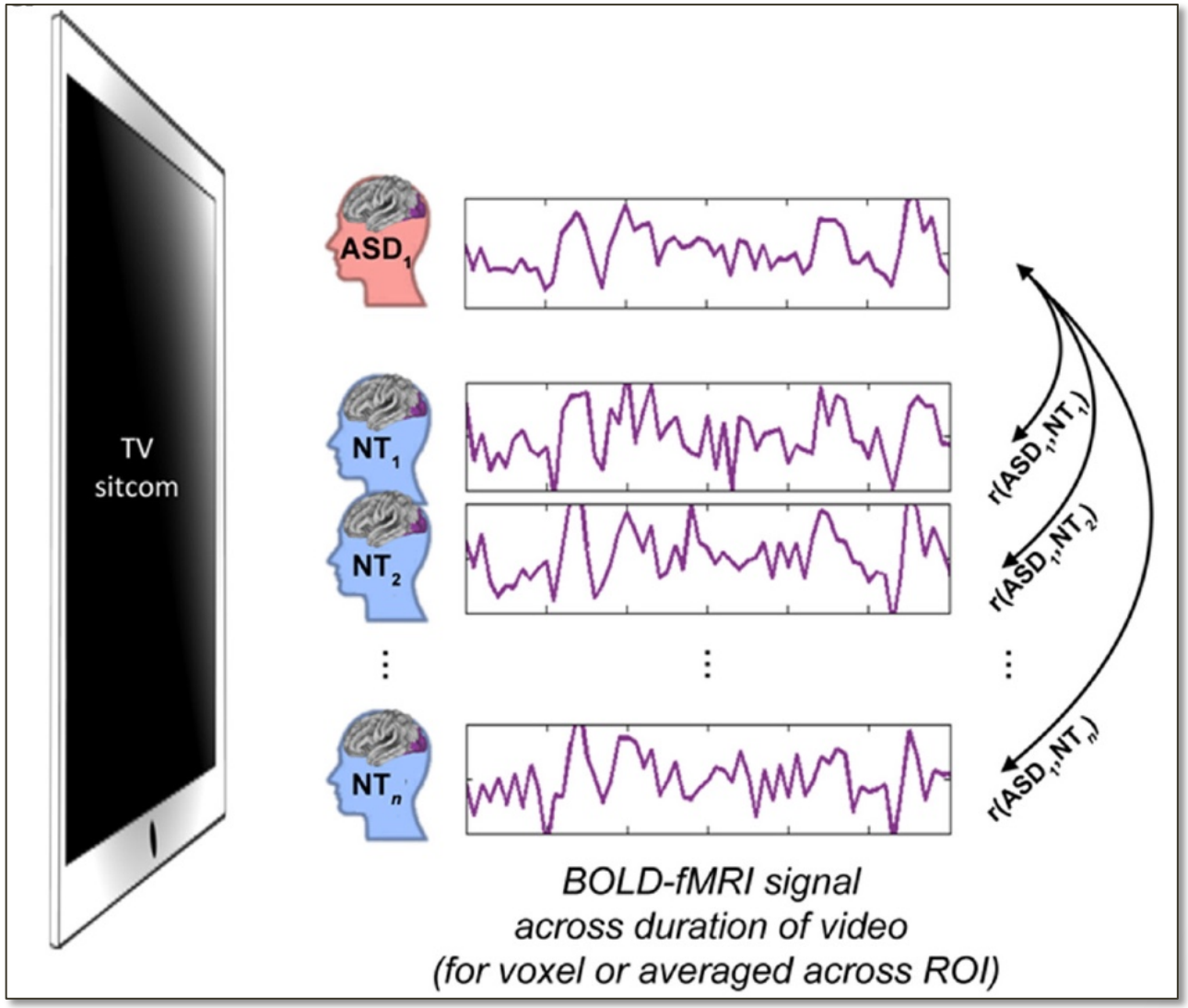


Fig. 3 The cluster of voxels for which we observed a significant group difference (NT > ASD), shown on a gradient from red to orange. These sagittal cross sections go from lateral (left) to medial (right): $x = 62, 58, 56, 50$. The cluster straddles predefined RTPJ and RSTS regions; outlined here in blue and yellow, respectively.

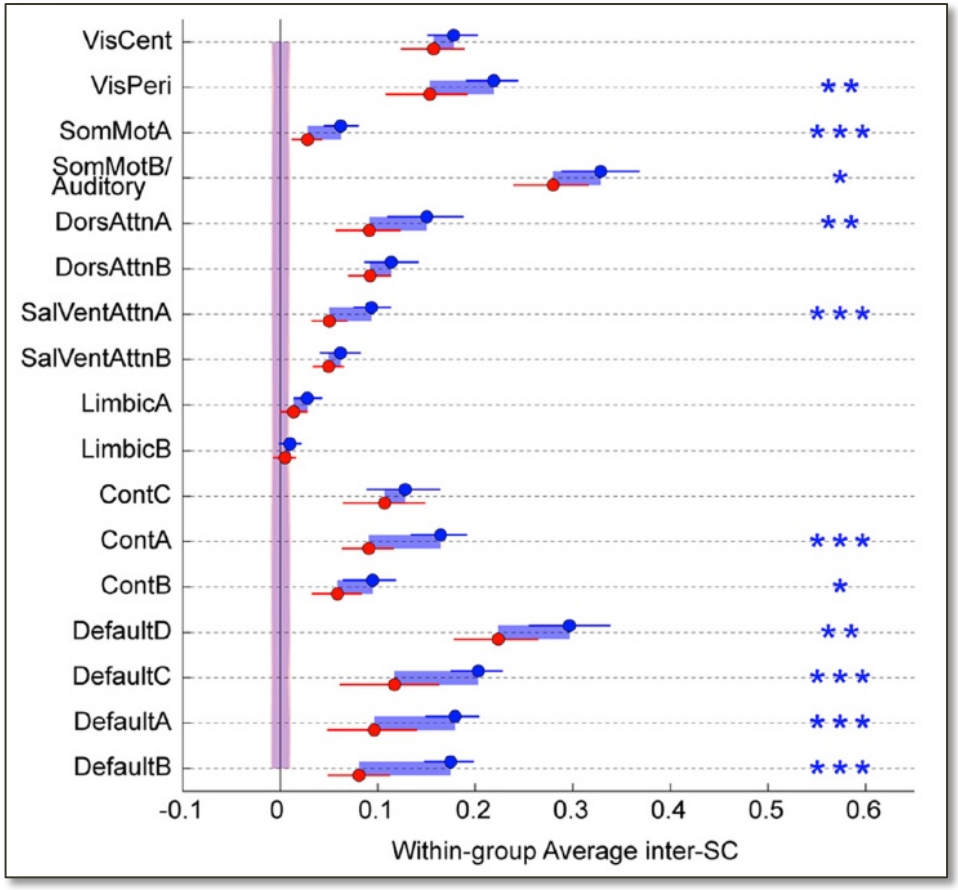
Pantelis, et al., 2015

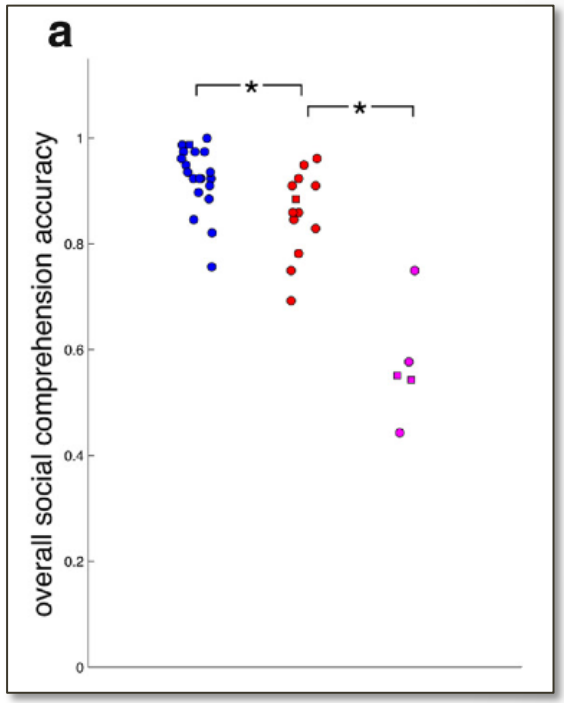
Brain synchrony in ASD



Byrge et al., 2015

Brain synchrony in ASD





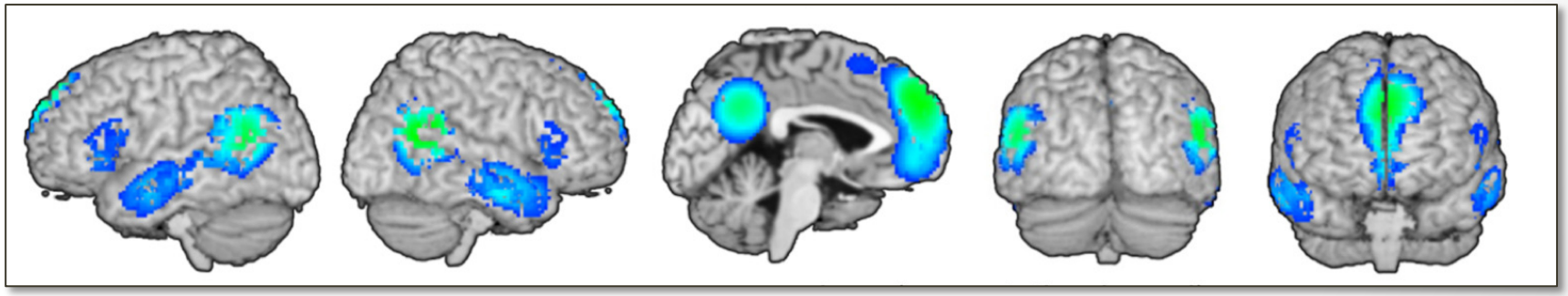
NT ASD

Less brain synchrony in ASD, but this is a result of 5 very atypical participants with ASD

Byrge et al., 2015

Theory of mind summary

- Social brain network is activated during theory of mind tasks
- Similar brain activation during theory of mind stories in ASD compared to NT controls
- Trial-based tasks may not capture the rich processing that occurs in the real world
- Using naturalistic viewing, the social brain responds to social awkwardness more so in NT compared to ASD
- Individuals with ASD do not synchronize with NT controls



Schurz et al., 2014

Reward processing and ASD

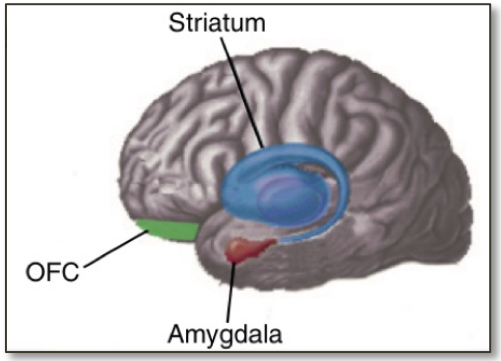
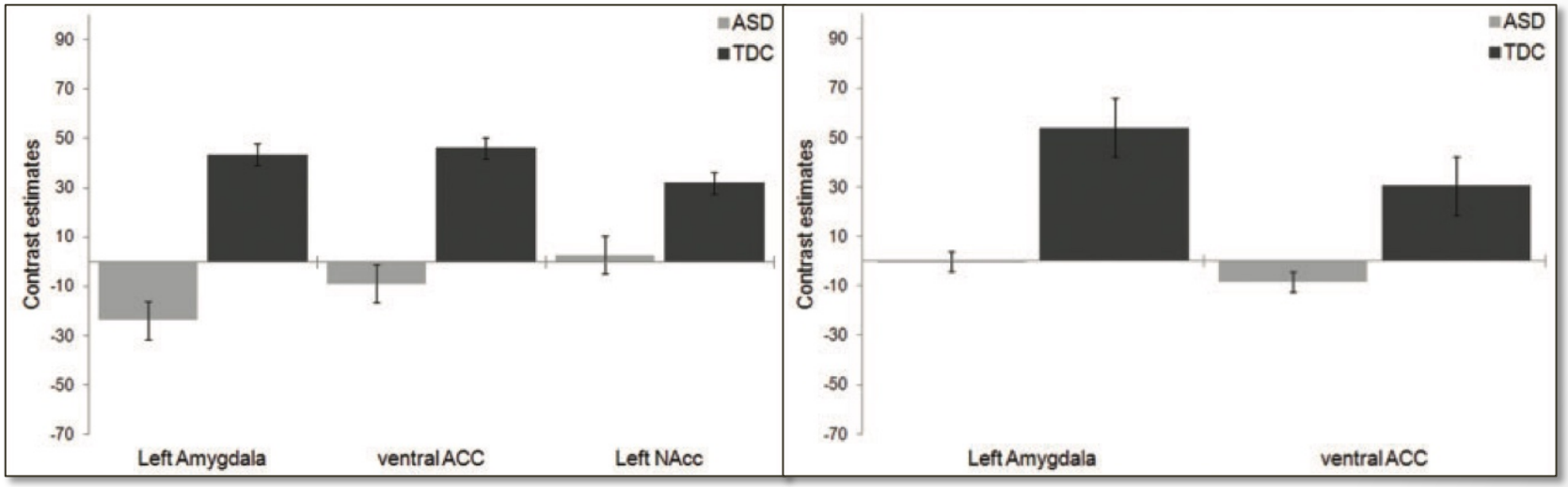


Image from Chevallier et al., 2014

Monetary Reward vs. No Reward

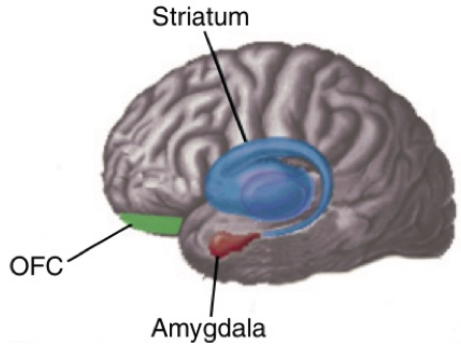
'Social' Reward vs. No Reward



Kohls et al., 2014

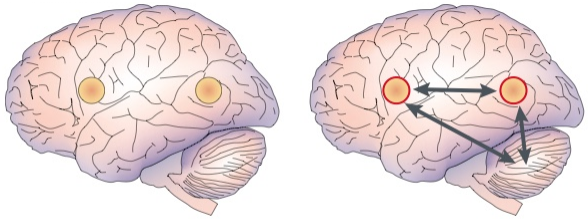
The Social Motivation Theory

Motivation to interact with others



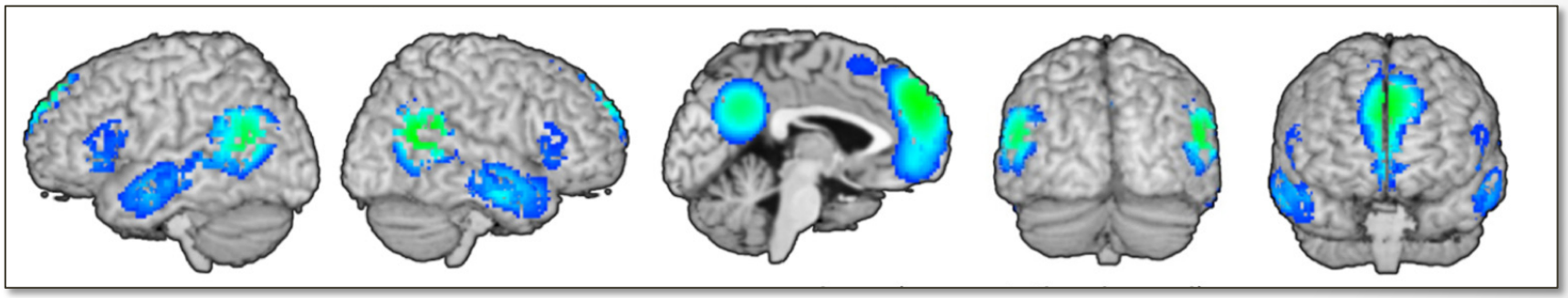
Chevallier et al., 2014

Interactive specialization



Johnson, 2001

Higher-order social processing (like theory of mind)



Schurz et al., 2014

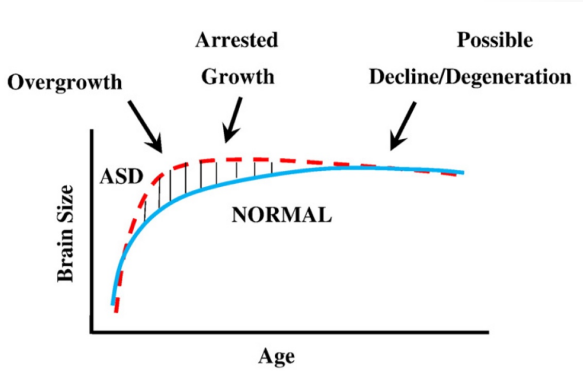
Make ‘social’ more social

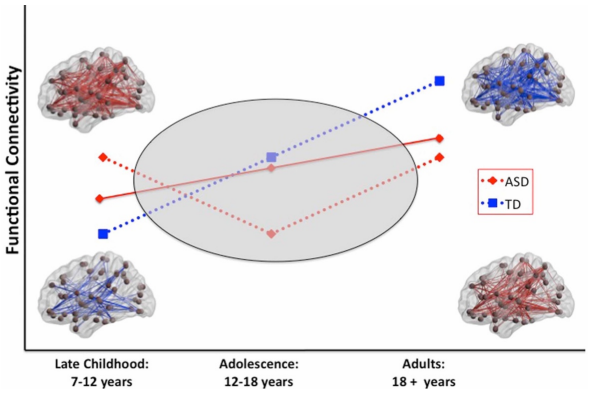
≠

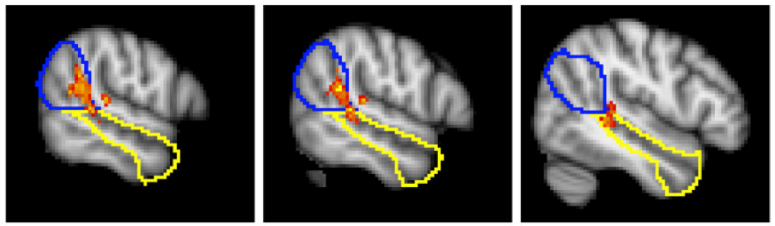
Stay tuned!!

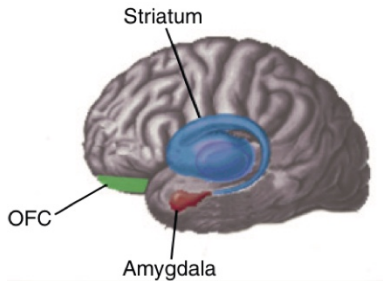
Summary

- Brain overgrowth in the first years of life
- Hyper- and hypo- functional connectivity
- Neural differences during naturalistic viewing
- The Social Motivation Theory









Diagnosis?

- Possible biomarkers:
  - Head circumference changes
  - Attention to faces
  - Response to social and language cues
- No reliable neuroimaging markers… yet

- With big data and fully appreciating heterogeneity, neuroimaging could help differentiate subtypes of individuals who could be more successful with certain treatments compared to others

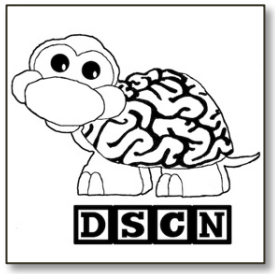
Unanswered questions

- Is autism one disorder?
  - Rdoc approach (Research Domain Criteria)
  - What about those on the lower end of the spectrum?
- We need to better understand the heterogeneity and how individuals with potentially different subtypes differentially respond to treatments.
- What causes autism?
- How early can we detect it?
- What about females?

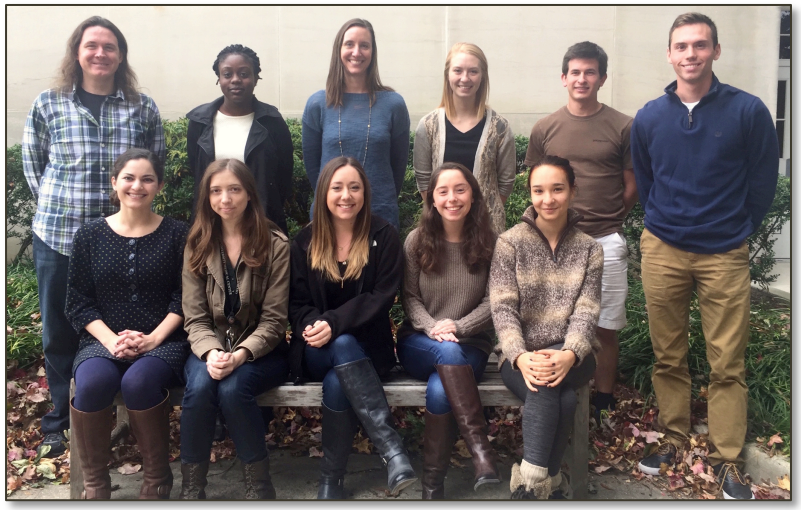
Future Directions

- BIG DATA
  - ABIDE, ABIDE II, extensive longitudinal studies that follow children from birth
  - Understand individual differences better
  - Machine learning and prediction (e.g. Hazlett et al., 2017)
  - Inclusion of more females into samples
- Multimodal approaches
  - Environmental, sociological, developmental, behavioral, cognitive, systems neuroscience (e.g. MRI), cellular neuroscience (not just neurons!), genetics, epigenetics
- Integrating neuroscience with clinical psychology to aid in diagnosis and treatment

Thanks!



Elizabeth Redcay
Nan Ratner
Kim Martin
Laura Kirby



Any questions?