Autism and the Brain

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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

- Gray matter
- White matter
- Ventricles

Diagram showing the structure of a neuron:
- Nucleus
- Soma (cell body)
- Dendrites
- Axon terminals
- Myelin Sheaths
- Axon
How does the brain develop?

However...

Almost all neurons are in place before birth!

(Rakic, 1995)
How does the brain develop?
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**
- Whole brain size
- Cortical thickness (processing)

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

Fox & Raichle, 2007
How should we think of functional differences in ASD?

- Maturation, localization, and the lesion model

- Interactive specialization to understand atypical development (Johnson, 2002)
ASD as a disorder of brain connectivity

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

$r = .84$

$r = .06$

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
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

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

Schurz et al., 2014
Theory of Mind and ASD

No difference between ASD and neurotypical adults

Dufour et al., 2013
Naturalistic viewing
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 RFPJ and RSTS regions; outlined here in blue and yellow, respectively.
Brain synchrony in ASD

Byrge et al., 2015
Brain synchrony in 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

Monetary Reward vs. No Reward

‘Social’ Reward vs. No Reward

Image from Chevallier et al., 2014

Kohls et al., 2014
The Social Motivation Theory

Motivation to interact with others

Interactive specialization

Higher-order social processing (like theory of mind)

Chevallier et al., 2014

Johnson, 2001

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!

Any questions?

Elizabeth Redcay
Nan Ratner
Kim Martin
Laura Kirby