Neuroimaging Project Update

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11-15-2017

Plan

* Recruit groups of 45 (PAE) and 45 (control)
  * During the first 3 years
* Age range: 10 – 16 years old
* All will receive dysmorphology
* MRI scan
* 3-hour neurocognitive / behavioral session testing
  * Including Dr. Mattson's short, digital battery (iPads)
* 15 month interval
* Second MRI scan

Phase IV Progress

* Two new coordinators hired (Mariah & Priya)
* Training with Dr. Mattson's group in San Diego
* Imaging protocol finalized and tested
* IRB approval secured (Nov 6)
* Batch 1 of recruitment letters sent (Nov 7)
* Recruitment at local conference (Nov 9-10)
* First participants (mid-late November)

Phase III Data analyses… ongoing

Hendrickson, T.J., Mueller, B.A., Sowell, E.R., Mattson, S.N., Coles,C.D., Kable, J.A., Jones, K.L., Boys, C.J., Lim, K.O., Riley, E.P., & Wozniak, J.R. (2017). Cortical gyrification is abnormal in children with Prenatal Alcohol Exposure. *Neuroimage: Clinical. 15, 391-400; doi.org/10.1016.j.nicl.2017.05.015.* PMCID: PMC5447653.

Uban, K.A., Herting, M.M., Wozniak, J.R., & Sowell, E.R. (2017). Sex differences in associations between white matter microstructure and gonadal hormones in children and adolescents with prenatal alcohol exposure. *Psychoneuroendocrinology, DOI: 10.1016/j.psyneuen.2017.05.019. PMID: 28609669.*

Gross, L.A., Moore, E.M., Coles, C.D., Kable, J.A., Sowell, E.R., **Wozniak, J.R.**, Jones, K.L., Riley, E.P., Mattson, S.N., & the CIFASD. (2017). Neural correlates of verbal memory in youth with heavy prenatal alcohol exposure. *Brain Imaging and Behavior; doi: 10.1007/s11682-017-9739-2. PMID:28656347.*

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Uban, K.A., Kan, E., Wozniak, J.R., Mattson, S.N., Coles, C.D., Sowell, E.R. (revision under review). The relationship between socioeconomic status and brain development is attenuated in children and adolescents with prenatal alcohol exposure.

Phase III Data analyses… ongoing

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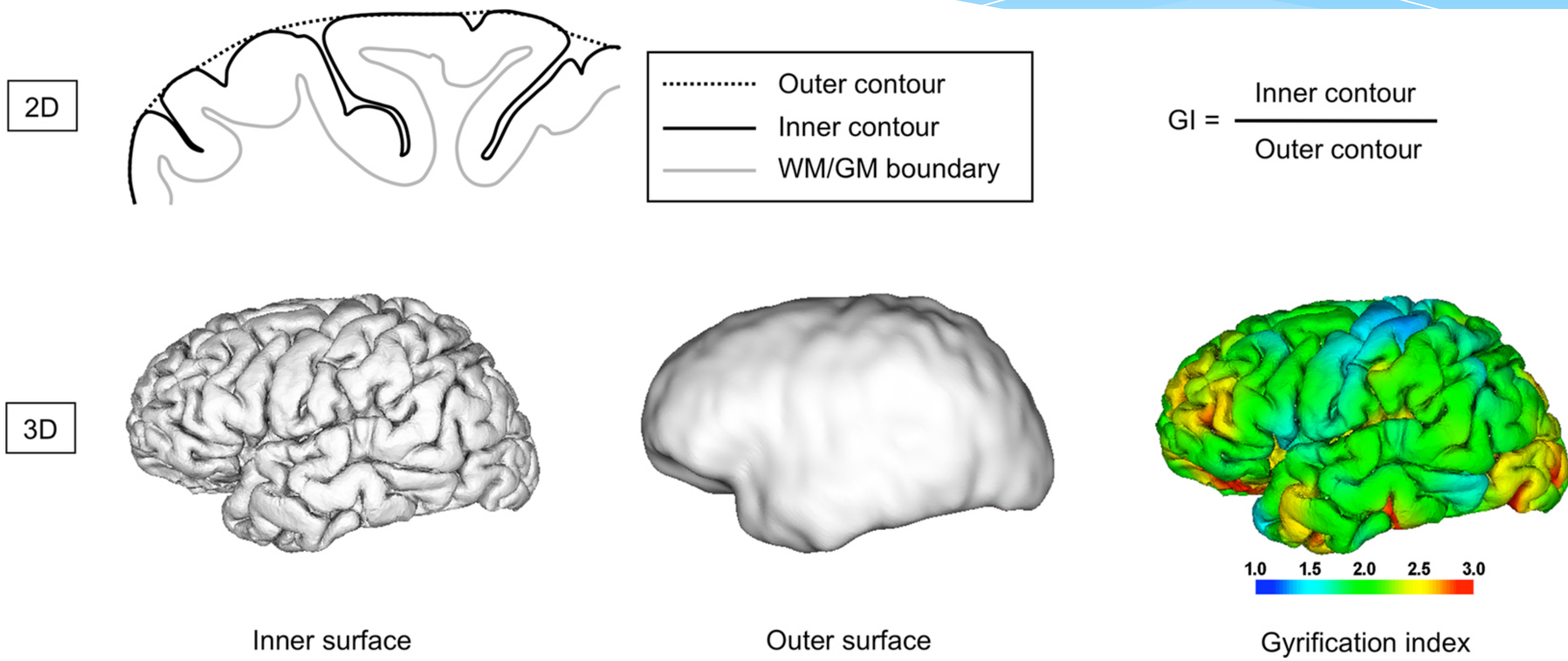
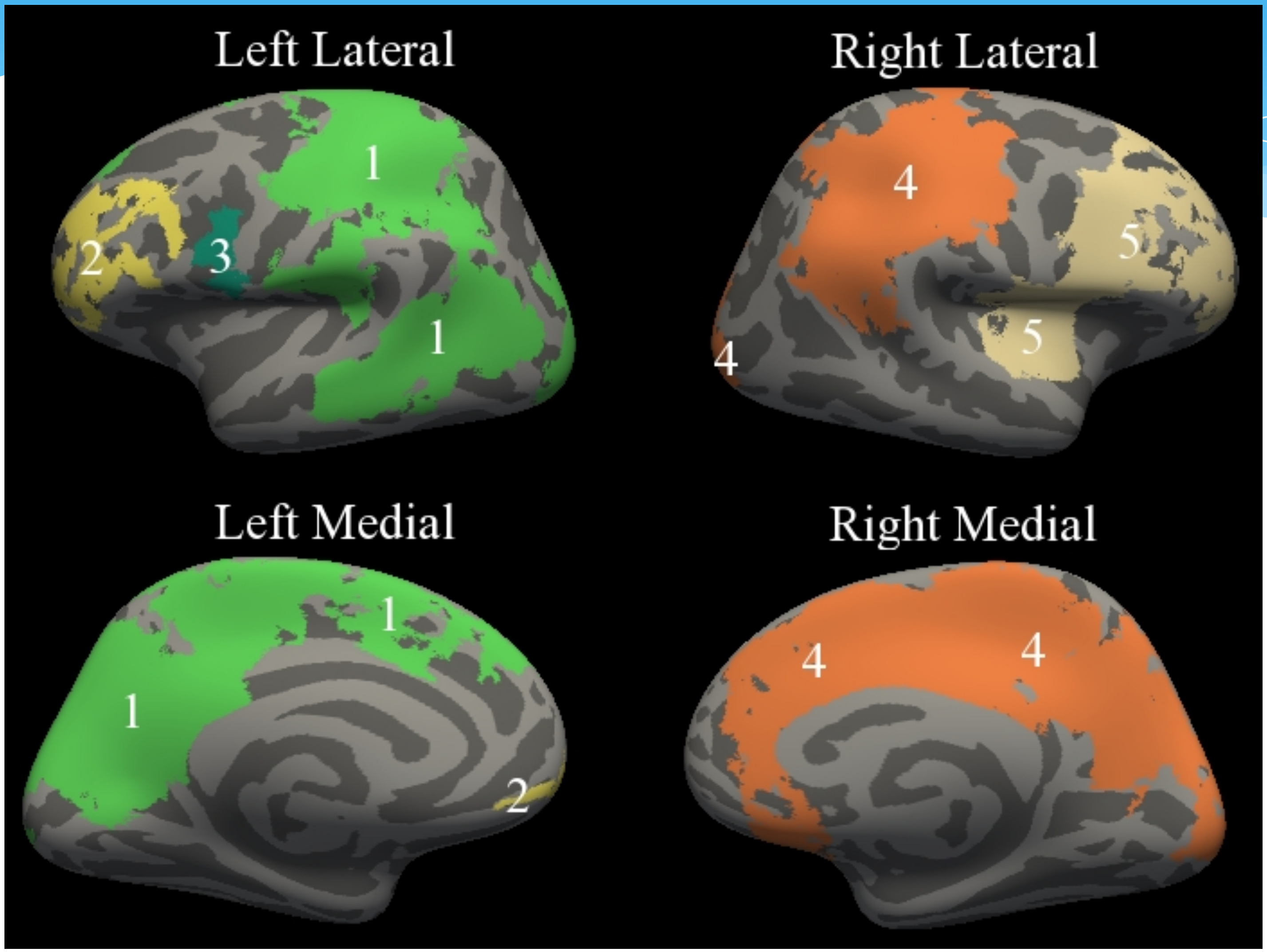
Cortical gyrification



Cross Sectional Brain Anomalies (LGI)



4 Sites
Ages 9-16
92 PAE
83 Controls

T. J. Hendrickson, B. A. Mueller, E. R. Sowell, S. N. Mattson, C. D. Coles, J. A. Kable, K. L. Jones, C. J. Boys, K. O. Lim, E. P. Riley, and J. R. Wozniak, "Cortical gyrification is abnormal in children with prenatal alcohol exposure," NeuroImage Clin., vol. 15, pp. 391–400, Jan. 2017.

Cluster sizes and significance

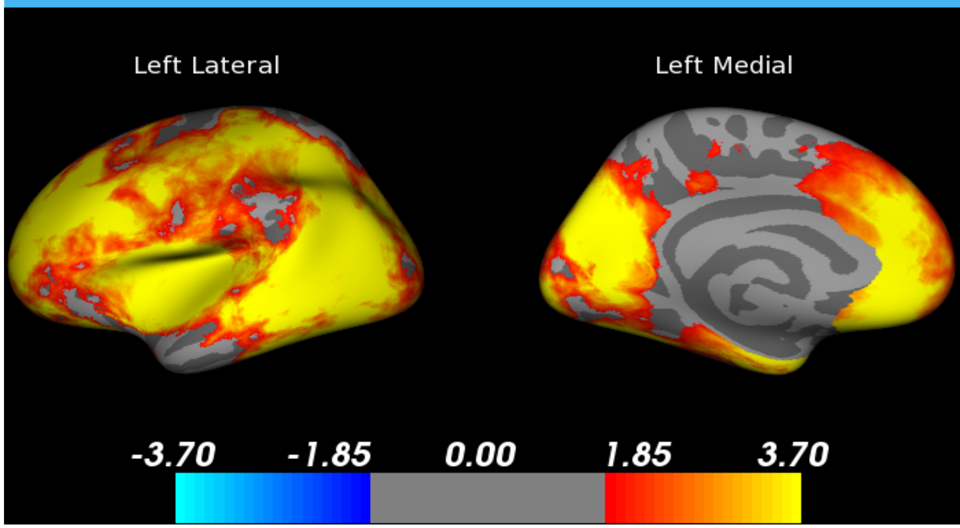
Table 3

Cluster summary. Clusters showing differences between the PAE and Control groups controlling for study site, sex, age, and total intracranial volume (TIV) (cluster forming threshold, $p < 0.05$; clusters for multiple comparisons, $p < 0.05$).

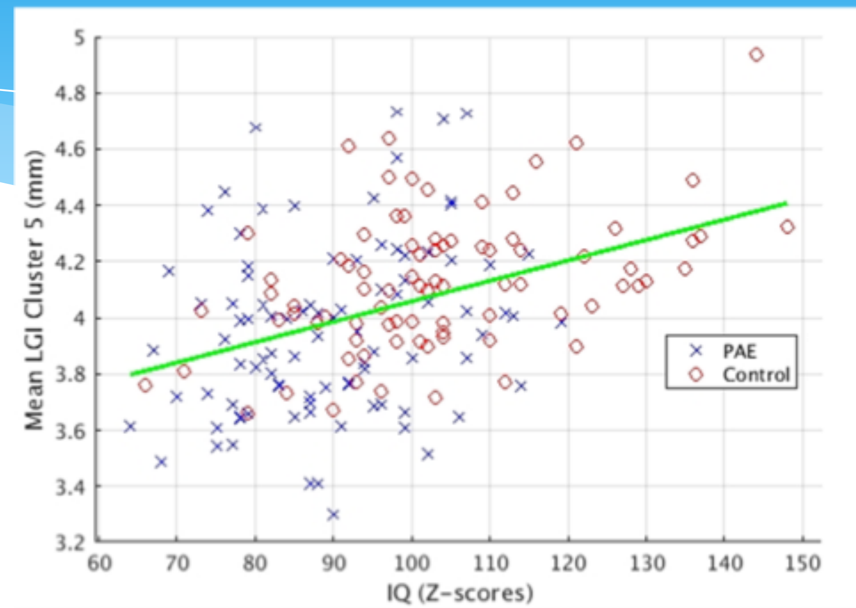
Peak vertex cluster *p*-value	Cluster number Findings	Size (mm^2)	Number of vertices		Peak vertex MNI (x,y,z)	Clusterwise
L postcentral	1	26,684	55,883	(− 27.8, − 35.1, 58.8)	0.00020	Con > PAE
L rostralmiddlefrontal	2	3720	5499	(− 22.6, 49.3, 21.9)	0.00020	Con > PAE
L precentral	3	731	1681	(− 46.7, 2.2, 22.5)	0.00340	Con > PAE
R postcentral	4	22,912	49,464	(37.3, −30.2, 64.0)	0.00020	Con > PAE
R rostralmiddlefrontal	5	8780	17,431	(35.2, 28.9, 40.6)	0.00020	Con > PAE

Note: R = right hemisphere, L = left hemisphere; Con = Control group, PAE = Prenatal Alcohol Exposure group, MNI = Montreal Neurological Institute (coordinate system). Monte Carlo Z Simulation test was applied for multiple comparisons. Confidence interval was 90% for all clusters, and had the following ranges for each respective clusterwise *p*-value: 0.00020 (0–0.00040), and 0.00340 (0.00240–0.00440).

Correlation Between Gyrification and IQ



Left Hemisphere



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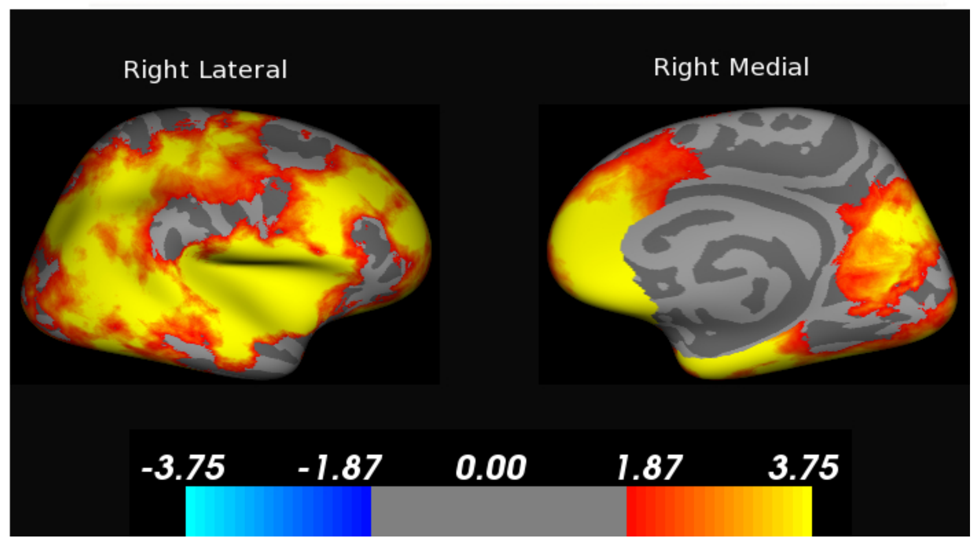


Right Hemisphere

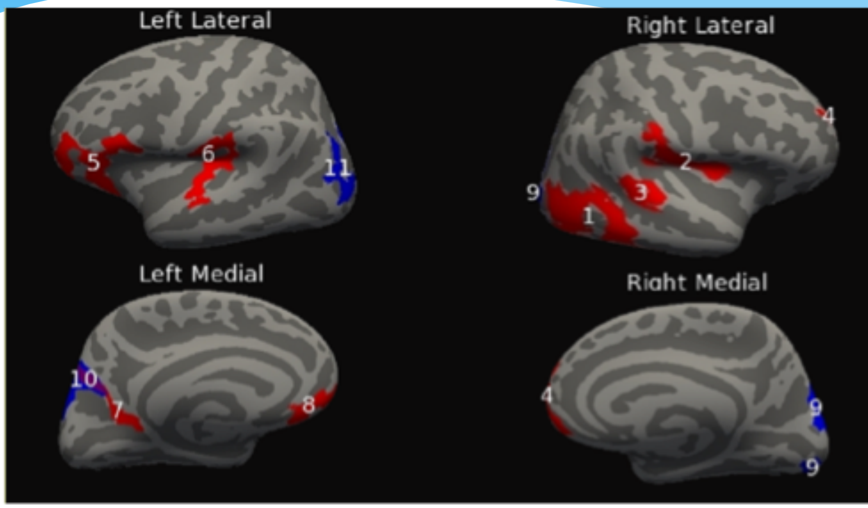
Longitudinal Brain Anomalies

- 58 PAE and 52 Control
- Ages 6 to 17 years
- Four sites (LA, San Diego, Minnesota, Atlanta)
- Two MRI scans – 2 years apart on average
- Multiple measures of cortex
  - Gyrification
  - Thickness
  - Surface Area Volume
- Symmetrized Percent Change (SPC)

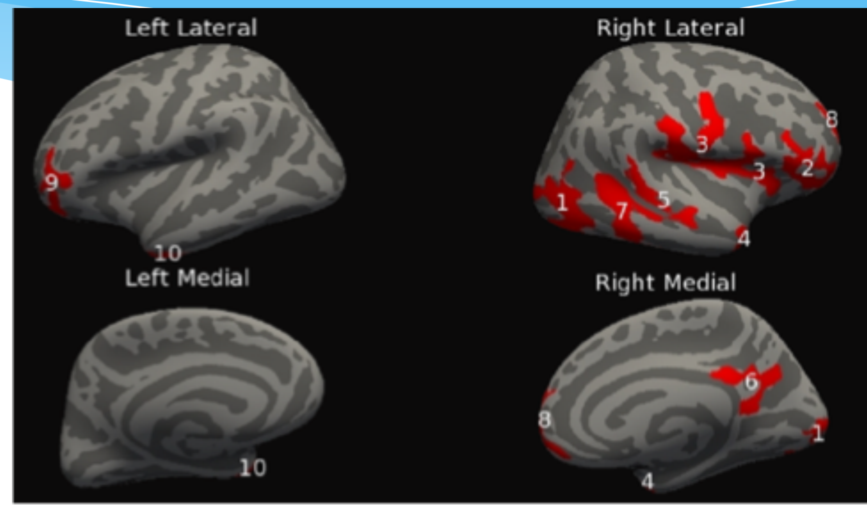
T. J. Hendrickson, B. A. Mueller, E. R. Sowell, S. N. Mattson, C. D. Coles, J. A. Kable, K. L. Jones, C. J. Boys, S. Lee, K. O. Lim, E. P. Riley, and J. R. Wozniak, "Two-year cortical trajectories are abnormal in children and adolescents with prenatal alcohol exposure." (revision under review).

Longitudinal Brain Anomalies

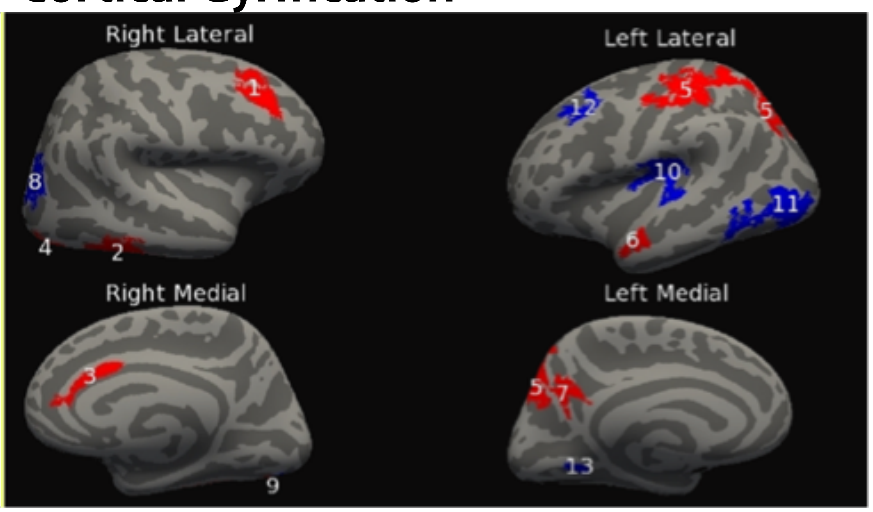
Cortical Thickness



Cortical Volume

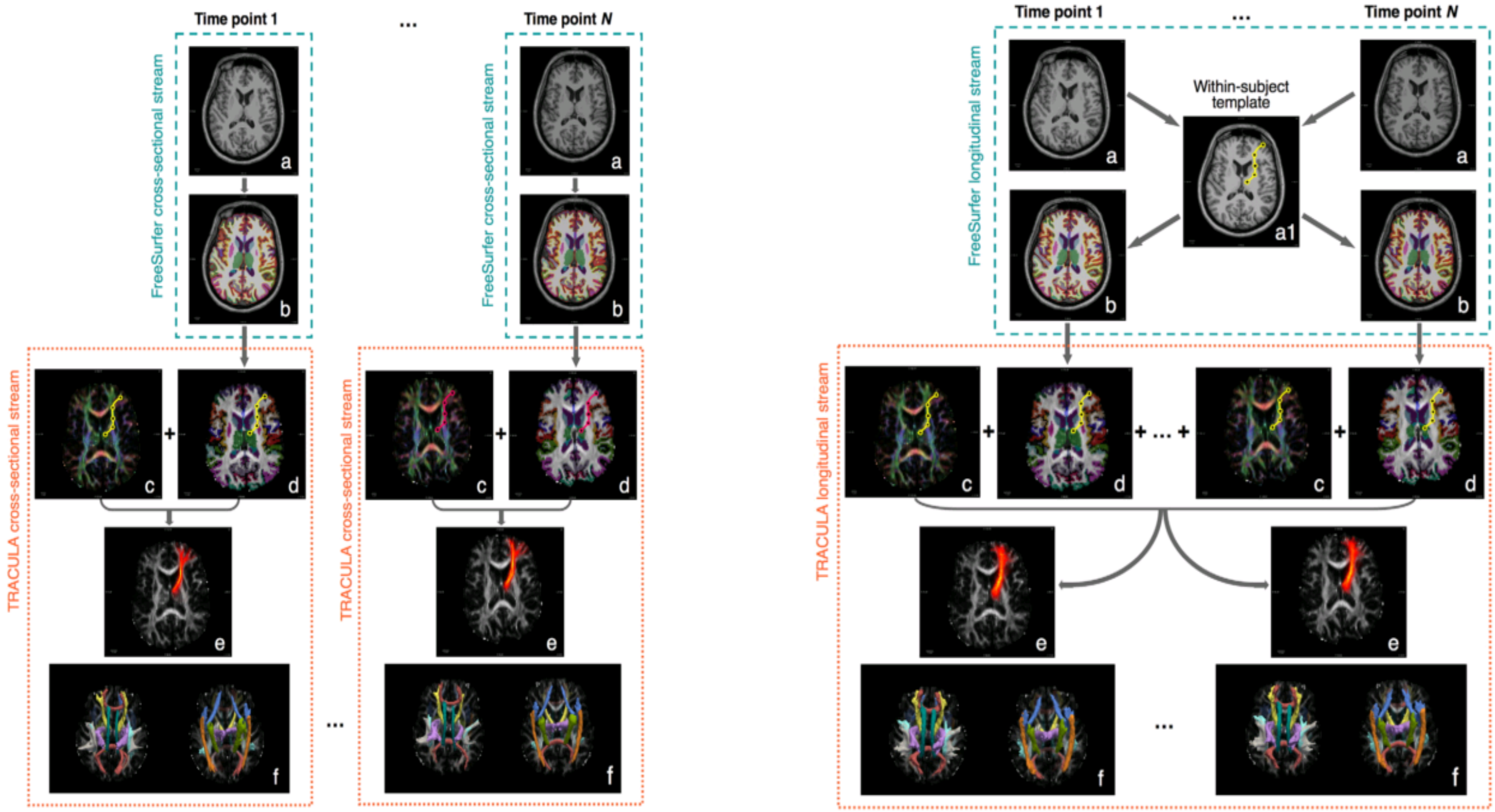


Cortical Gyrification



Thickness: PAE > change than Control at older ages (change was a thinning)
LGI: PAE < change than Control (change was increasing curvature)
Volume: none
Surface area: none

Ongoing Analysis: Longitudinal TRACULA



A. Yendiki, M. Reuter, P. Wilkens, H. D. Rosas, and B. Fischl, “Joint reconstruction of white-matter pathways from longitudinal diffusion MRI data with anatomical priors,” *Neuroimage*, vol. 127, pp. 277–286, 2016.

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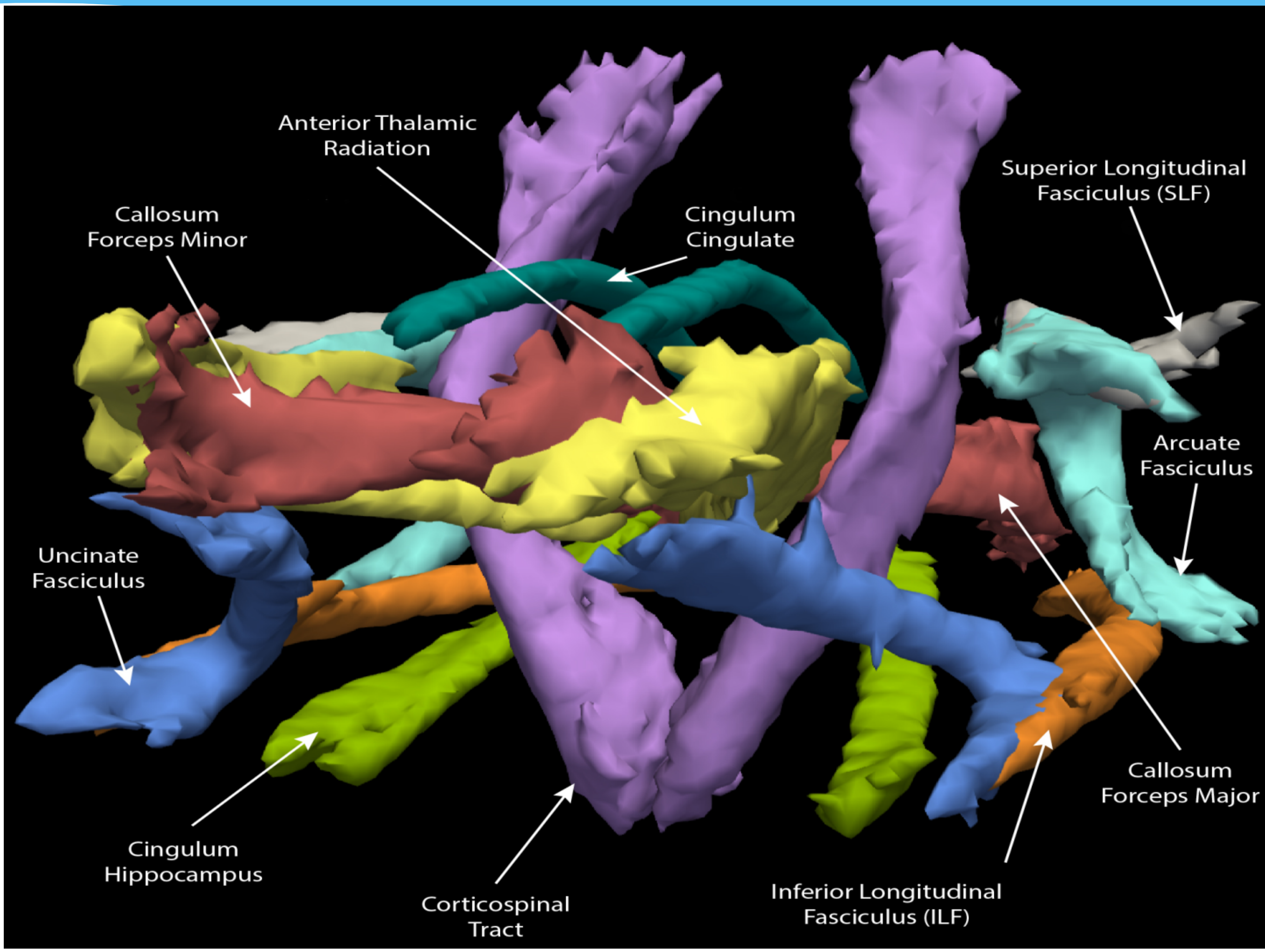

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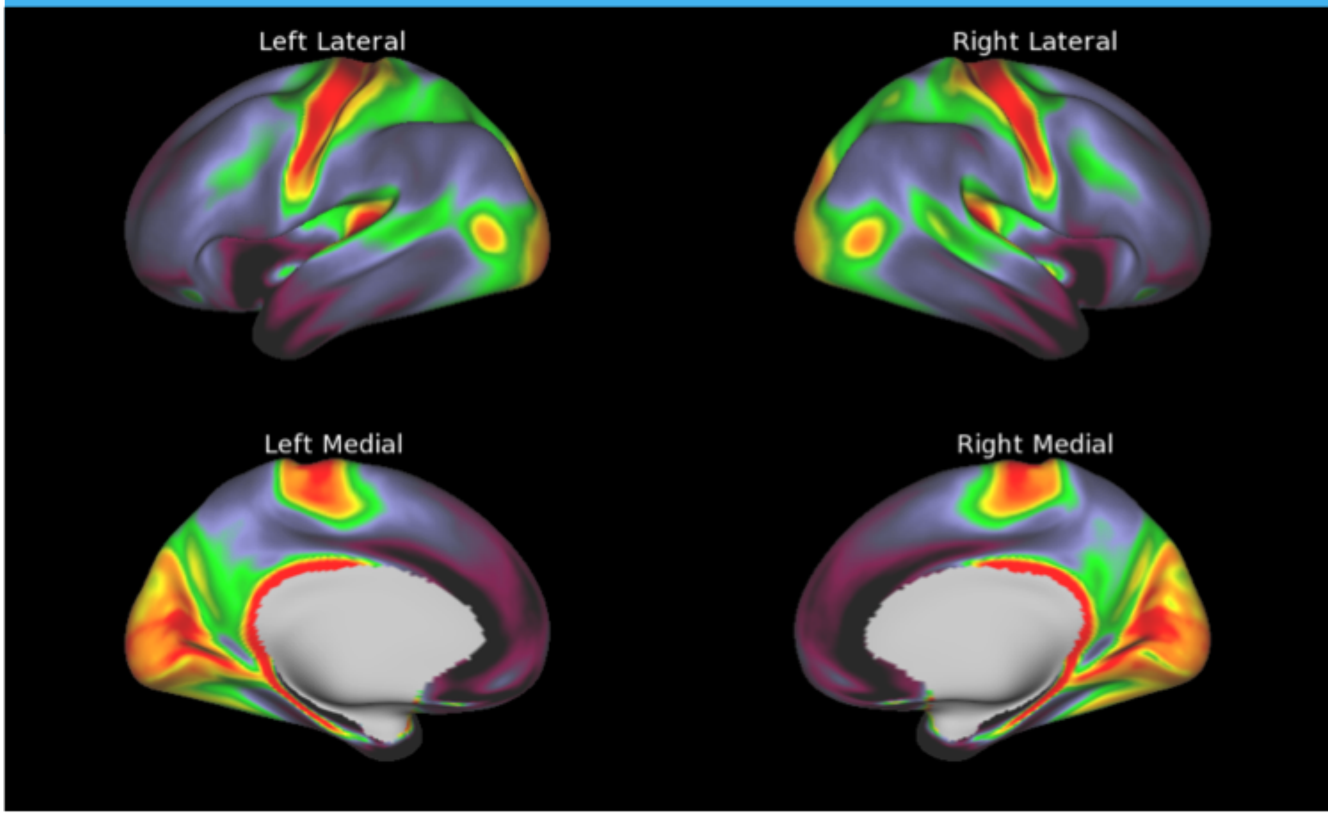
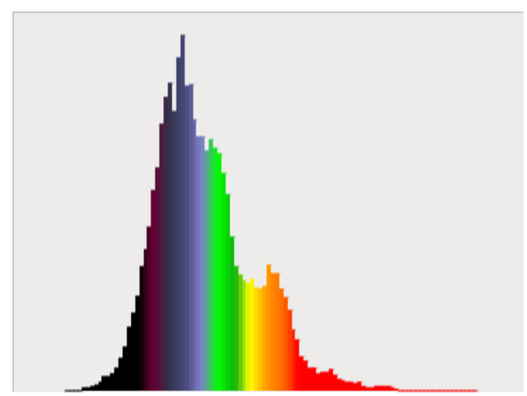
Next Steps: Myelin Maps

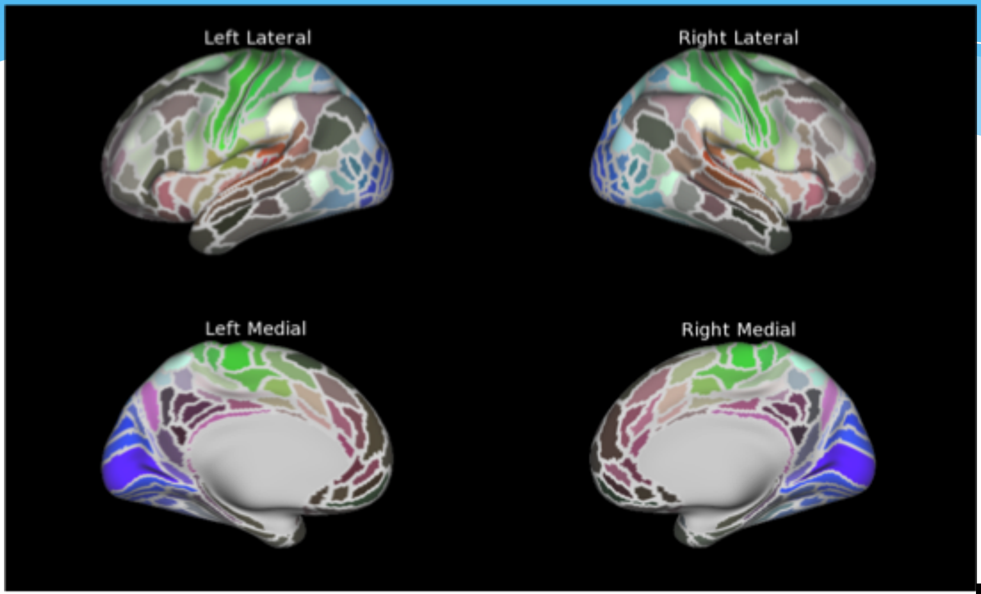


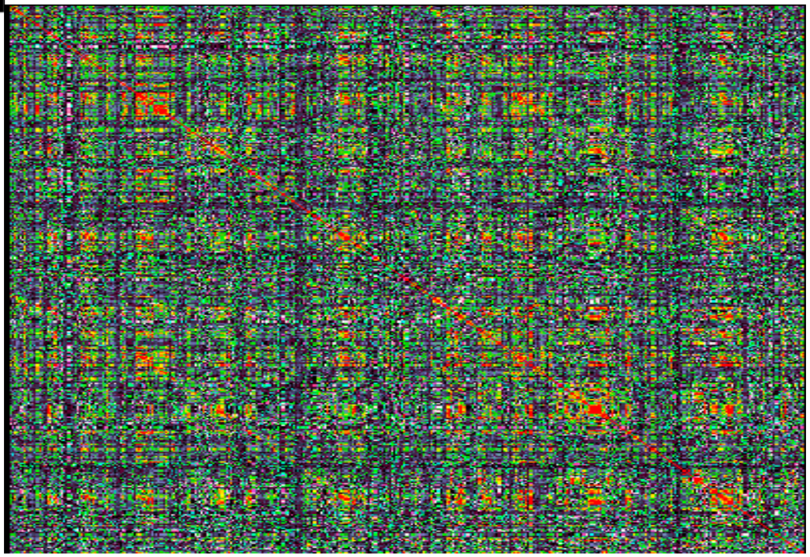


- Human Connectome methods
- Longitudinal assessment will be first of its kind in FASD
- Backdrop: >1000 children in Development project + our own controls

Glasser MF, and Van Essen DC. (2011). Mapping human cortical areas in vivo based on myelin content as revealed by T1- and T2-weighted MRI. J Neurosci. 31:11597-11616

Next Steps: Graph Theory with HCP's Multimodal Parcellation





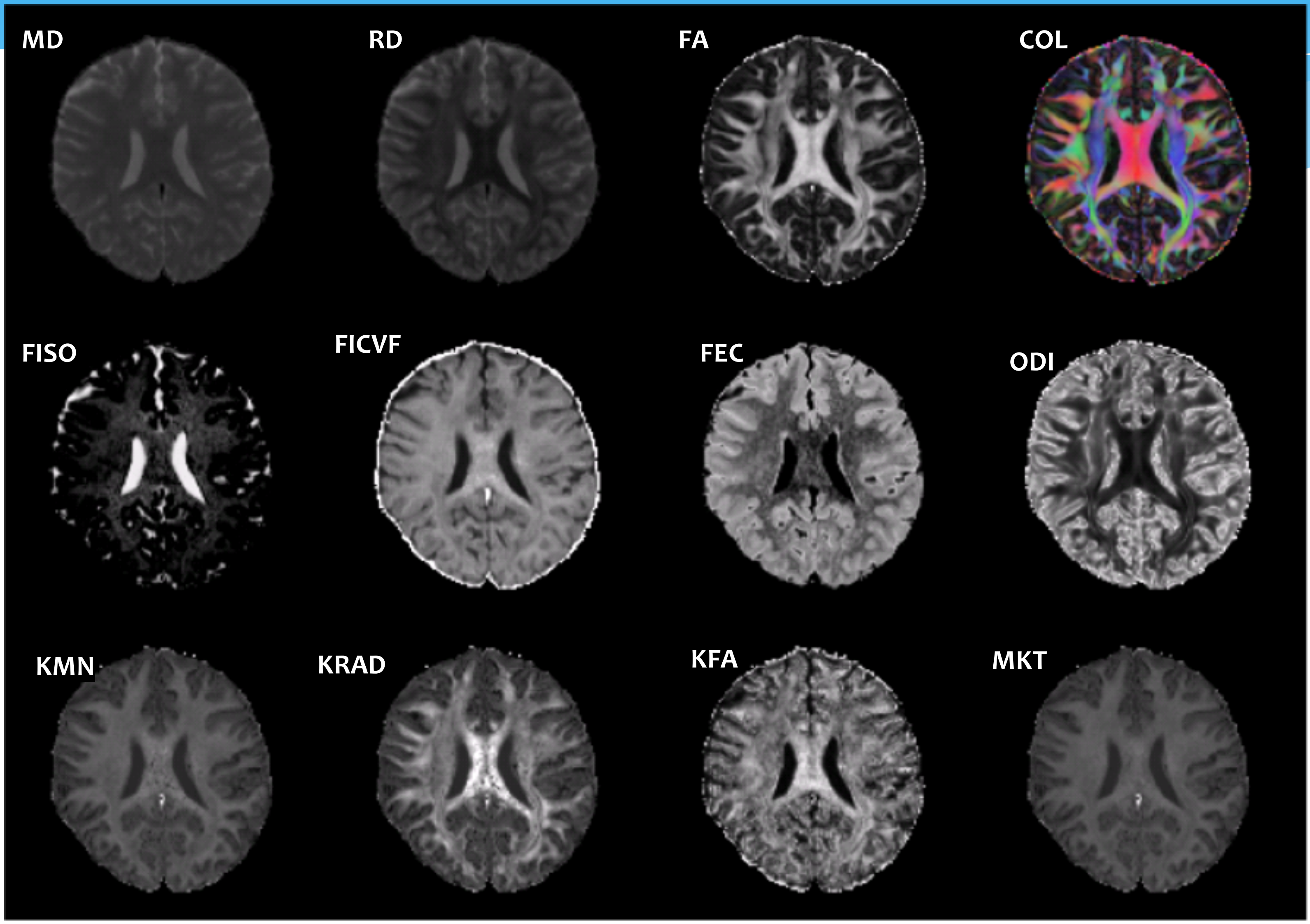
M. F. Glasser, T. S. Coalson, E. C. Robinson, C. D. Hacker, J. Harwell, E. Yacoub, K. Ugurbil, J. Andersson, C. F. Beckmann, M. Jenkinson, S. M. Smith, and D. C. Van Essen, "A multi-modal parcellation of human cerebral cortex," *Nature*, pp. 1–11, 2016.

Next Steps: Multi-Shell dMRI

DTI

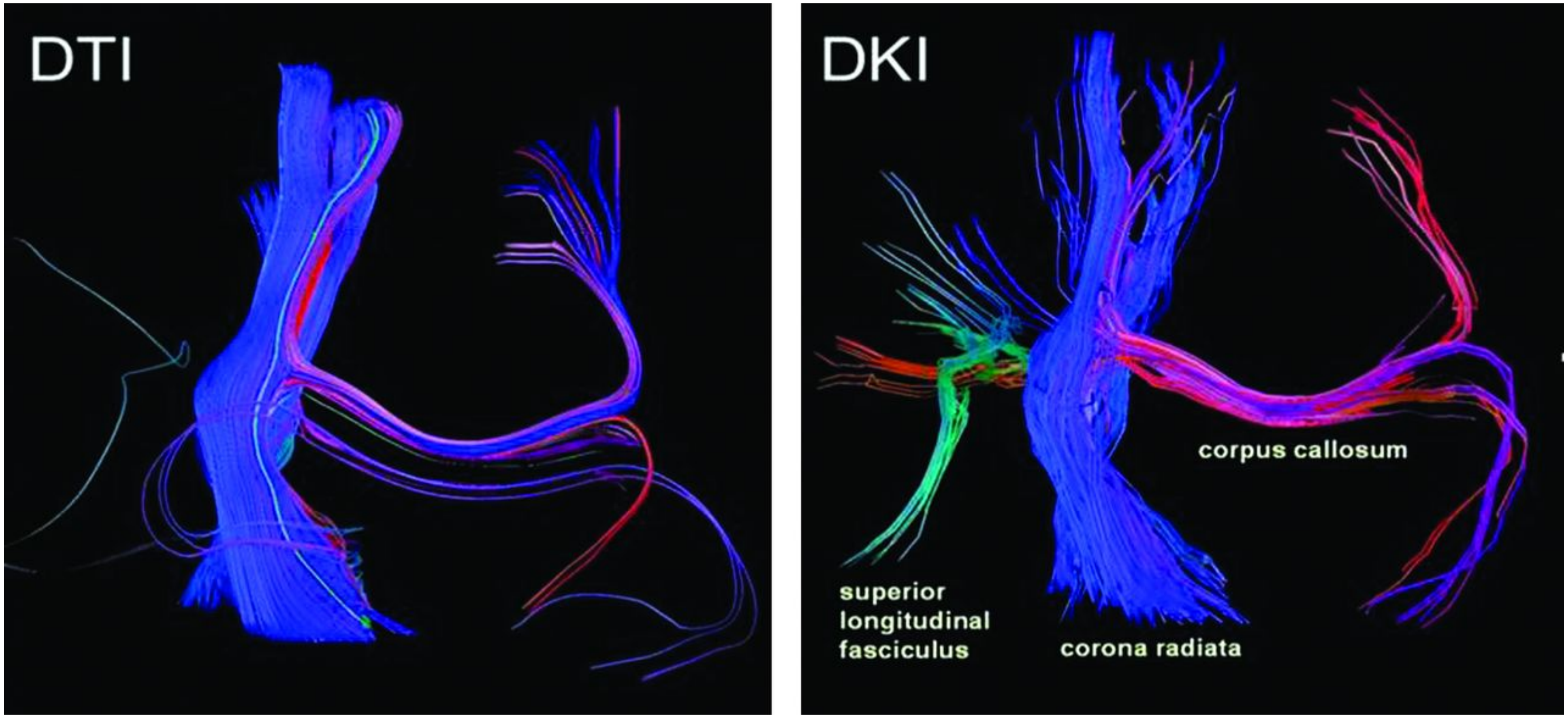
NODDI

DKI



Advantages of non-tensor models

(better handling of crossing fibers; less noise, esp important in longitudinal imaging work)



The dream

ID#	Group	Age	PFL %ile	IQ	Brain volume %ile	Network Efficiency %ile	Myelin fraction %ile	Gyrification %ile
1	Ct	10	28	110				
2	AE	14	24	84				
3	AE	10	26	76				
4	Ct	13	29	89				
5	AE	13	25	84				
6	Ct	12	28	96				

- Directly address the challenge of diagnosis
- Find evidence of neurodevelopmental abnormality in the undiagnosable
- Show the power of neuropsychological tools
- Share these data in a highly accessible manner with other researchers

Thanks

* UMN: Timothy Hendrickson, Bryon Mueller, Kelvin Lim, Dan Keefe, Judith K. Eckerle, Birgit A. Fink, Marisa Whitley, Christopher J. Boys, Susanne Lee
* CIFASD investigators: Elizabeth Sowell, Sarah Mattson, Claire Coles, Julie Kable, Ken Jones, Kristina Uban, Eric Kan, Helen Yezerets, Bill Barnett
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