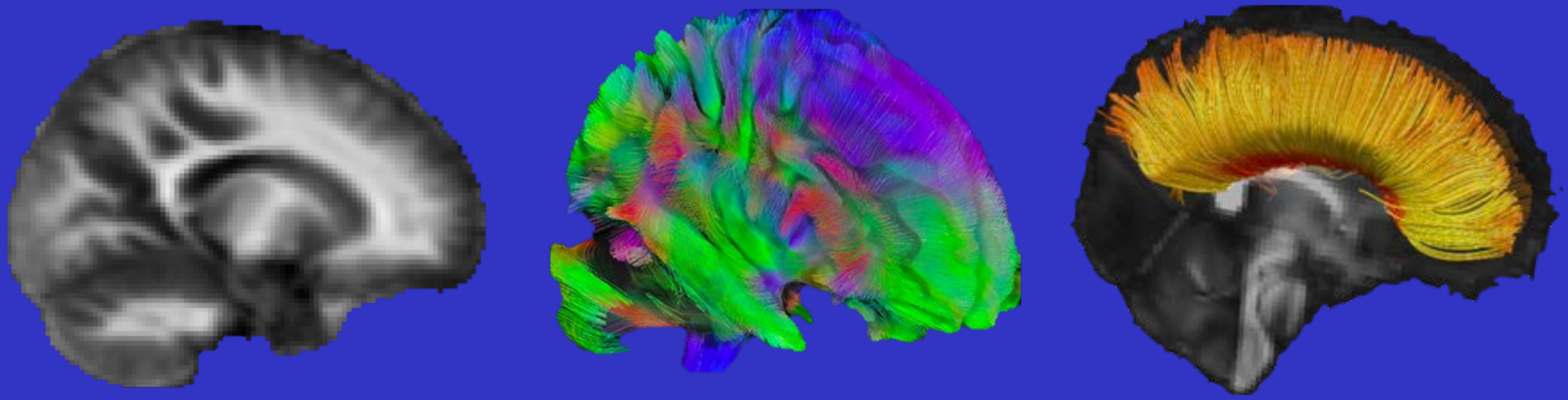


Quantitative Magnetic Resonance Imaging to Measure Brain Microstructure in ASD

Douglas C. Dean III, PhD
Waisman Center
University of Wisconsin–Madison


LEVEL

Research Program

Develop and apply advanced brain imaging techniques to:

- Determine changes in the brain specific to autism and linked to symptoms and outcomes
- Identify brain-based biomarkers that inform on causes of autism, neural mechanisms involved, aid in early diagnosis, preventive interventions, and treatment

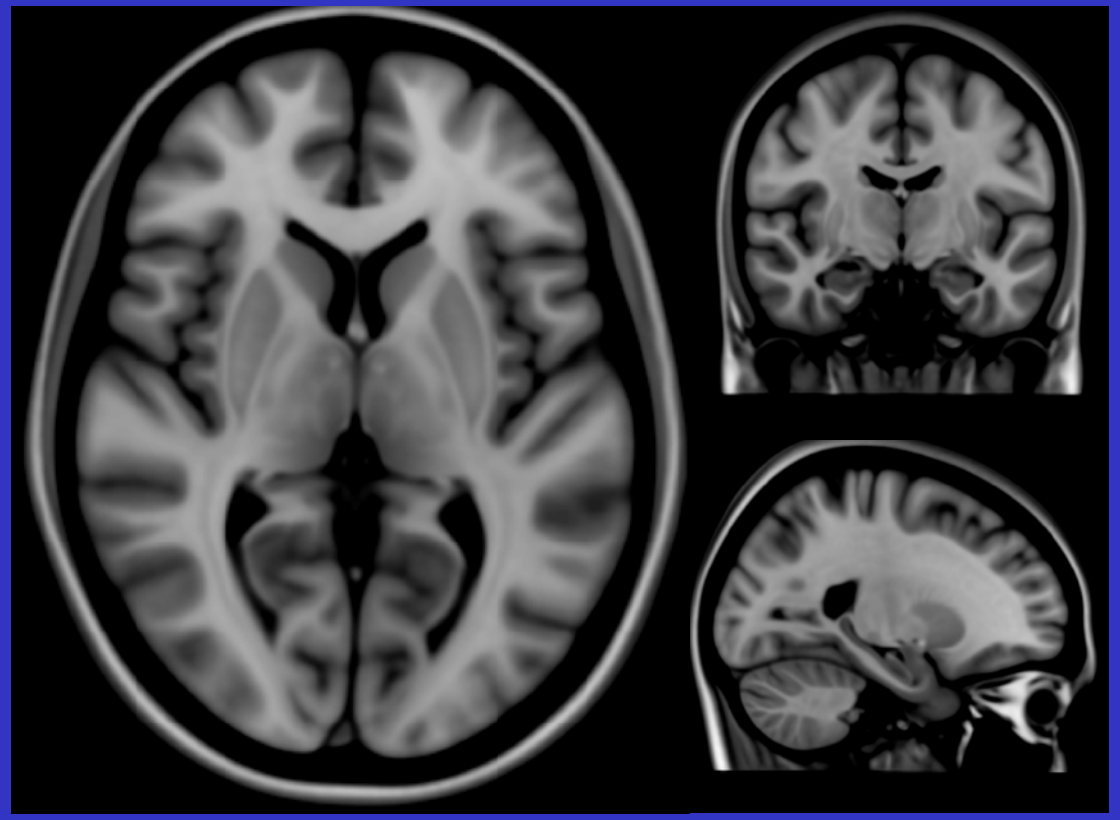
Brain Imaging

Brain Camera

Brain Image

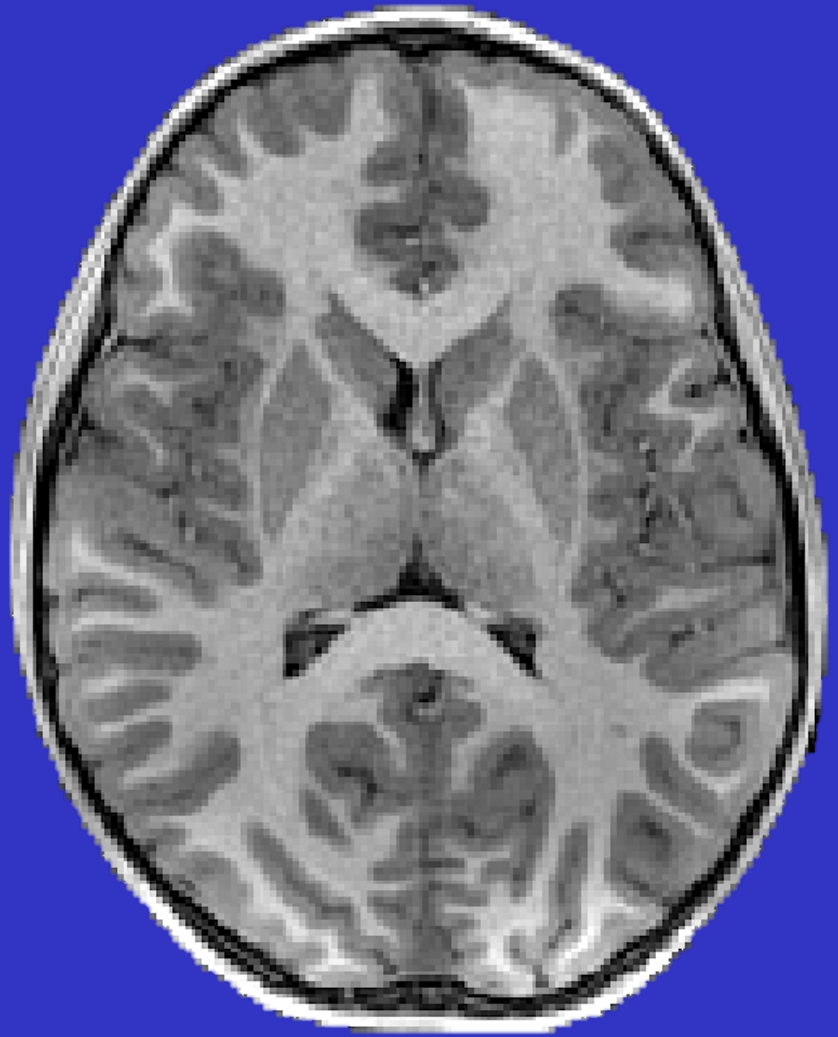
Magnetic Resonance Imaging

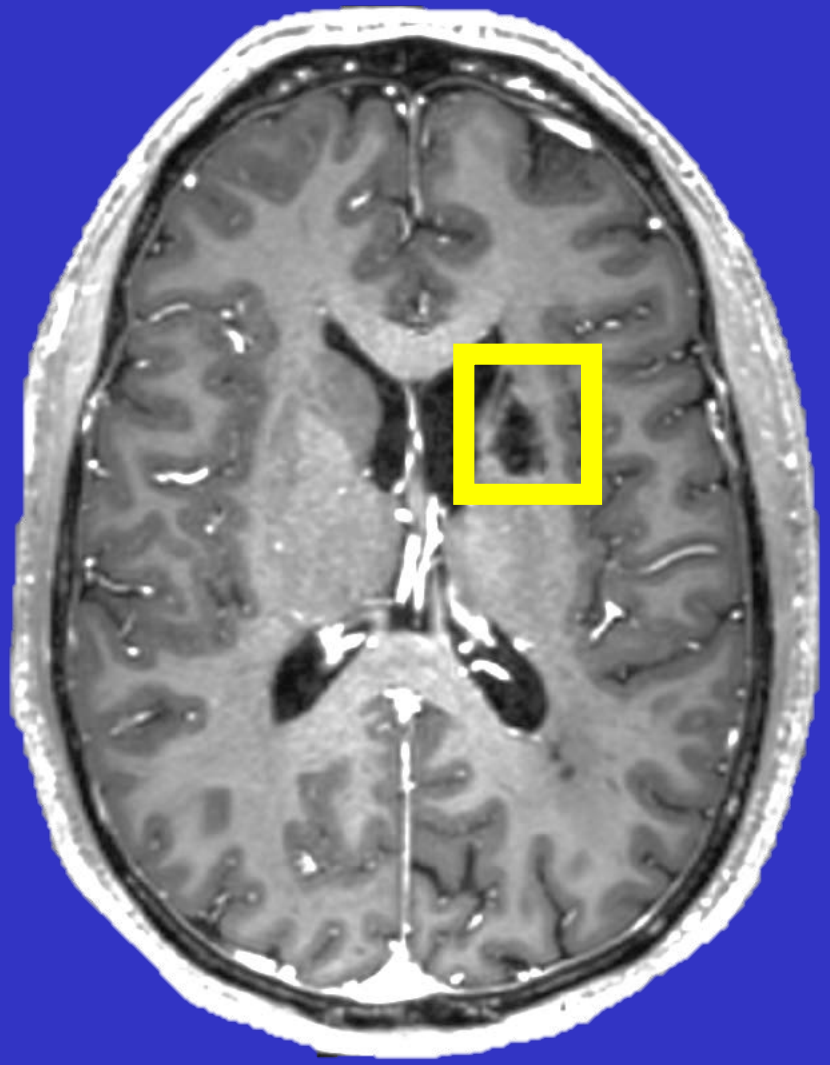
Brain Camera



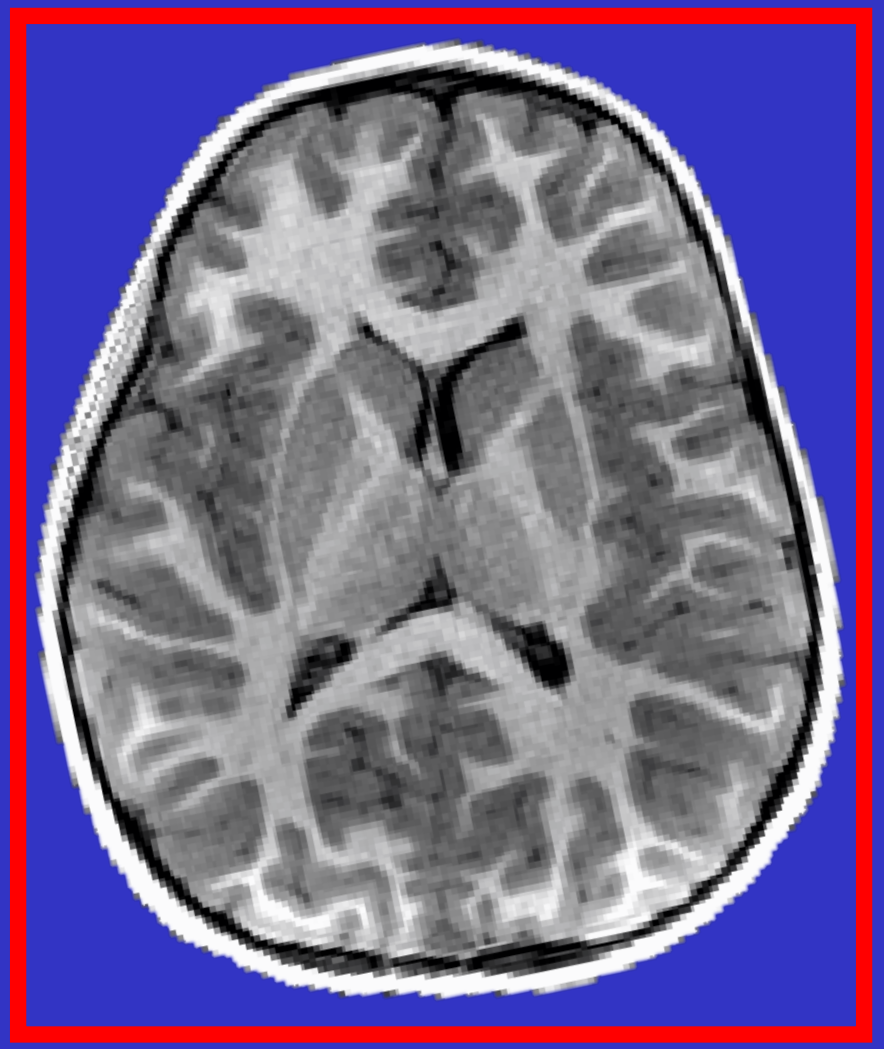
Brain Image

Magnetic Resonance Imaging





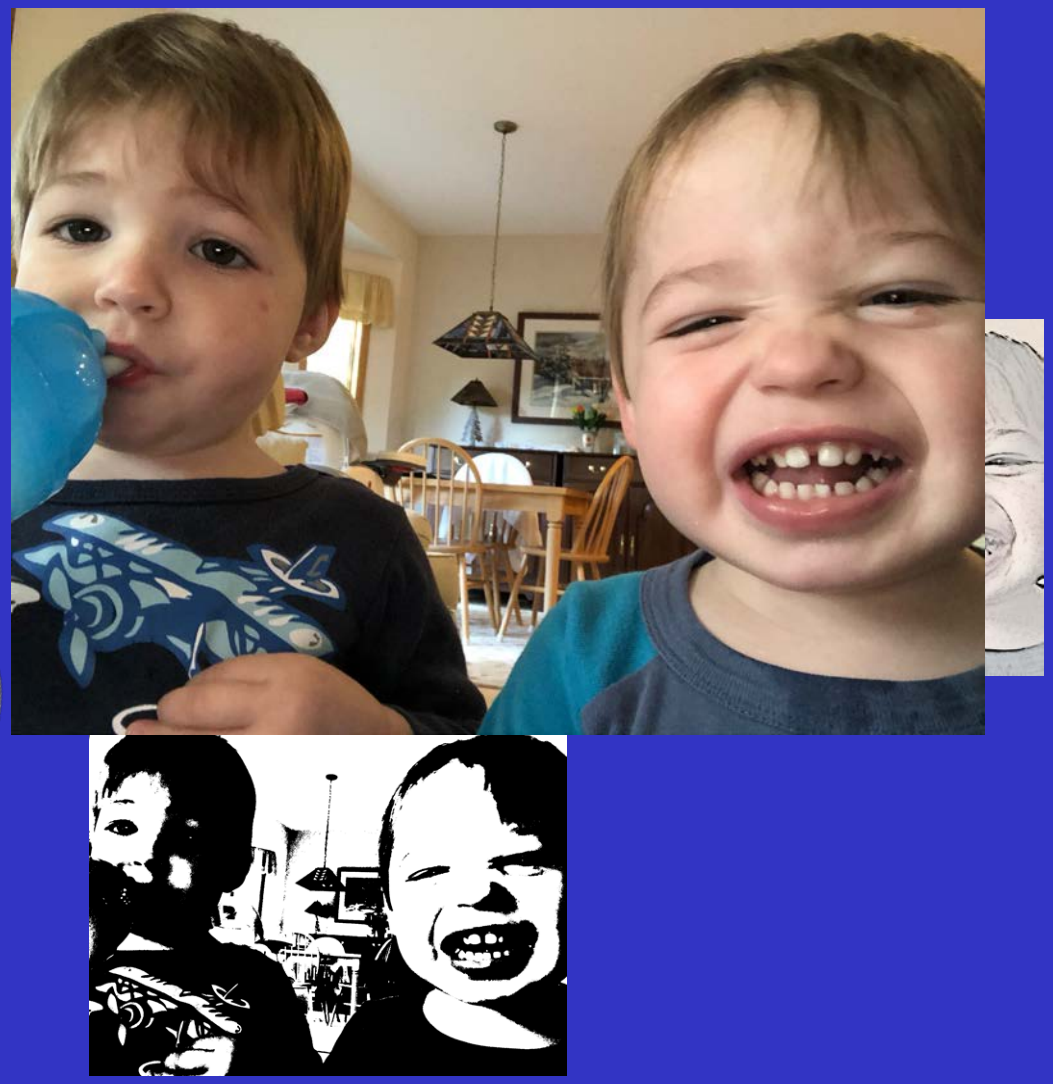
Magnetic Resonance Imaging in ASD



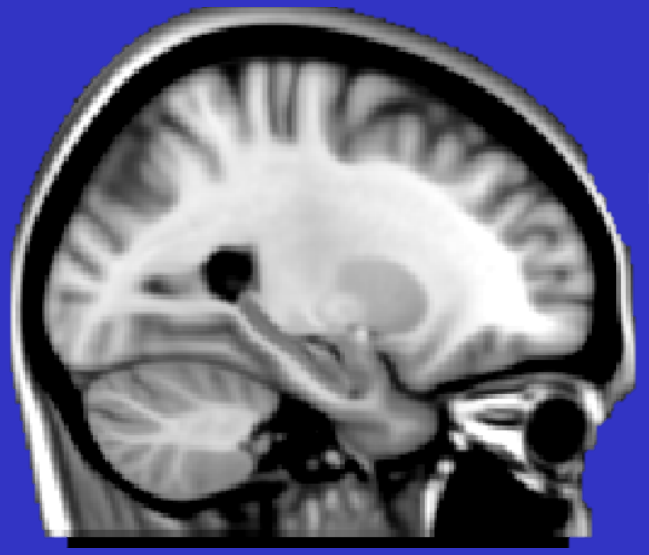
Participant 1

Participant 2

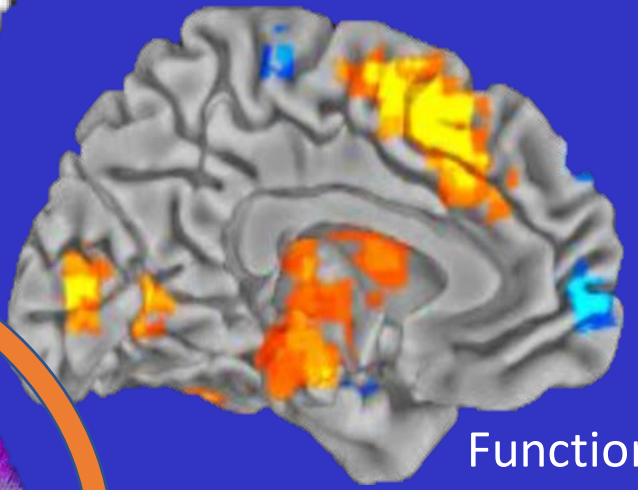
Magnetic Resonance Imaging



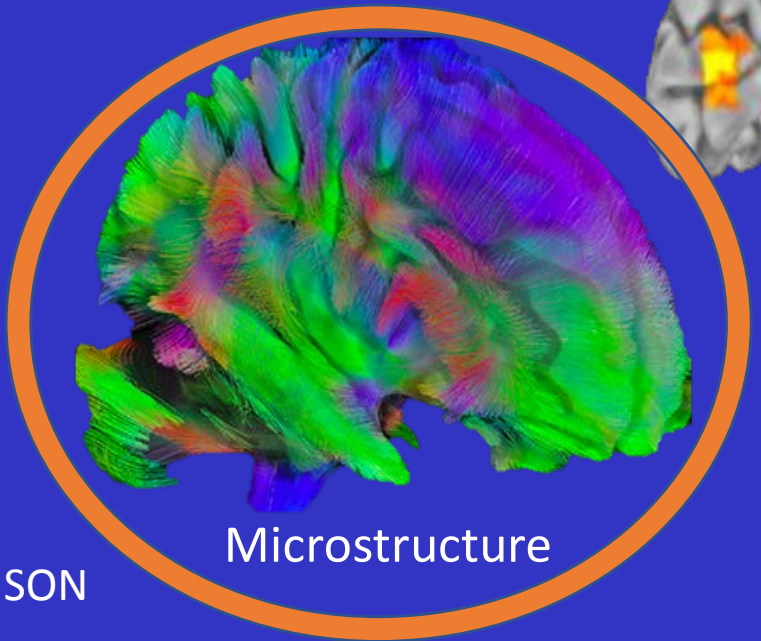
Magnetic Resonance Imaging



Anatomy /
Brain Structure



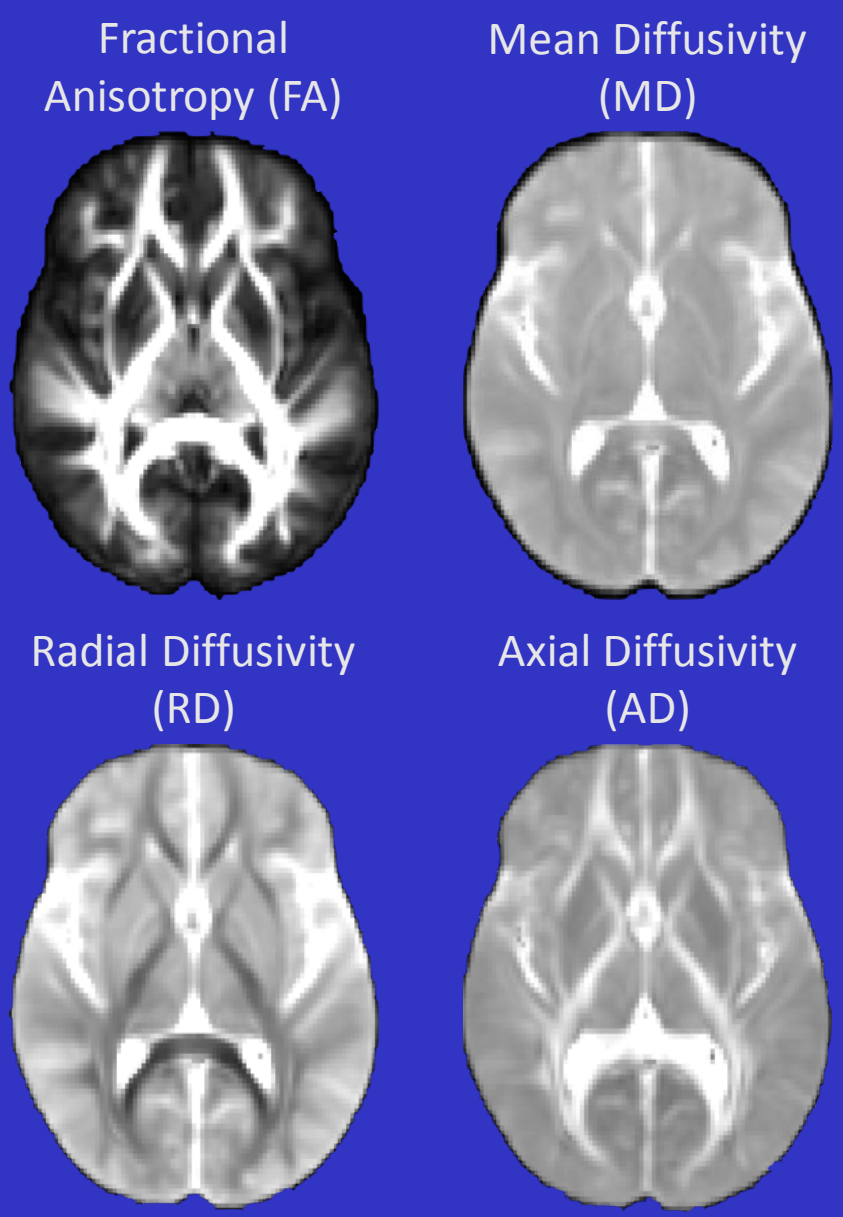
Function



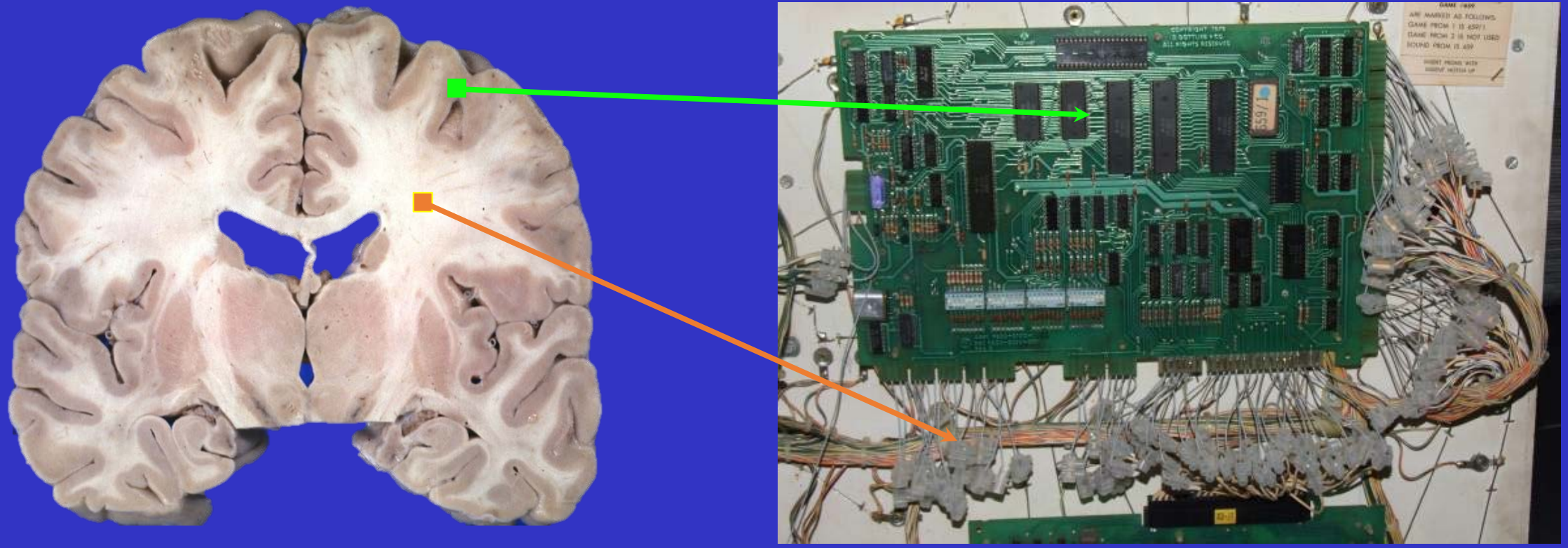
Microstructure

Diffusion Tensor Imaging

- Probes tissue microstructure by investigating how water molecules diffuse throughout the brain.
- Diffusion Tensor Imaging (DTI): provides quantitative measures sensitive to underlying white matter microstructure



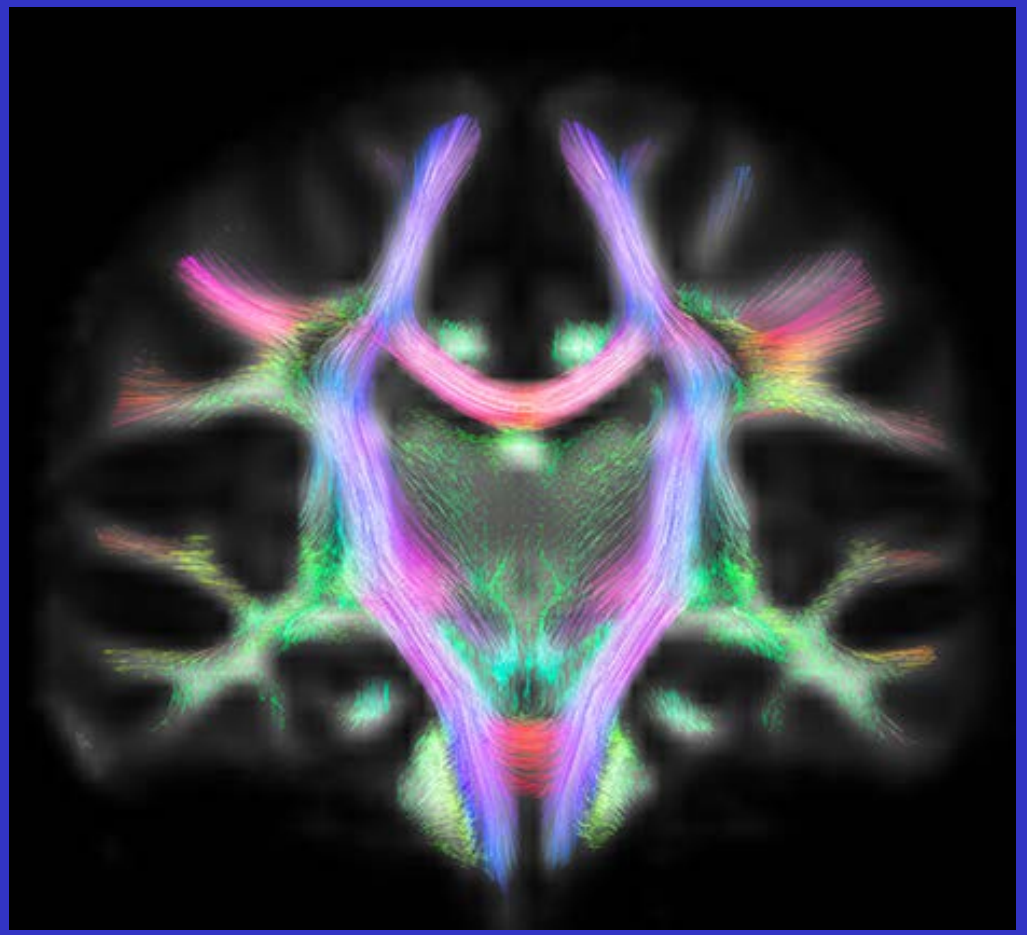
White Matter Matters

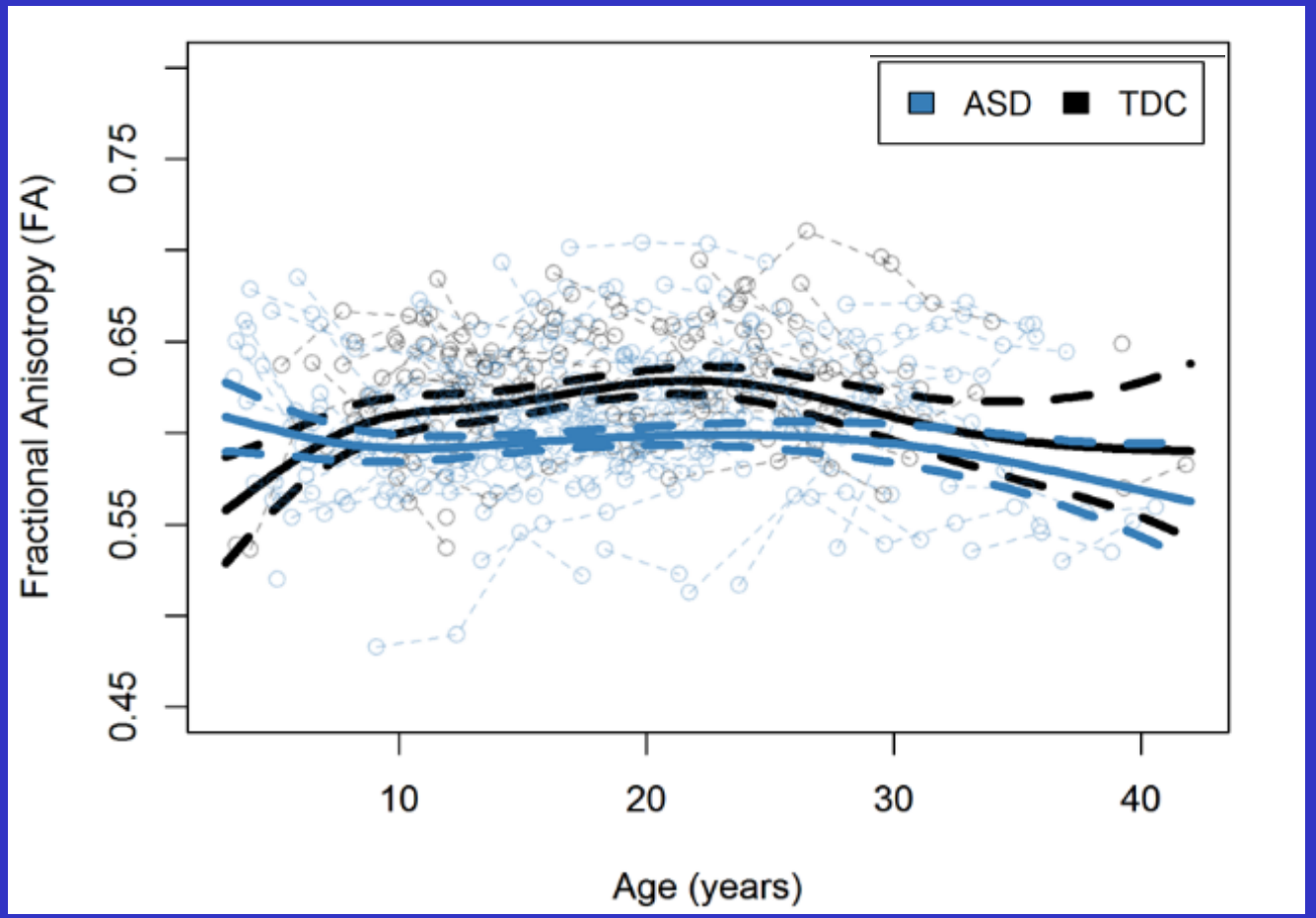


Gray Matter = ‘Processing Centers’ or ’Information Hubs’

White Matter = ‘Brain Wiring’ or ‘Information Highways’

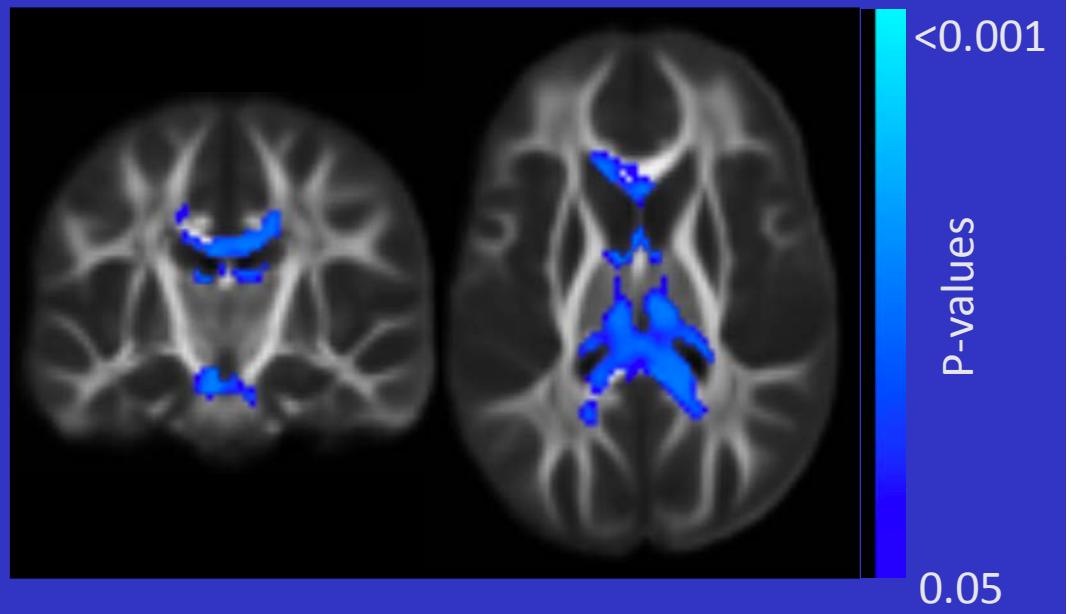
White Matter Matters in ASD

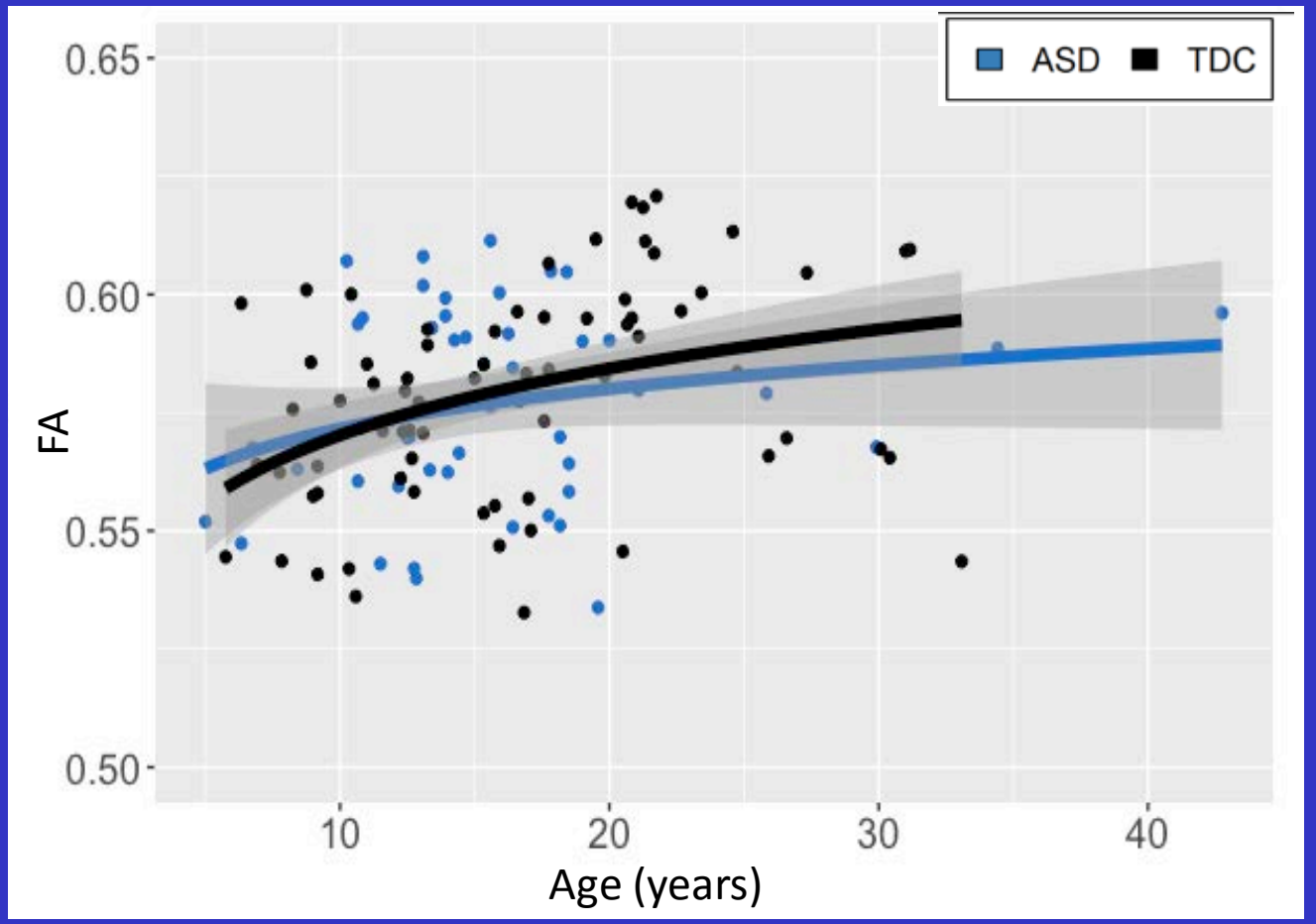




Travers et al., 2015

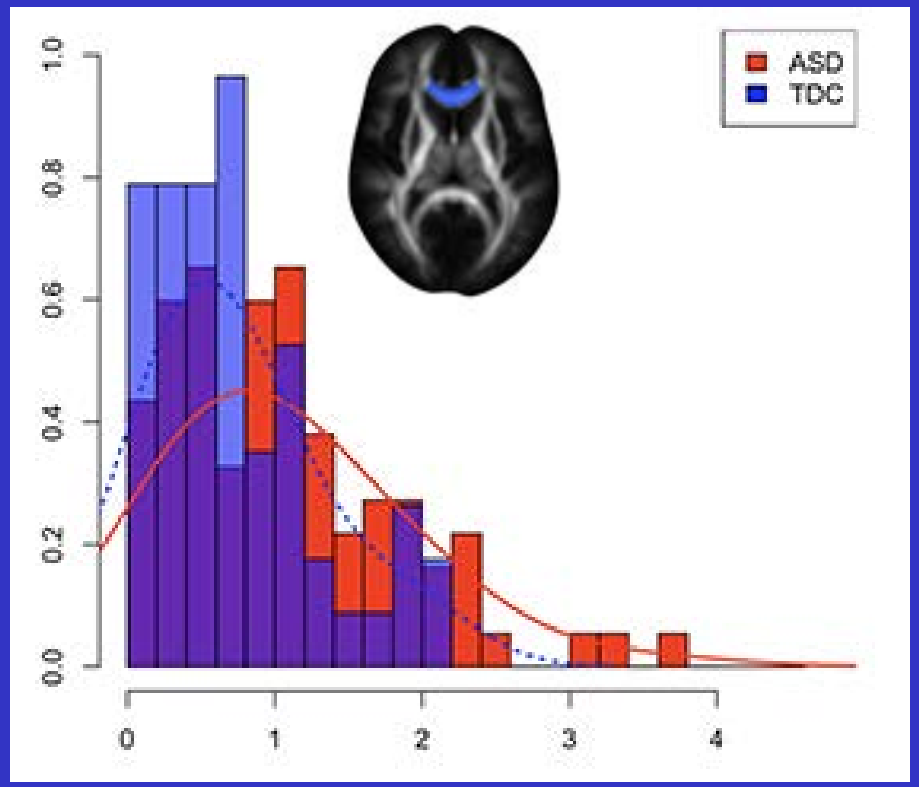
White Matter Matters in ASD

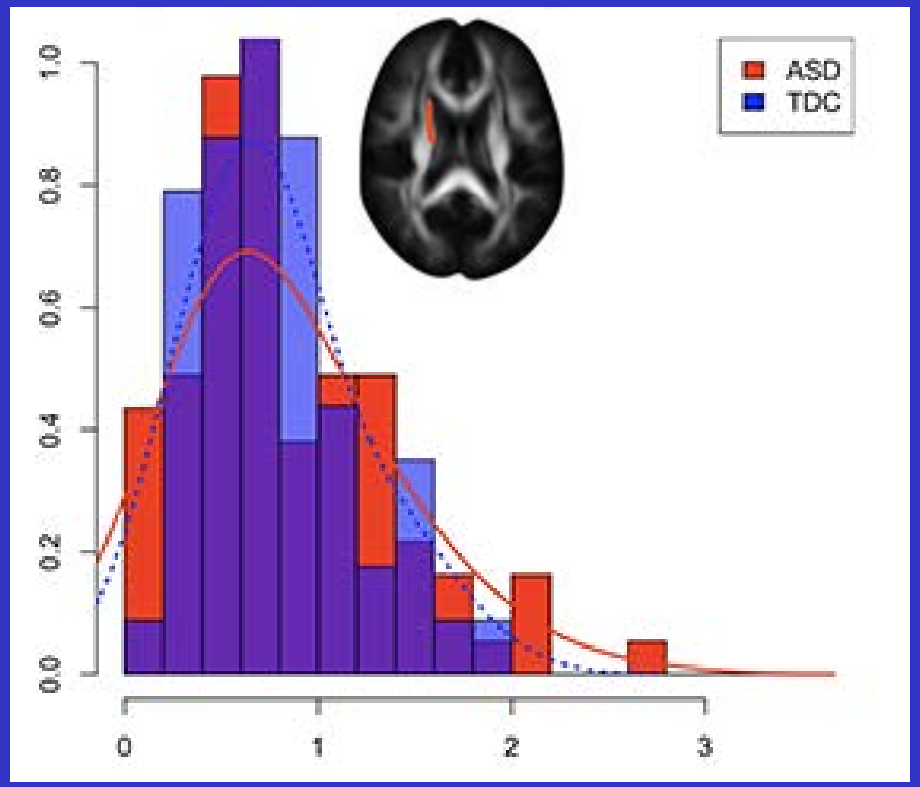




Dean et al., In Prep

White Matter Variation Across ASD

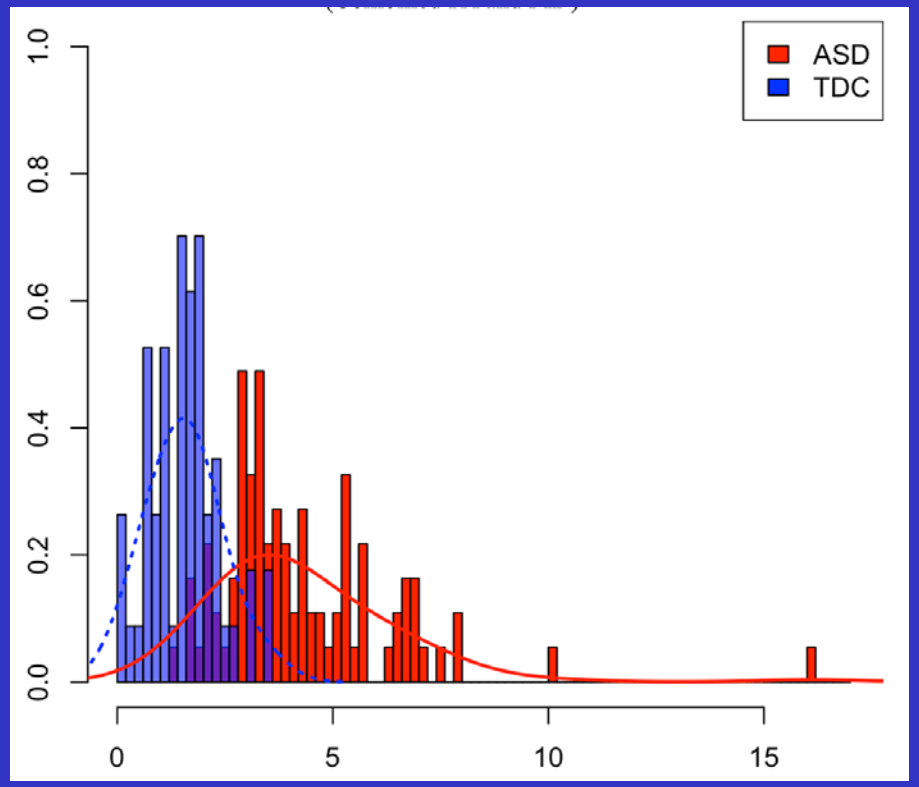


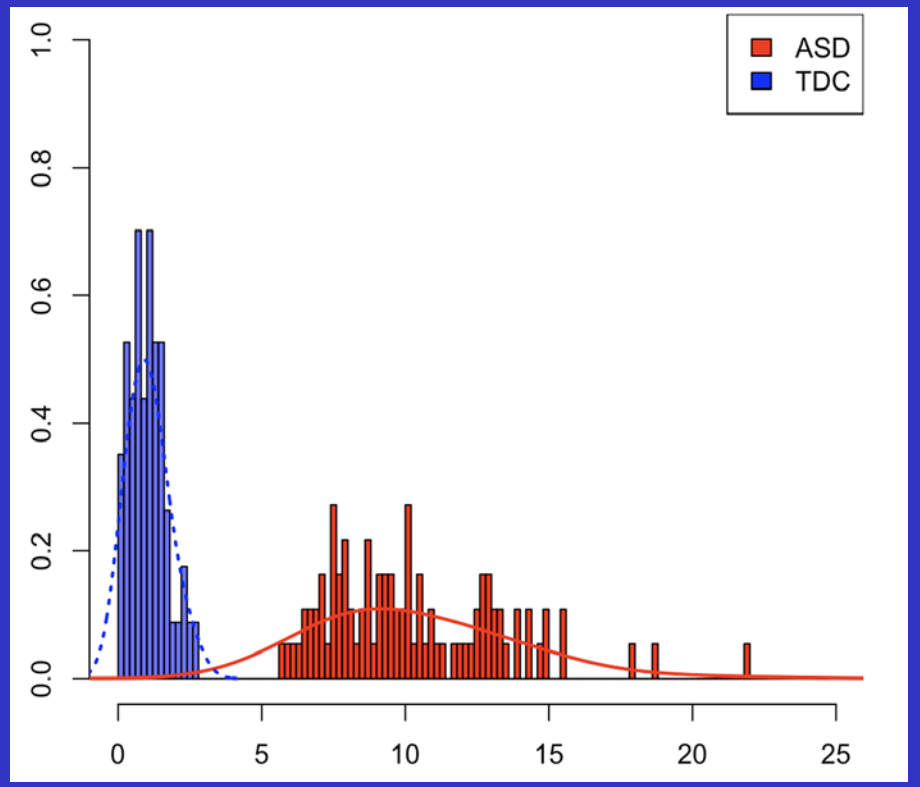


- Widespread heterogeneity across individual white matter regions
- Individual differences depend on white matter region

Dean et al., NeuroImage Clinical, 2017

White Matter Variation in ASD





- Combining multiple white matter measures together provides greater sensitivity for identifying ASD individuals than just looking at single brain regions.

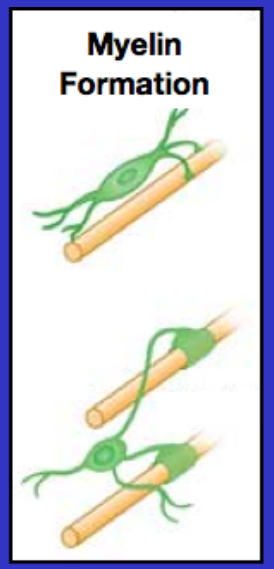
Dean et al., NeuroImage Clinical, 2017

Diffusion Tensor Imaging

Increasing FA

Increasing AD

Decreasing RD

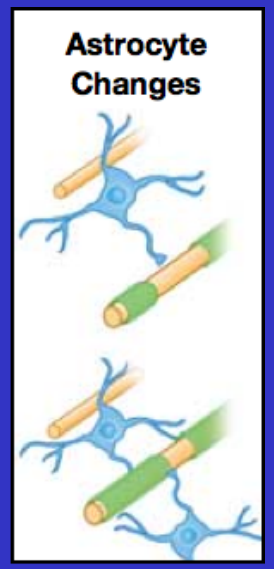


Increasing FA

Increasing AD

Decreasing RD

Increasing RD

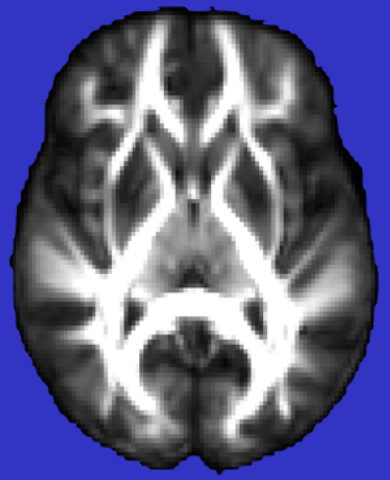


Decreasing FA

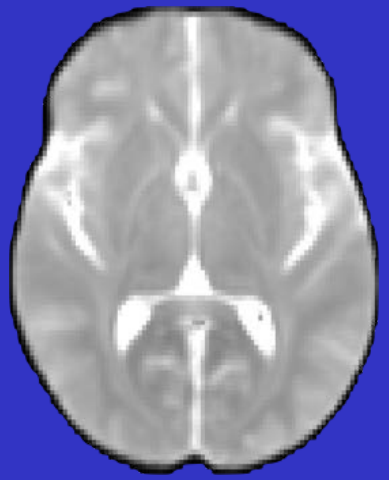
Decreasing AD

Non-specific!

Fractional Anisotropy (FA)

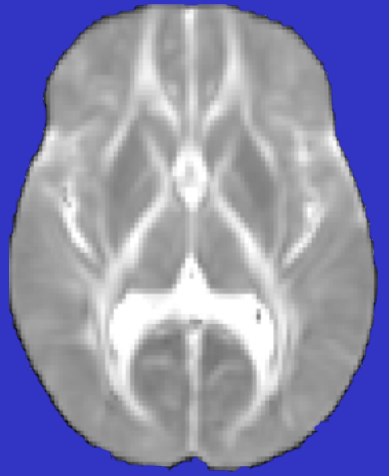


Mean Diffusivity (MD)



Radial Diffusivity (RD)

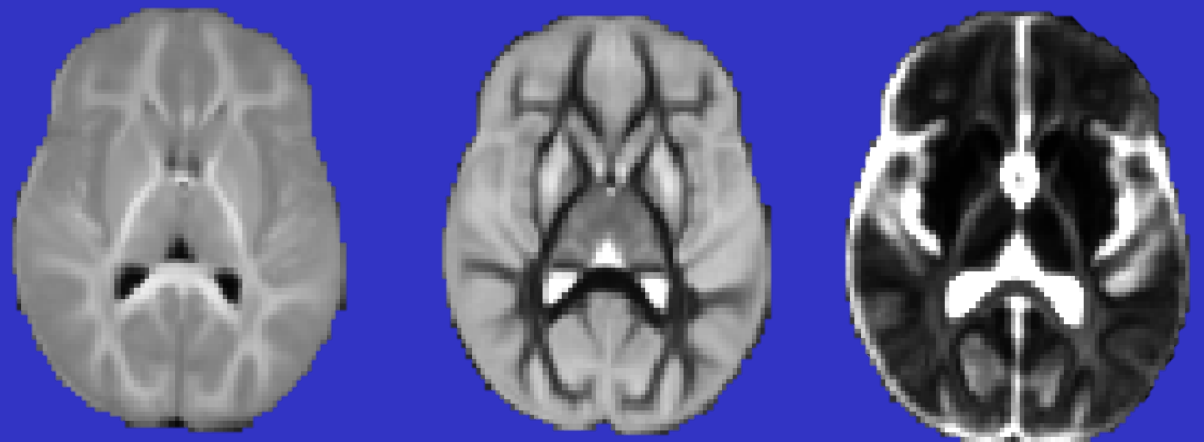
Axial Diffusivity (AD)



Advances in Microstructural Imaging

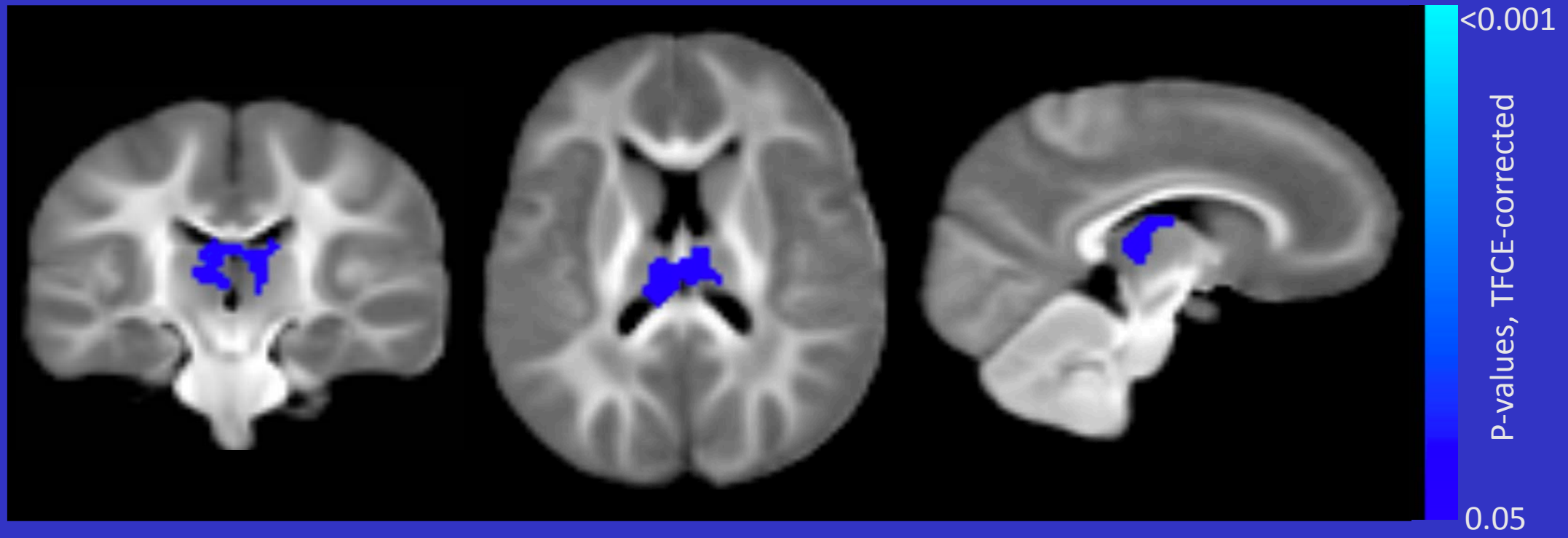
- Improved measurement and characterization of white matter is important for understanding processes underlying neural diversity in ASD.

- Neurite Orientation Dispersion and Density Imaging (NODDI)
  - Unique measures shown associated with microstructure,
  - Have not been extensively examined in ASD populations



FICVF ODI v_{ISO}

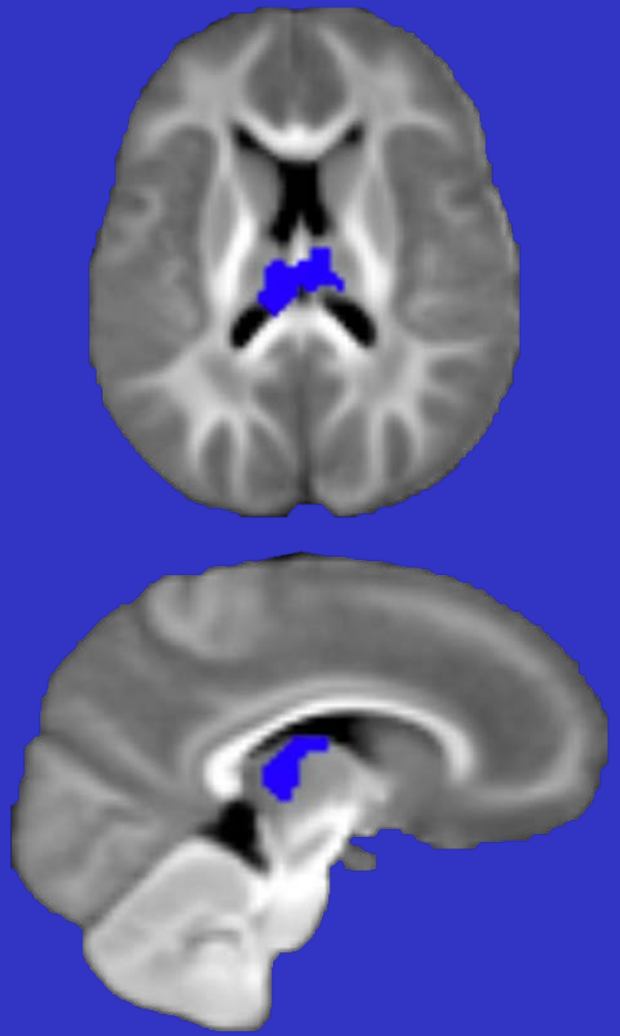
Microstructural Imaging in ASD

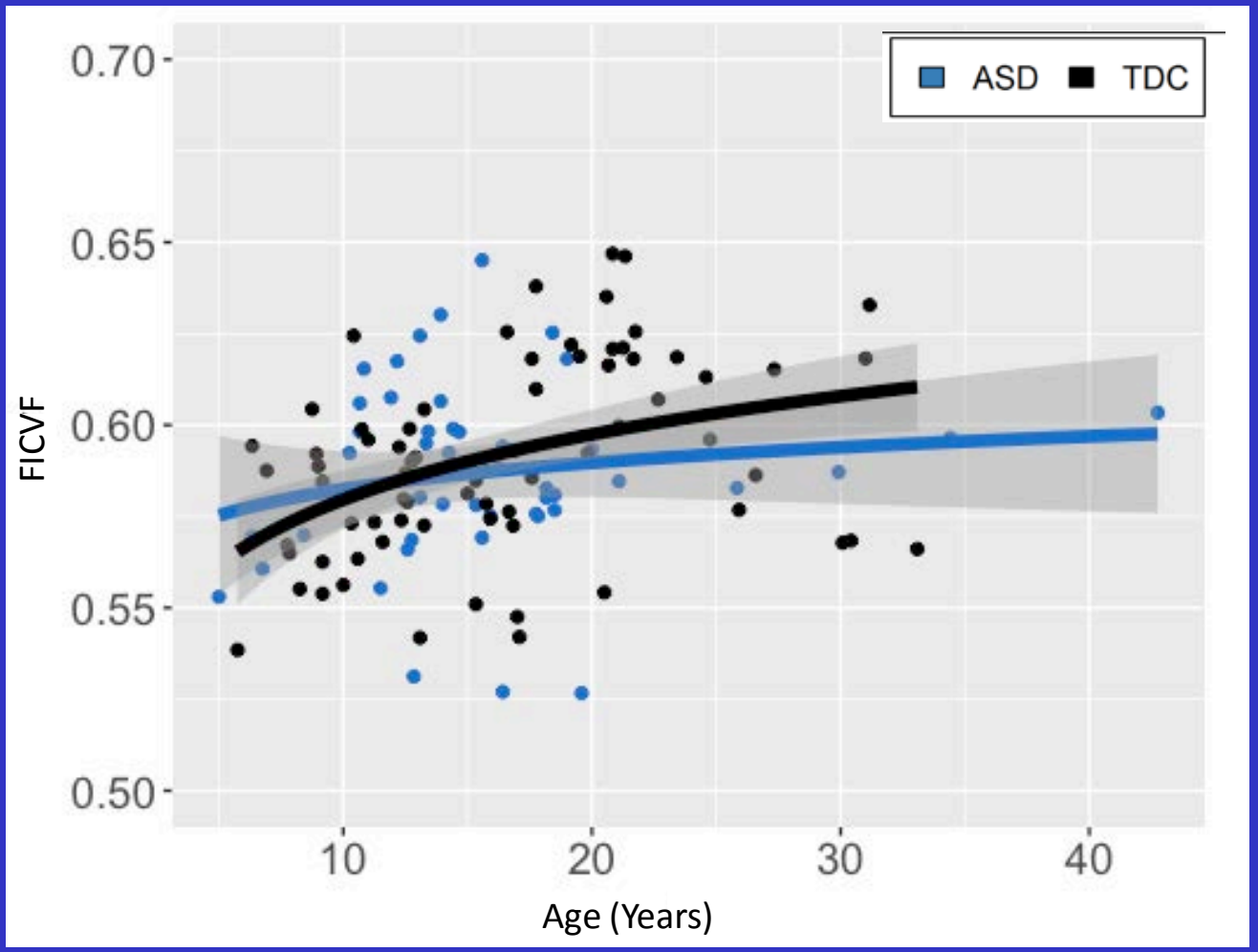


Lower FICVF (i.e. lower neurite density) bilateral thalamus

Dean et al., In Prep

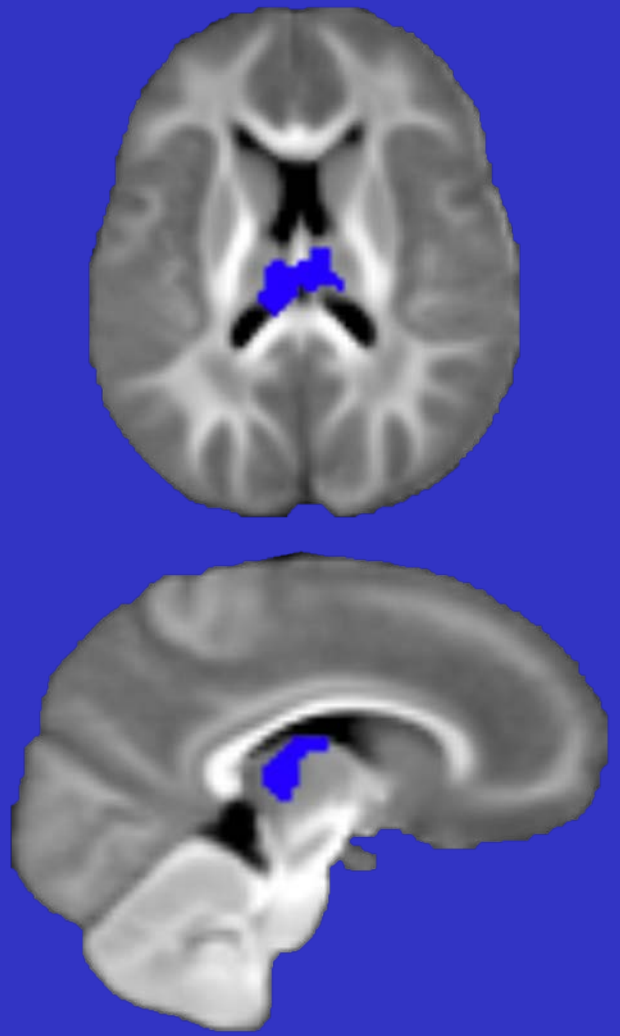
Microstructural Imaging in ASD

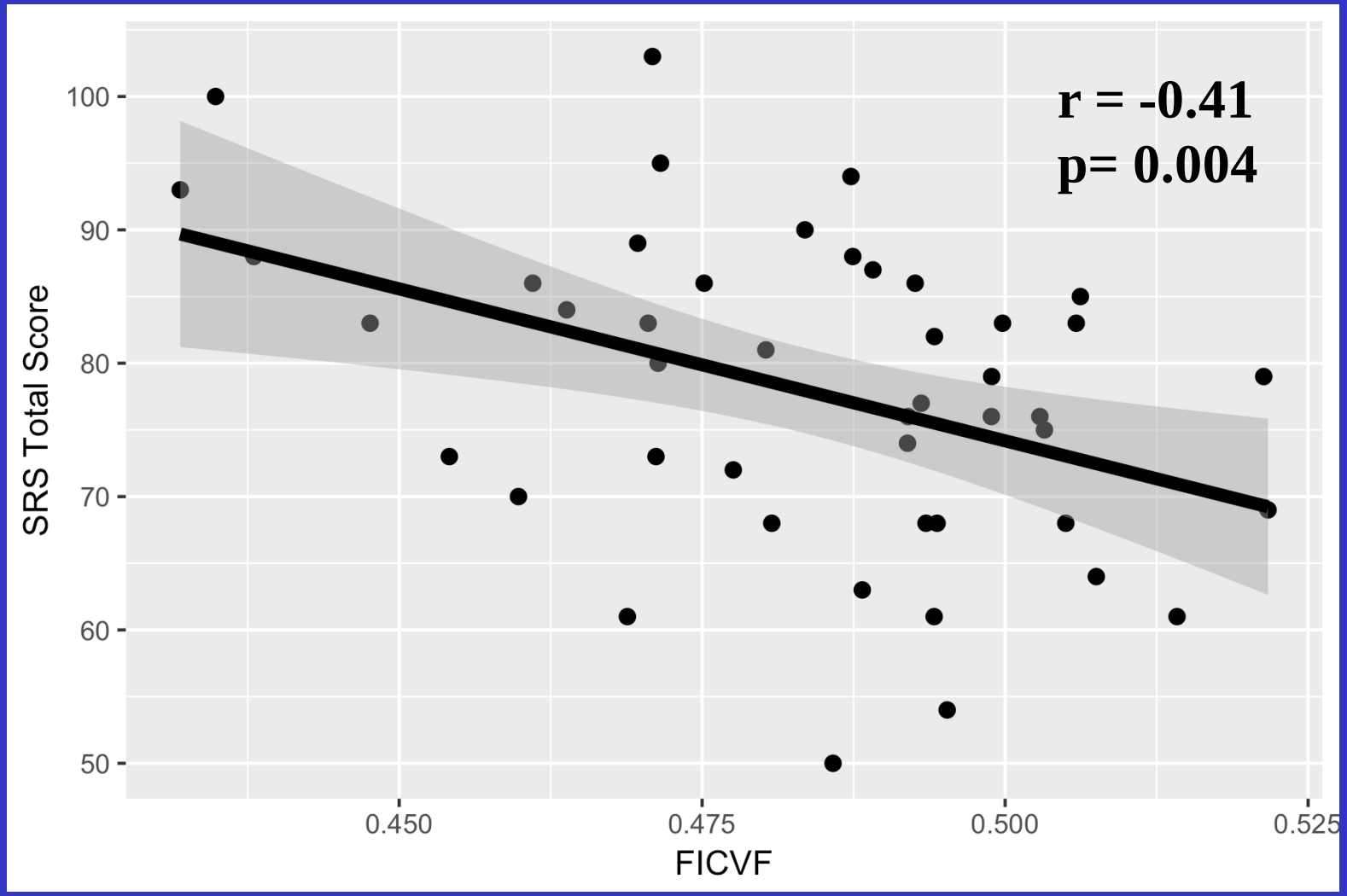




Dean et al., In Prep

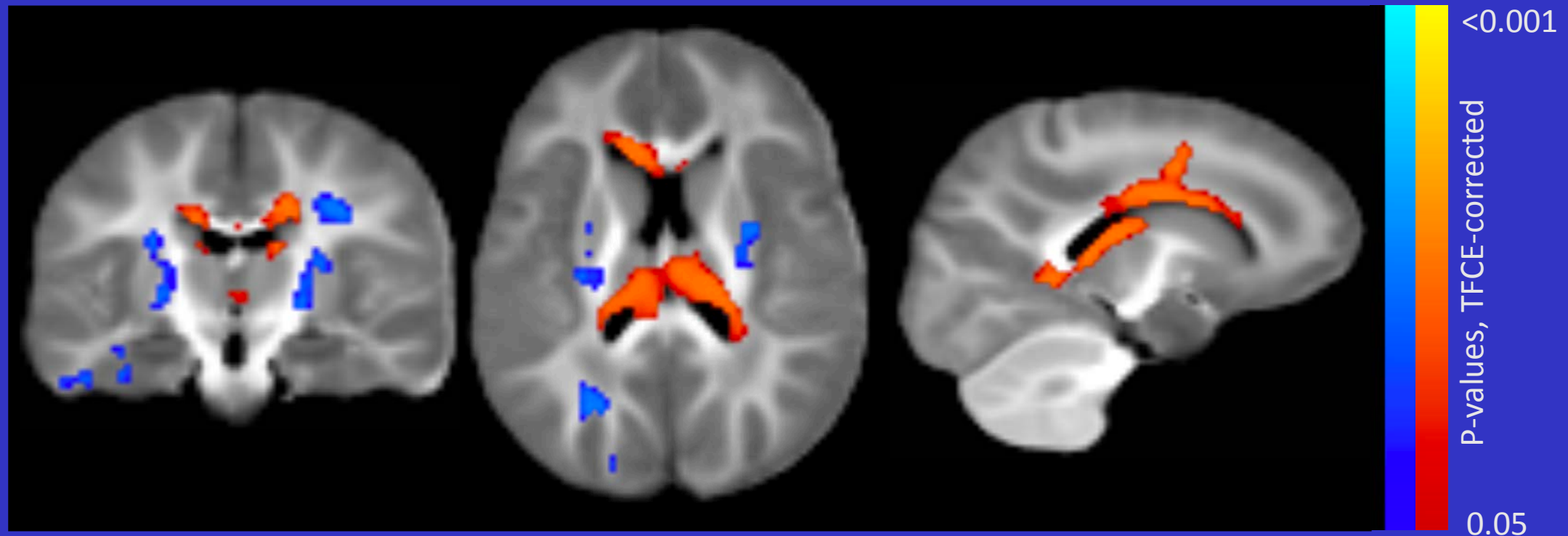
Microstructural Imaging in ASD





Dean et al., In Prep

Microstructural Imaging in ASD



Higher ODI (i.e. greater dispersion) in corpus callosum and thalamus

Lower ODI (i.e. less dispersion) in internal capsules and right superior longitudinal fasciculus

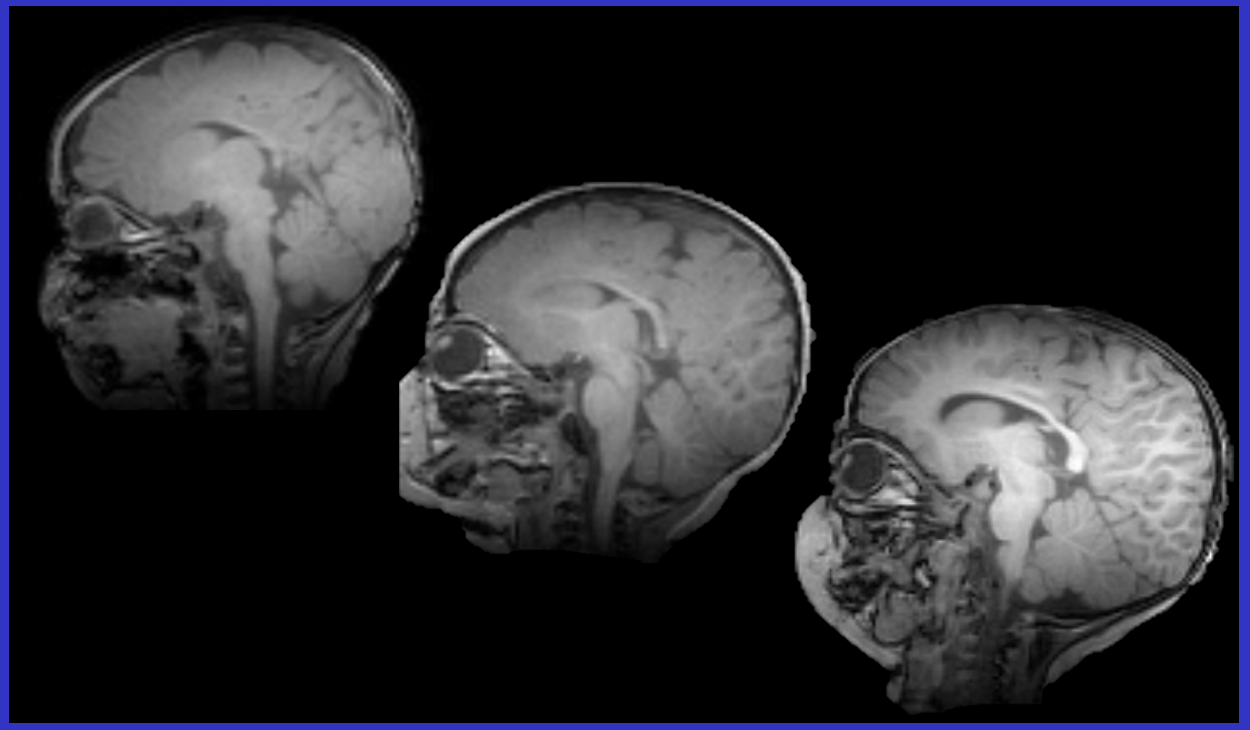
Dean et al., In Prep

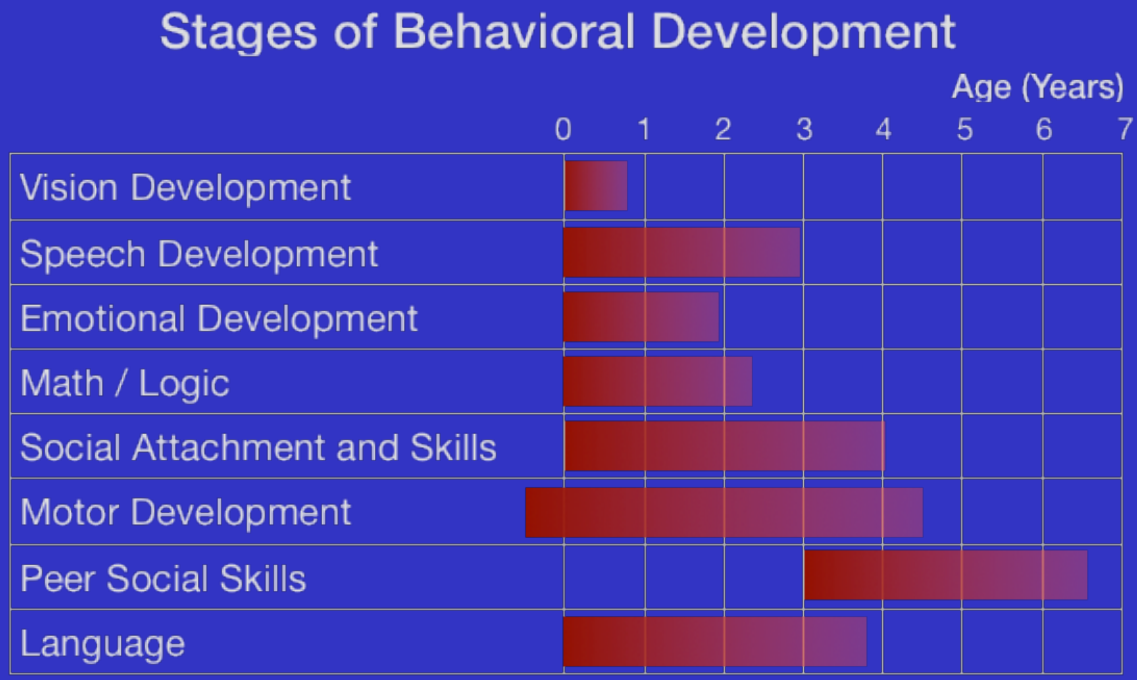
Summary

- White matter microstructure plays important role in neurobiology of ASD
- Despite group level differences between ASD individuals and typically developing controls, widespread individual variation exists within the brain.
- Emerging microstructural imaging techniques, like NODDI (and others), provide new approaches for studying white matter and may inform processes underlying microstructural diversity in ASD

Future Directions: Looking For Answers In Early Brain Development

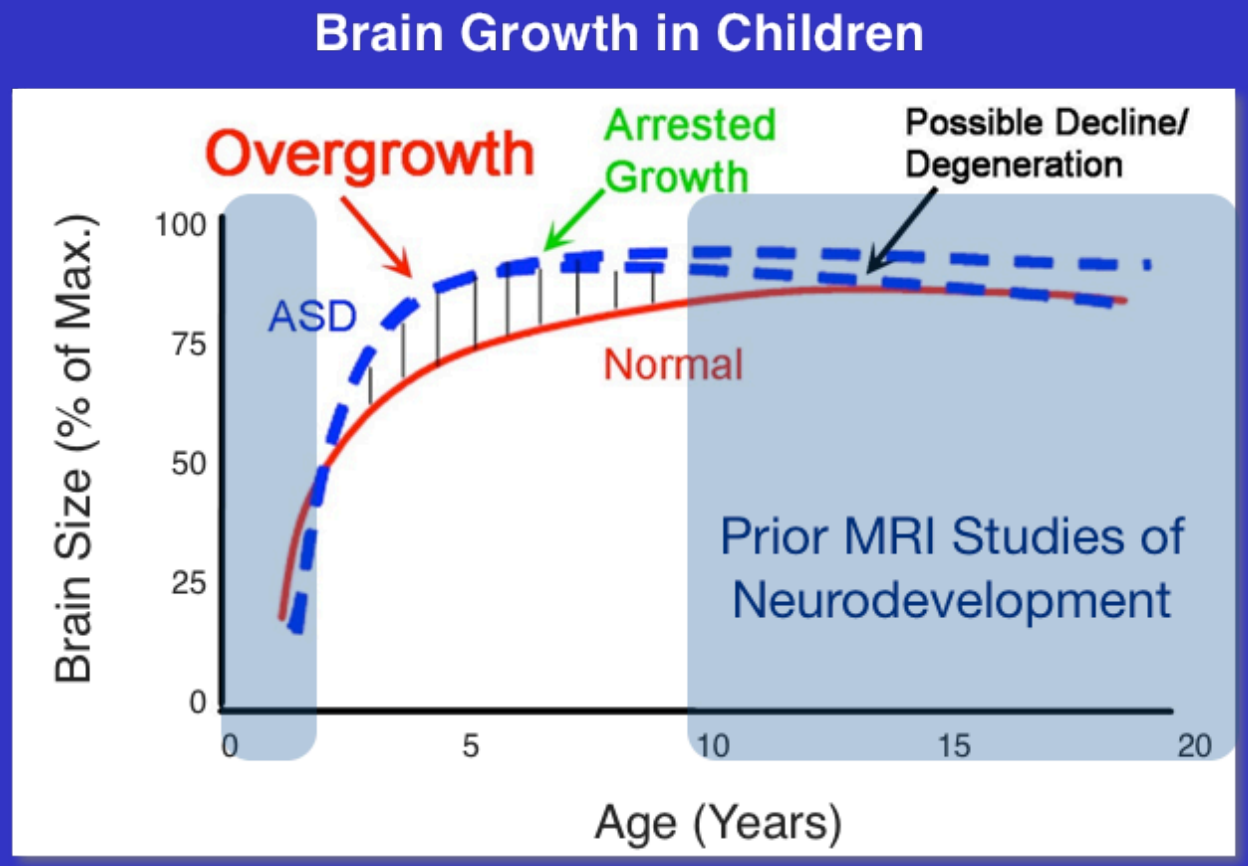
Future Directions: Looking For Answers In Early Brain Development





- Early brain development plays critical role in later brain development and development of behavior and cognition.

Future Directions: Looking For Answers In Early Brain Development



- Do not know how the neurodevelopmental trajectory of ASD during early life.
- Can microstructural imaging provide new information about ASD neurodevelopment

Acknowledgements

Collaborators:

Andy Alexander
Brittany Travers
Steve Kecskemeti
Nagesh Adluru
Greg Kirk
Aly Rameshk
Janet Lainhart
Nicholas Lange
Molly Prigge
Brandon Zieliniski
Abigail Freeman
Joaquin Villaruz
Erin Bigler
Tom Fletcher
Jeff Anderson
Mark Leppert
Nori Matsunami
Carolyn King

Sincerest gratitude to the participants and their families for making this research possible!

Funding:

U54 HD090256
T32 HD007489
R01 MH080826
R01 MH084795
R01 MH097464
K99 MH110596

NIH National Institute of Mental Health

NIMH National Institute of Mental Health

ISLA INTERDISCIPLINARY SCIENCE TO LEARN ABOUT AUTISM