

A Role for Fetal and Neonatal Imaging in Autism

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Overall outline

- Overview of functional connectomes
- Why fetal and neonatal connectomes?
- What connectomes can tell us about neurodevelopmental disorders?

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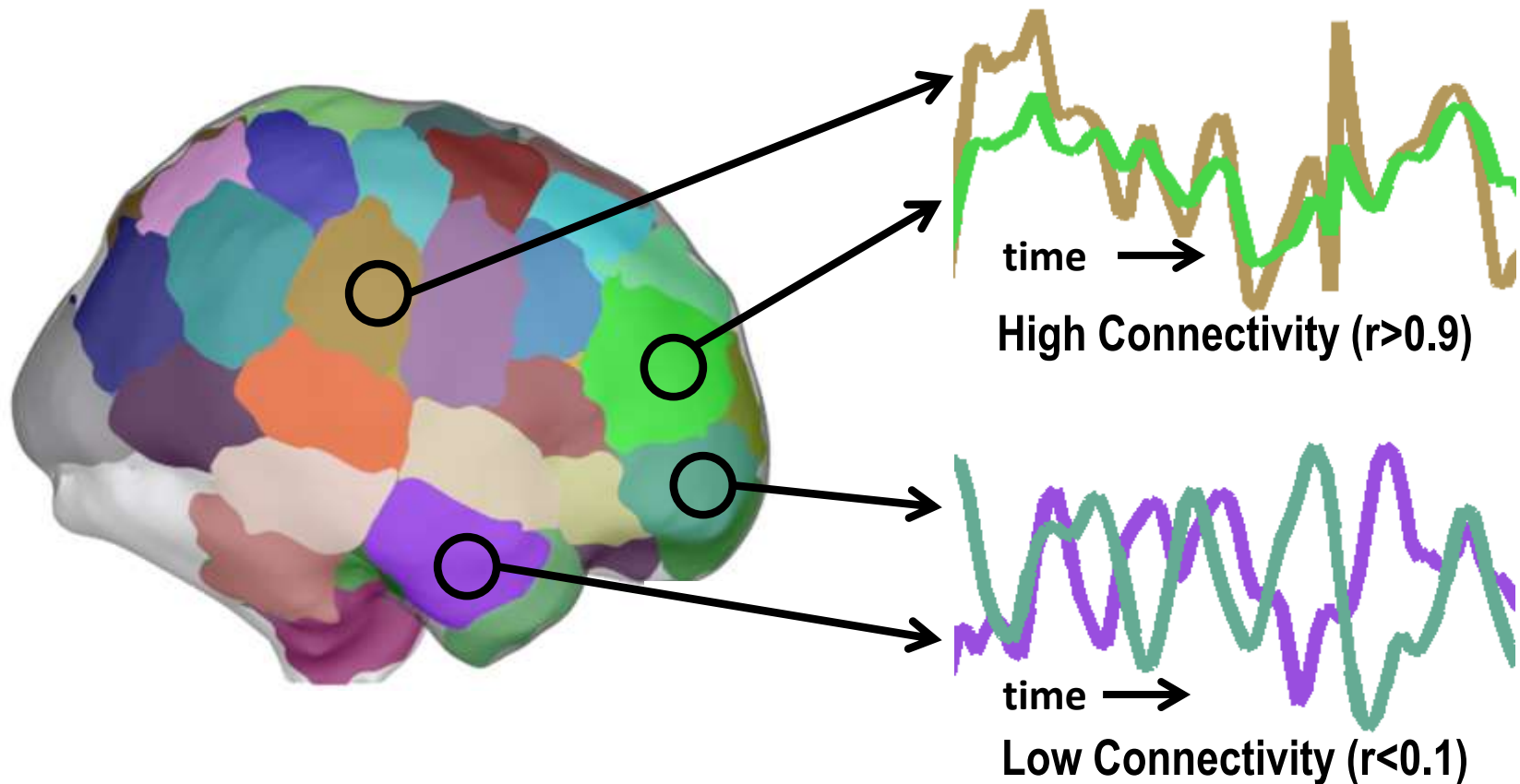
- **Overview of functional connectomes**
- Why fetal and neonatal connectomes?
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What's a Connectome??

- A comprehensive map of neural connections in the brain
 - “Wiring diagram” of the brain
- Functional connectomes
 - Functional connections or connectivity
 - Macro-level organization

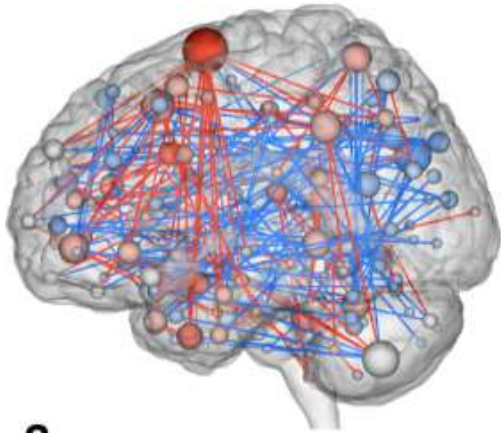
Functional connectivity

Goal: find synchrony between brain areas

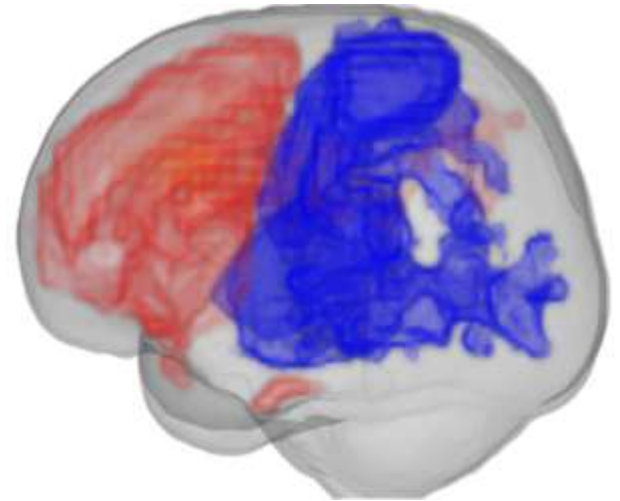
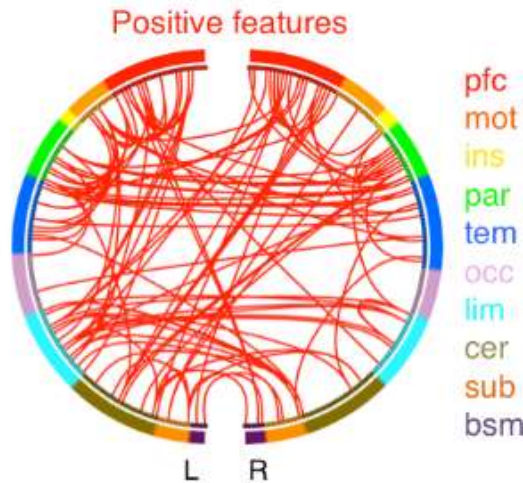


Visualizing connectomes

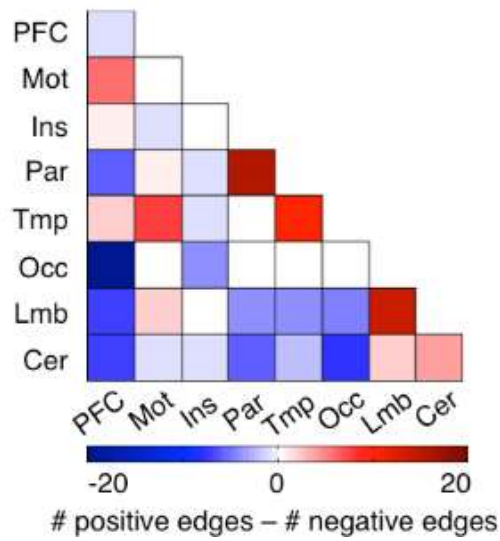
a



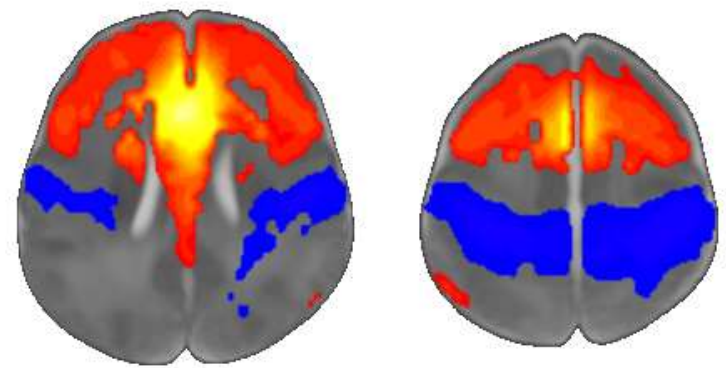
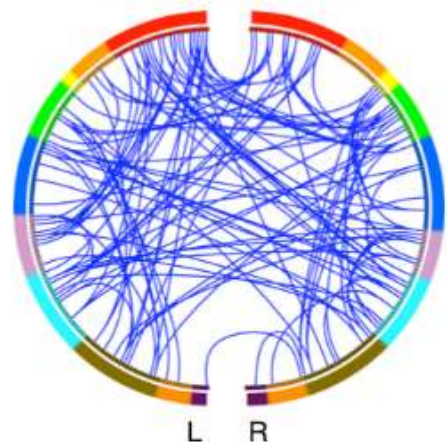
b



c



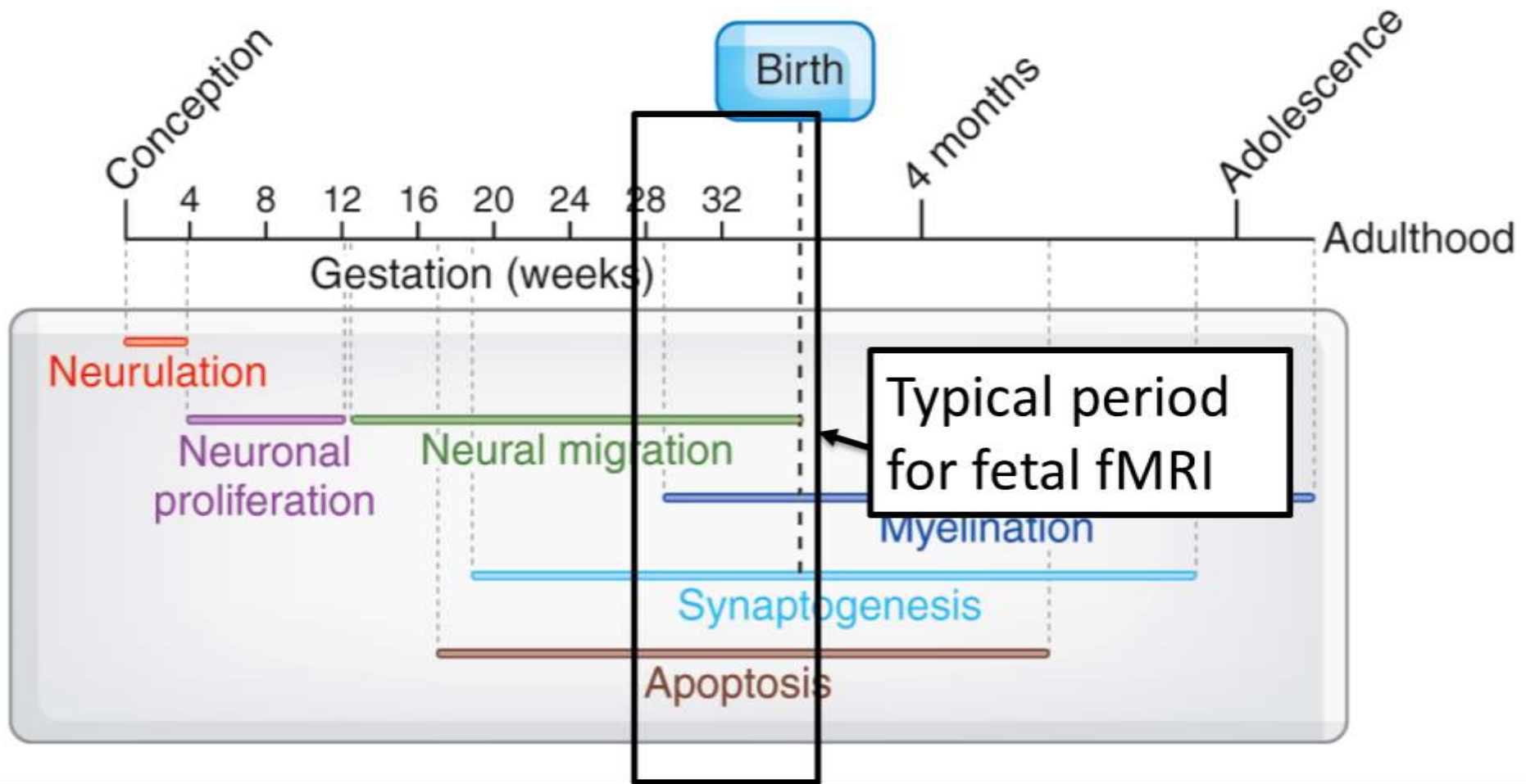
Negative features



Overall outline

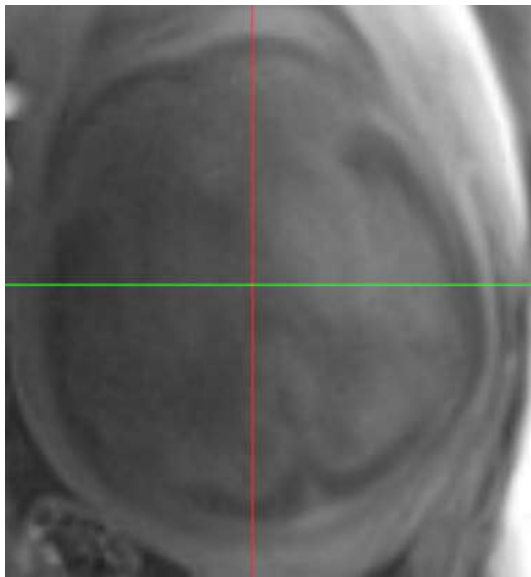
- Overview of functional connectomes
- **Why fetal and neonatal connectomes?**
- What connectomes can tell us about neurodevelopmental disorders?

Many neural processes end at birth

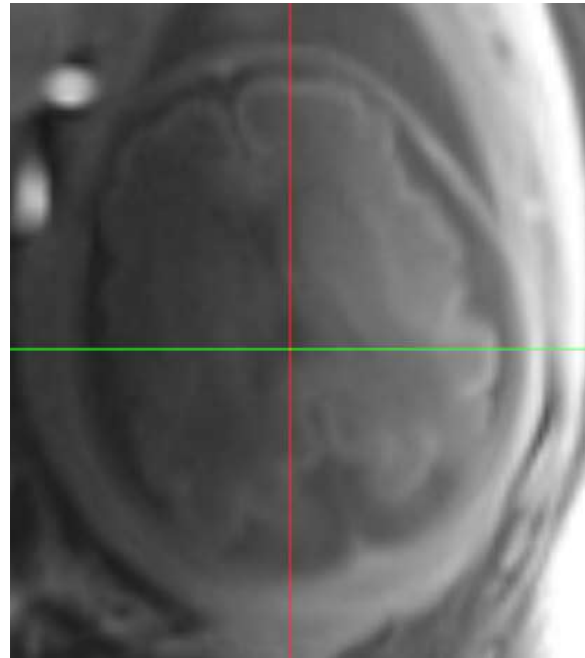


Rapid growth: single subject example

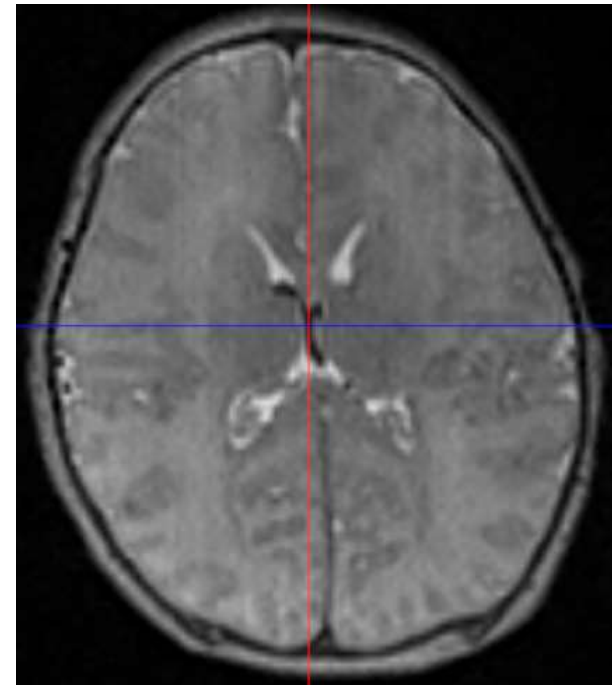
30 wks GA



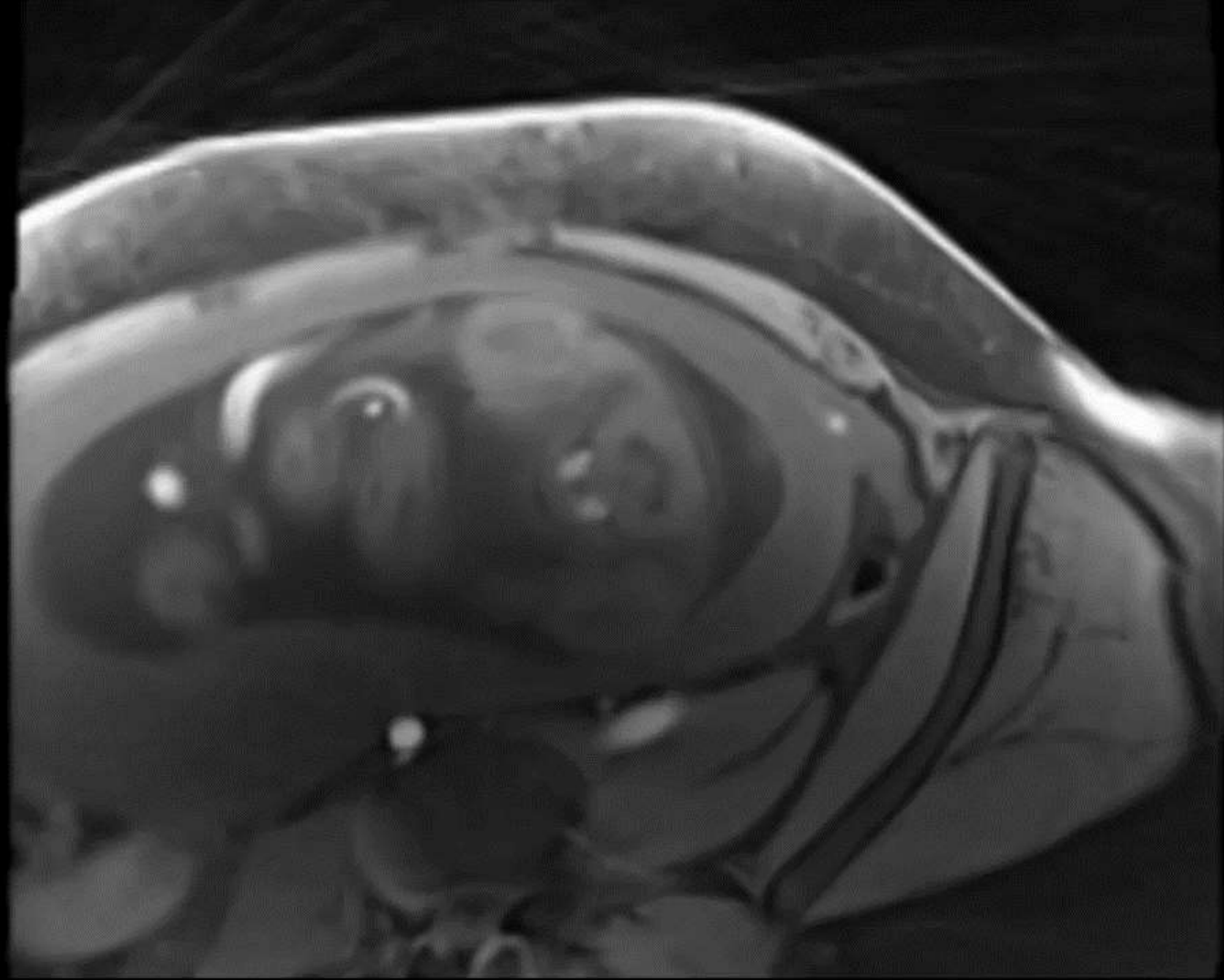
34 wks GA



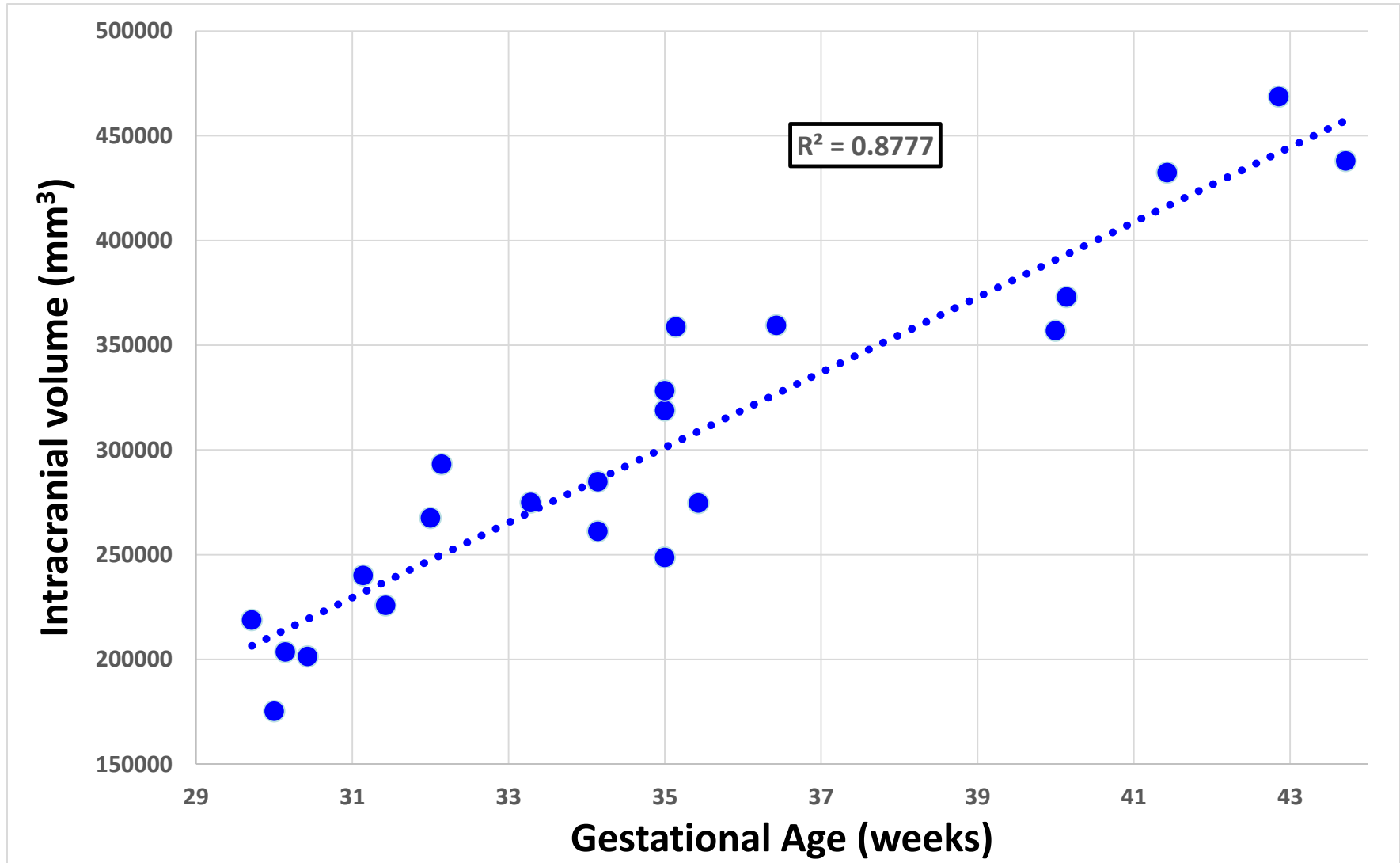
40 wks GA



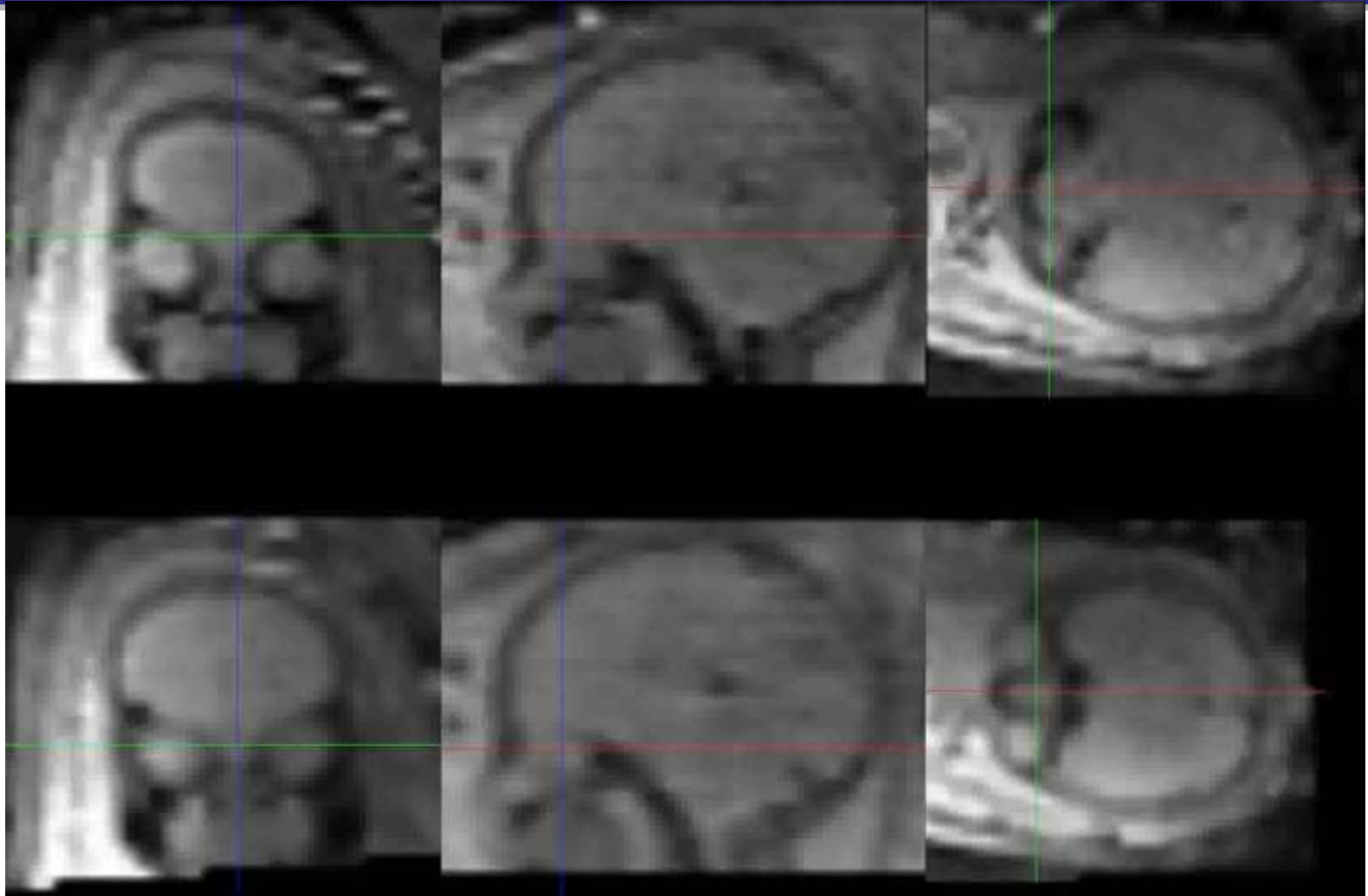
MRI of 30 week fetus: Axial images



The brain doubles in size in <3 months

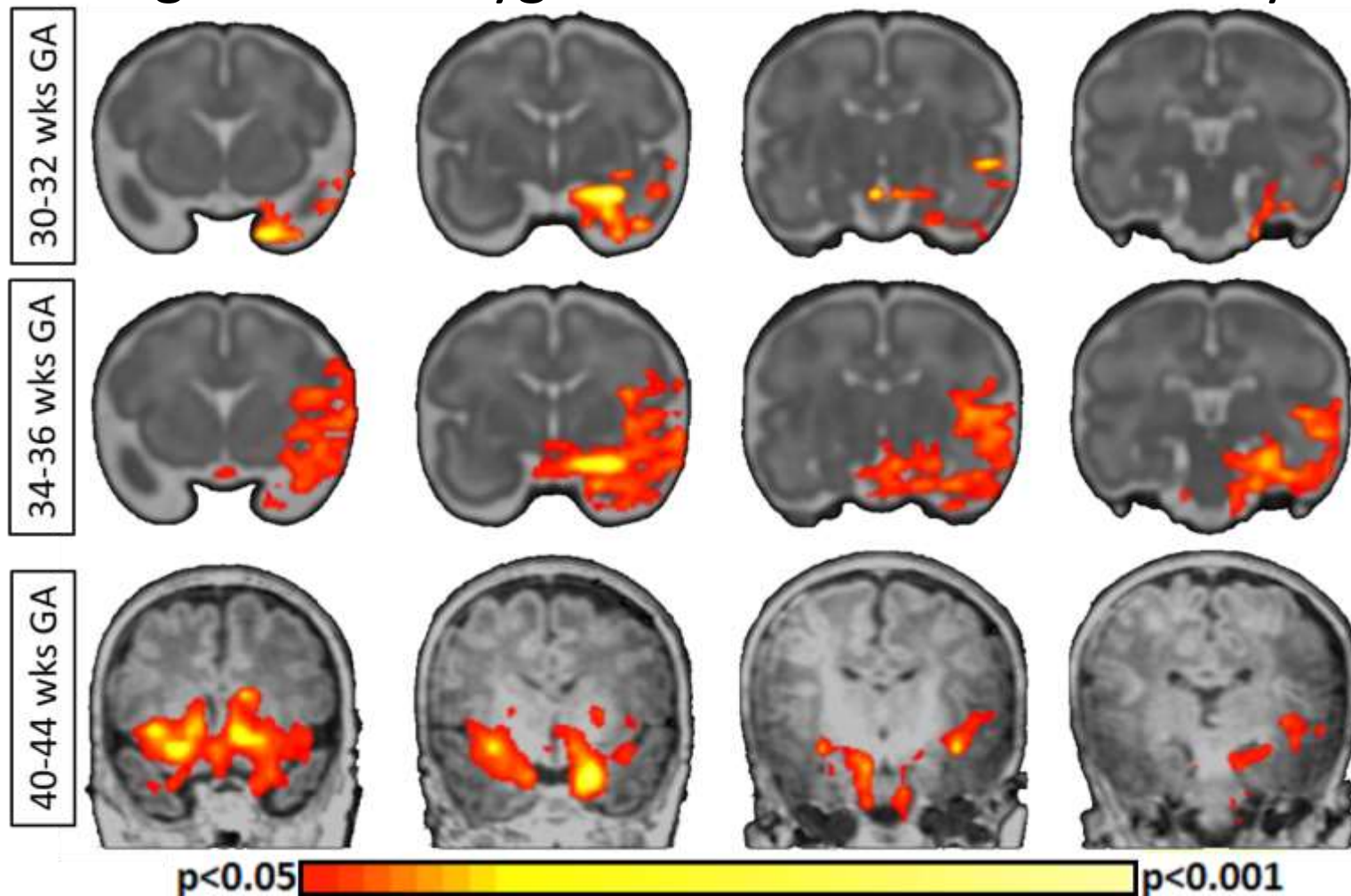


Functional MRI of 30 week fetus



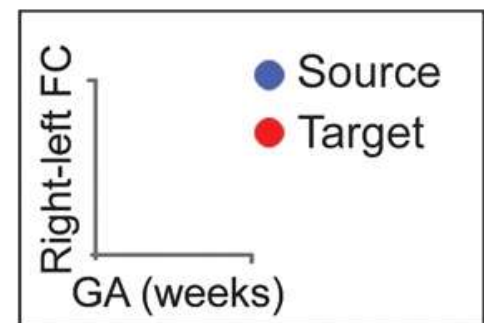
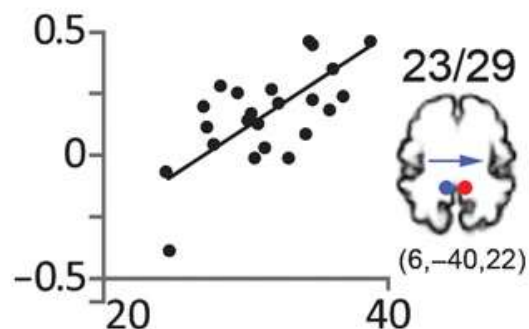
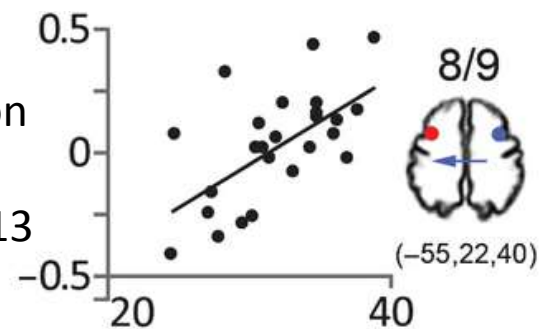
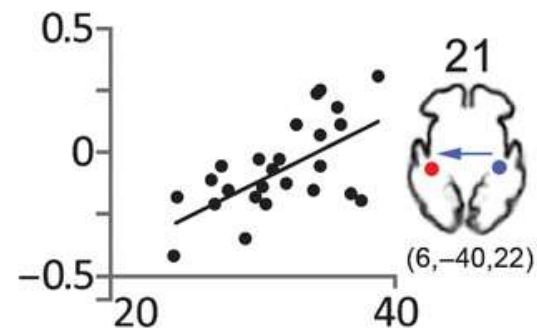
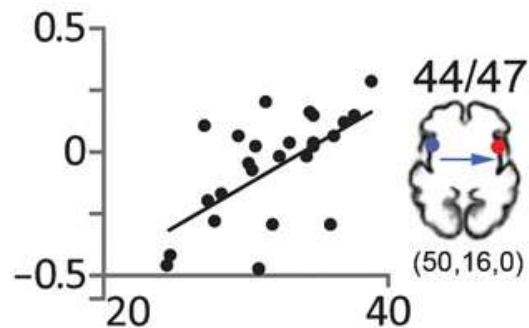
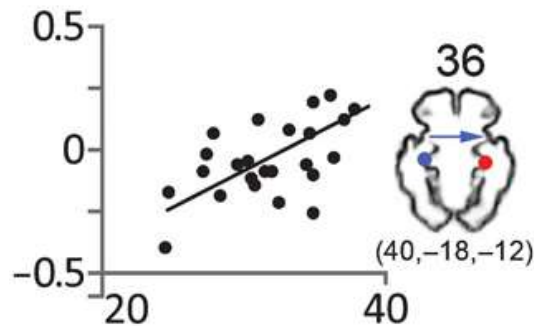
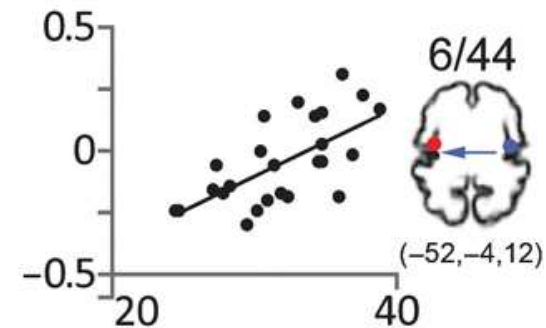
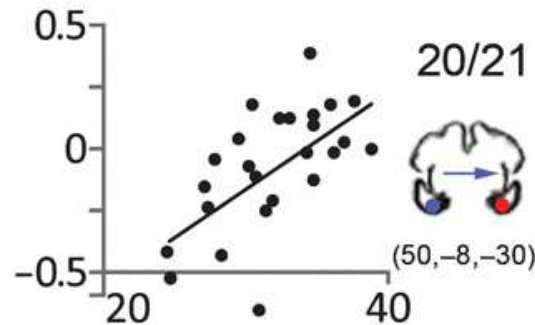
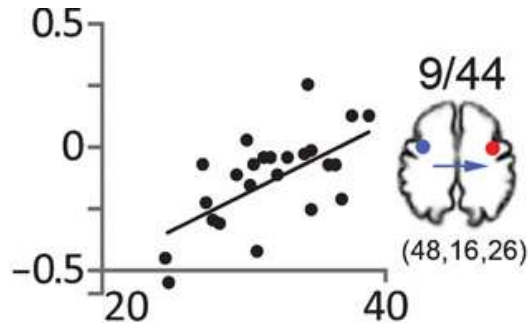
Connectomes develop across the 3rd trimester

Longitudinal amygdala functional connectivity



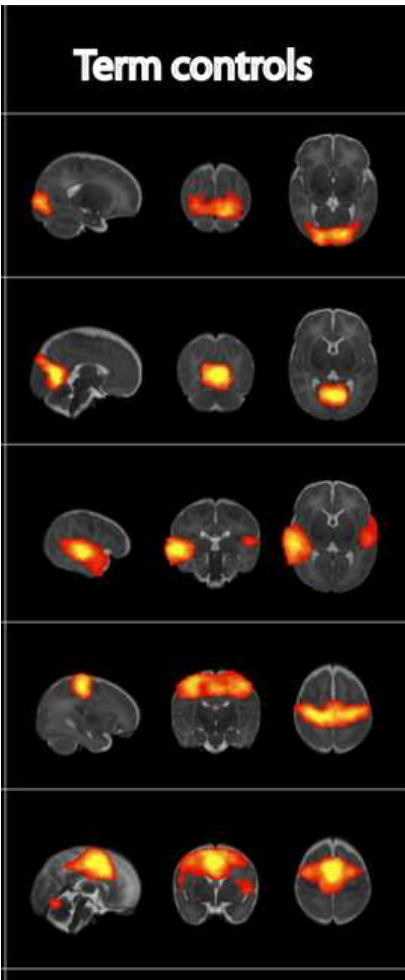
Scheinost
2016,
Pediatric
Research

Similar data from cross sectional studies



Thomason
Sci Trans
Med, 2013

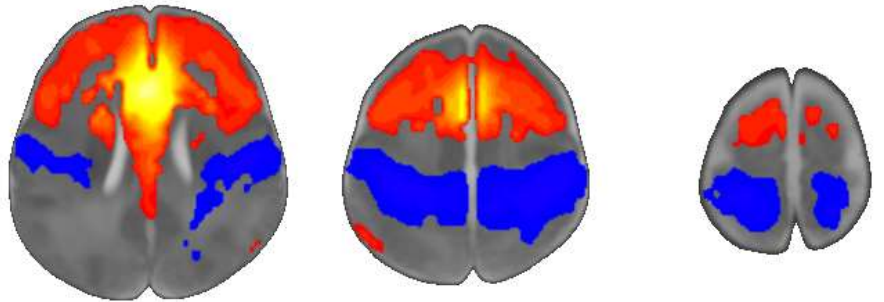
Functional connectomes are detectable at birth



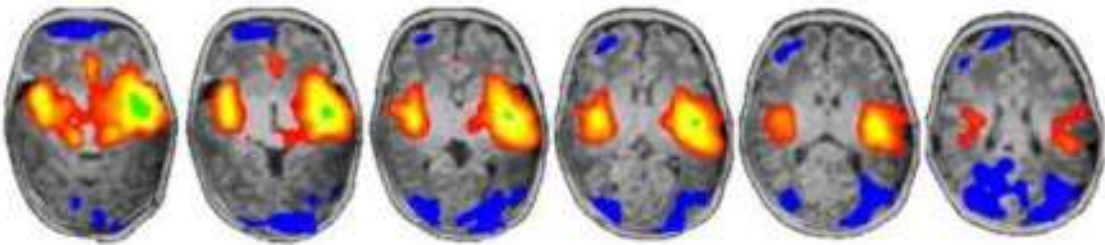
Doria, PNAS 2010

Term Control

Smyser cerebral cortex 2010

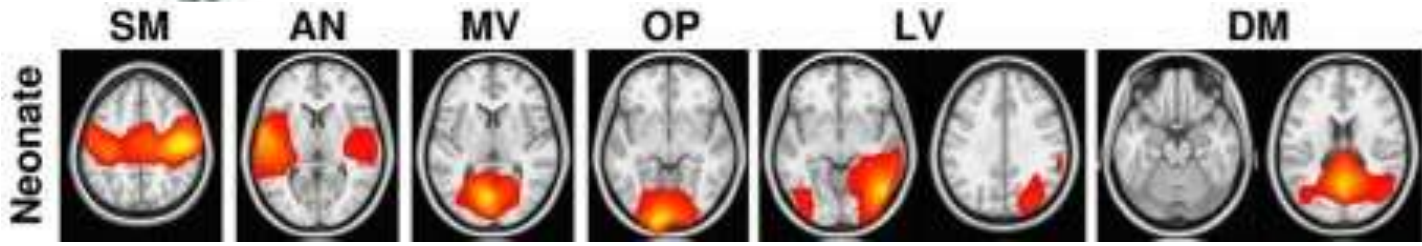


Spann J Neurosci 2018

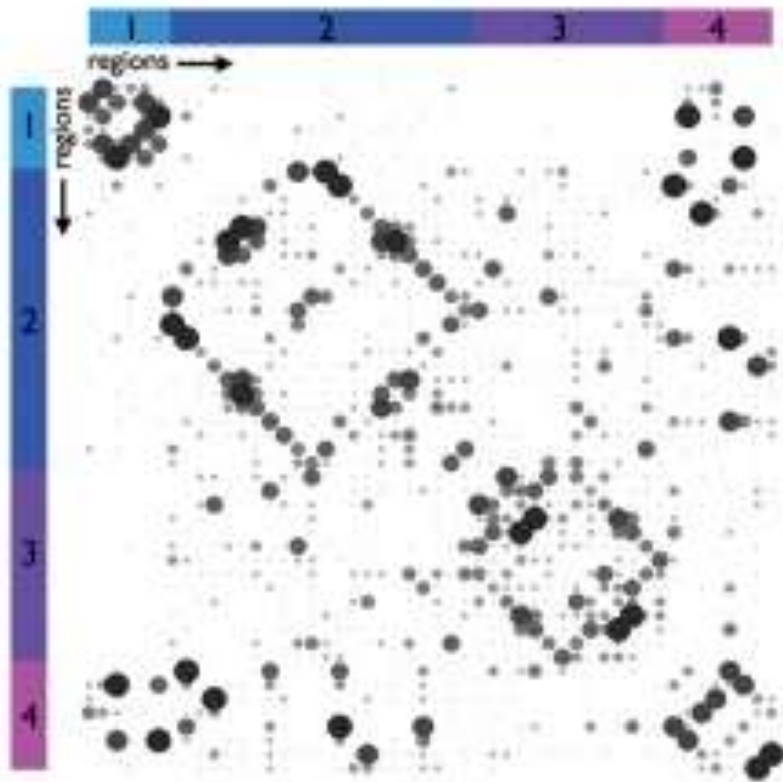


Kwon Neuroimage 2015

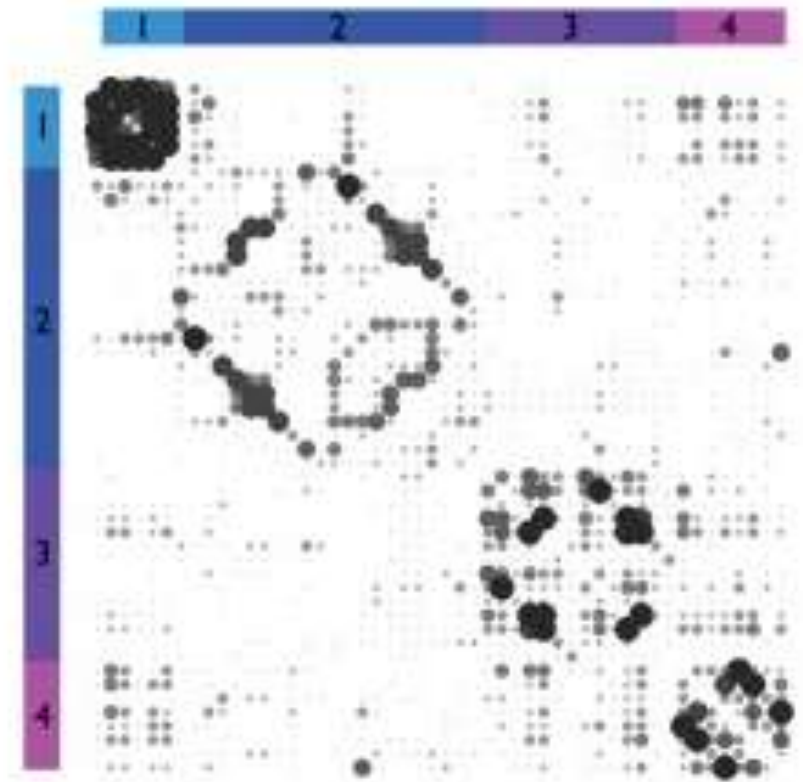
Alcauter J NeuroSci 2014



Baby connectomes are similar to adults'



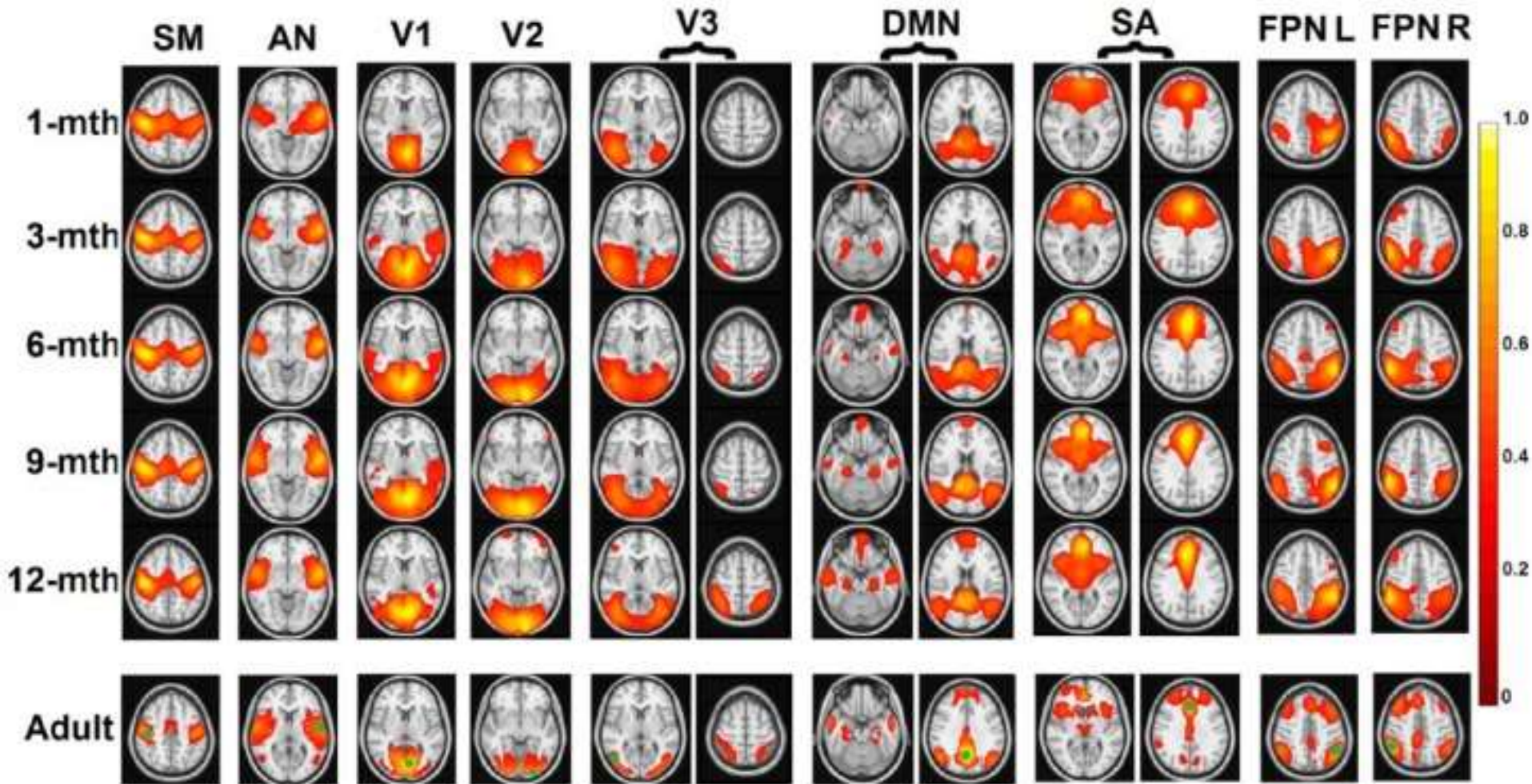
Neonate



Adult

overlap: 79%

But, they still have room to grow



Gao Cerebral Cortex 2015

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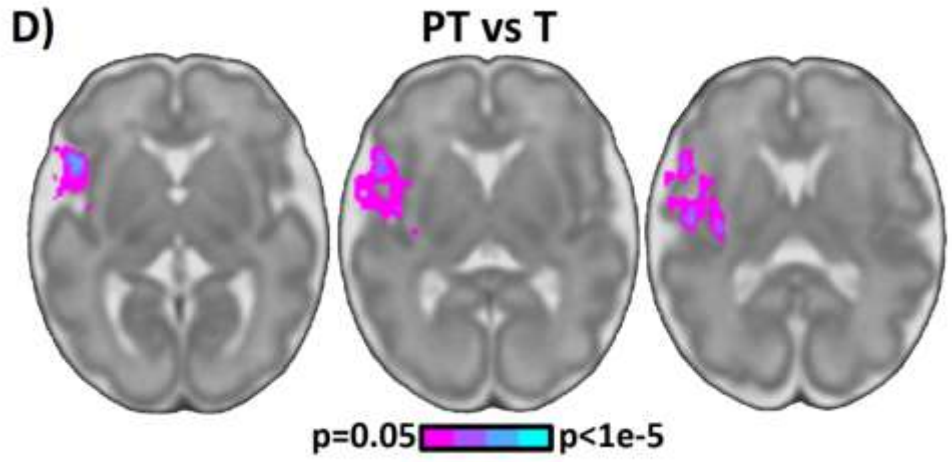
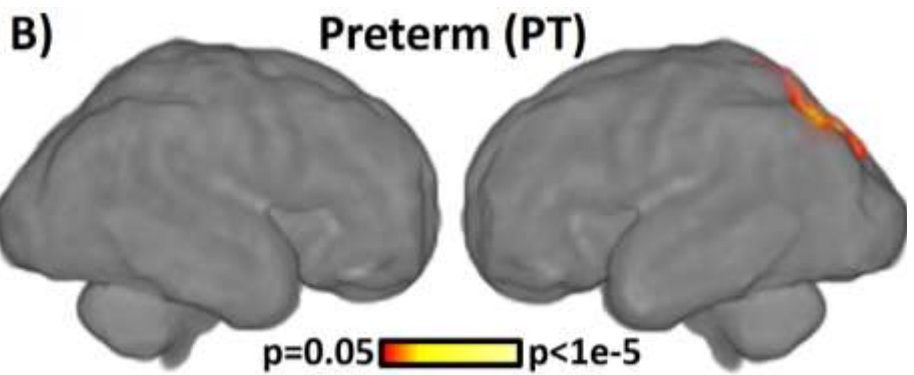
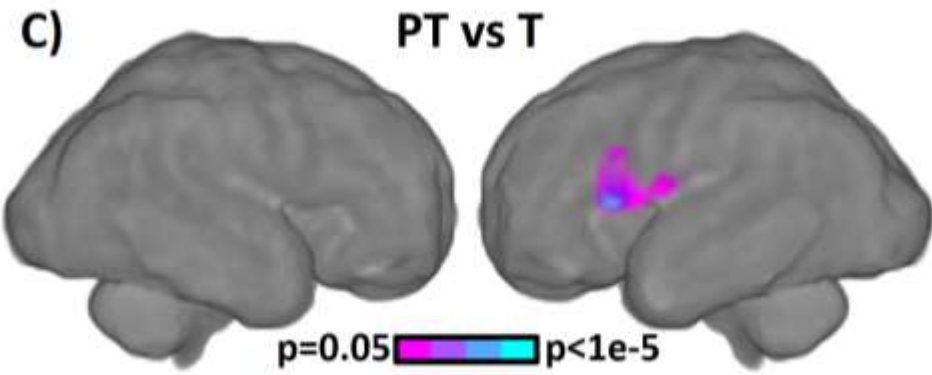
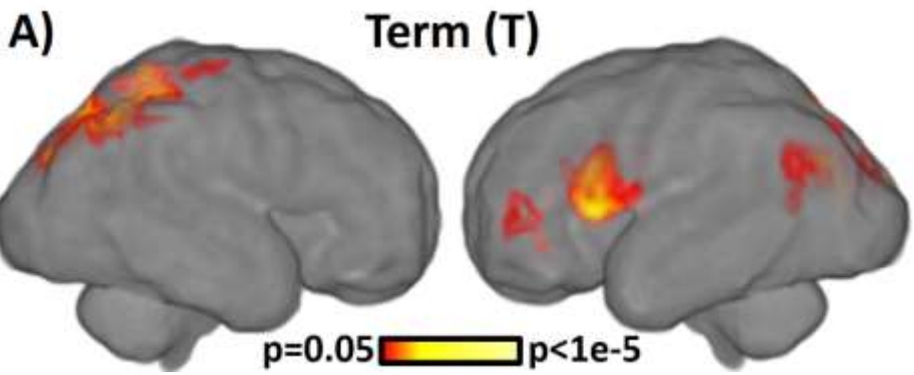
A promising example study

- Preterm birth
 - Birth before 37 week gestation
 - Long-term developmental delays
 - Altered connectomes
 - Infants, children, adolescents, adults
 - Mainly attributed to postnatal factors

What about connectomes before preterm birth?

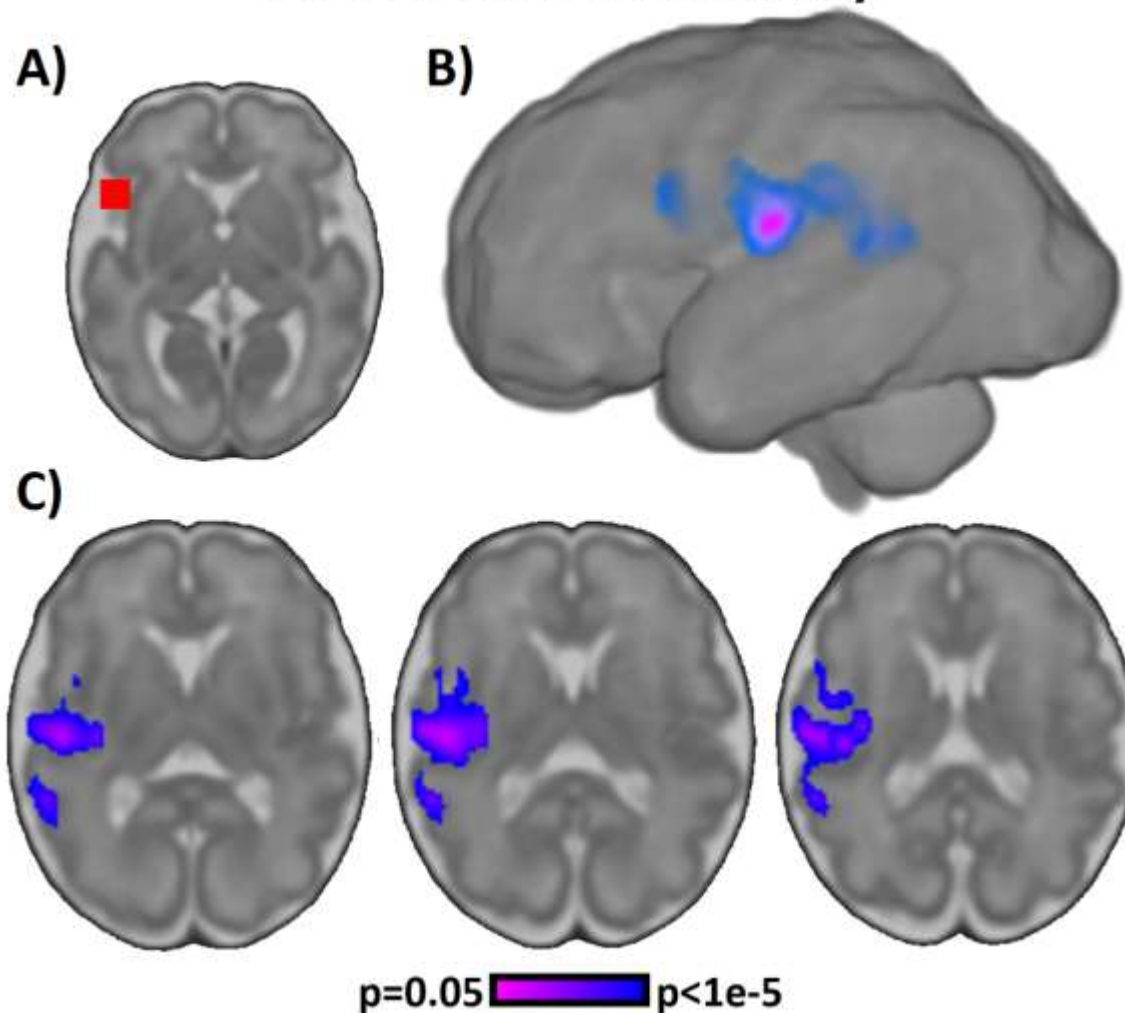
- Alterations before preterm birth
 - Suggests prenatal origins
 - Not purely postnatal factors
 - i.e. a neurodevelopmental disorder of “mis-wirings”
- Compare connectomes at 29 weeks
 - 18 fetus born term; 14 fetus born preterm

Disrupted connectomes in language regions



Lower connectivity within the language network

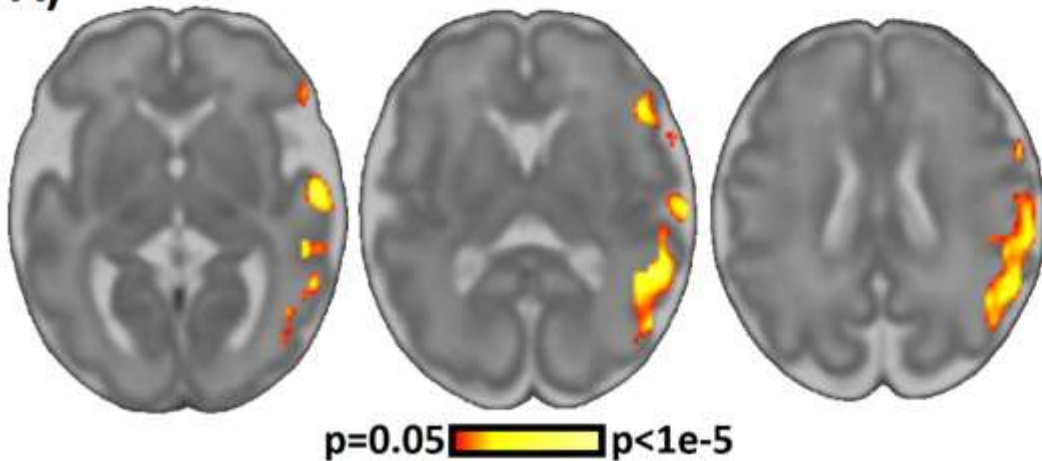
PT vs T: Seed connectivity



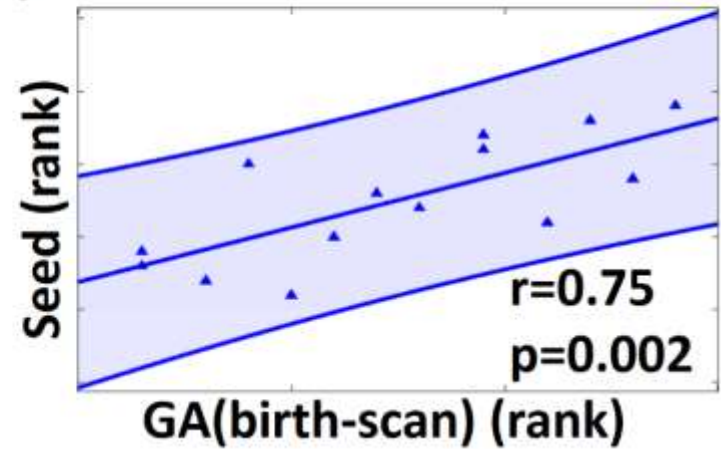
Alterations correlates age at birth

PT: Correlation between seed connectivity and GA(birth-scan)

A)

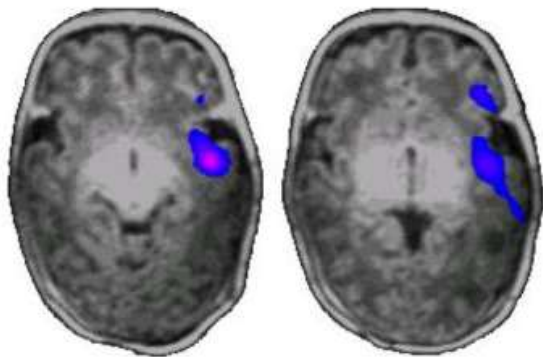


B)

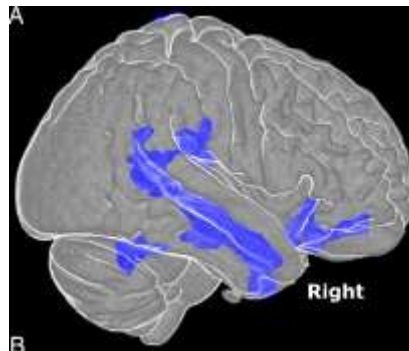


Making sense of these data

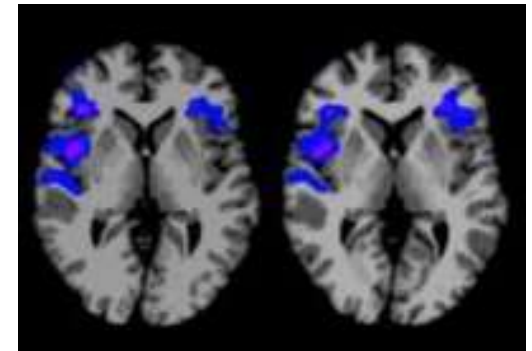
- Altered language connectivity is a “hallmark” of preterm birth



Infants



Children



Young adults

- But, origins are prenatal, not postnatal

On going and future work

- Early connectome based markers of ASD
 - Longitudinal scanning
 - Twice in the 3rd trimester
 - Once after birth
 - High risk group
 - Sibling(s) with ASD
 - Can we observe early neural correlates of ASD?

Summary

- Fetal and neonatal connectomes
 - How the brain's "wiring" develops
 - Rapid changes in 3rd trimester
- "Mis-wiring" gives insights to neurodevelopmental disorders
- Promising approach to studying ASD

Many thanks!

- Collaborators:

Laura Ment

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Fred Volkmar

Jamie McPartland

Joseph Chang

Kasia Chawarska

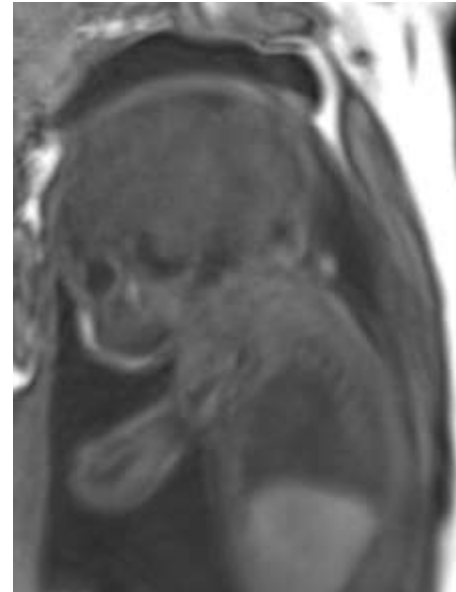
Kelly Powell

Suzanne Macari

Quan Wang

- Supported by:

NIH P50 MH115716 (ACE)



Questions?

