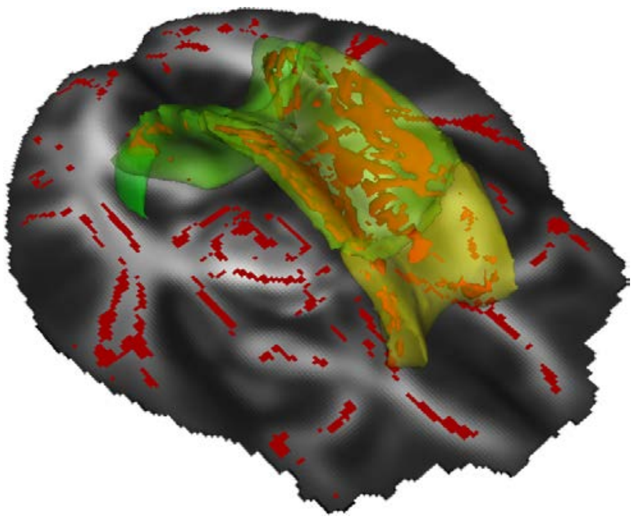
Age-Related Differences in Adolescent Brain Microstructure: Initial Findings from National Consortium on Alcohol & Neurodevelopment in Adolescence



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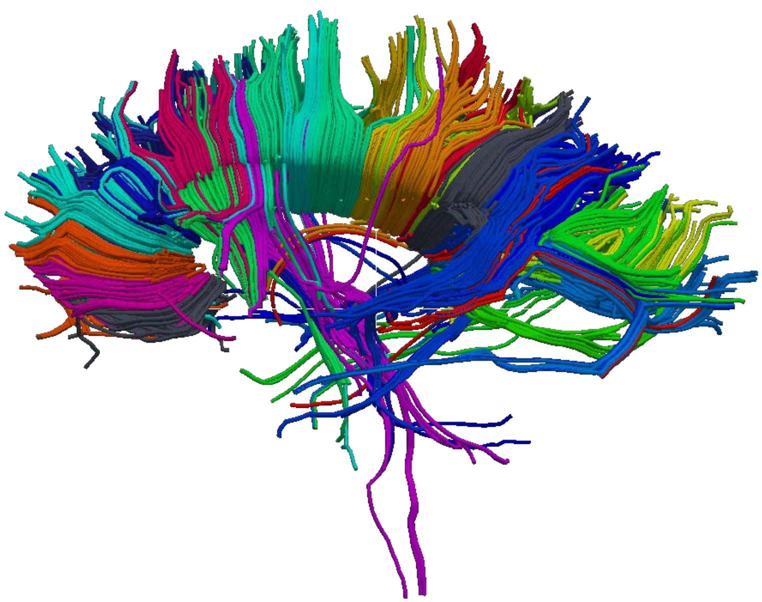
Financial Interest Disclosure

Salary and Research Support
of
Kilian M Pohl, Ph.D.

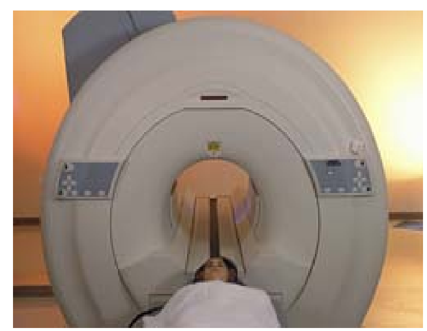
Goal

Investigate Aging of the White Matter Microstructure in Adolescents

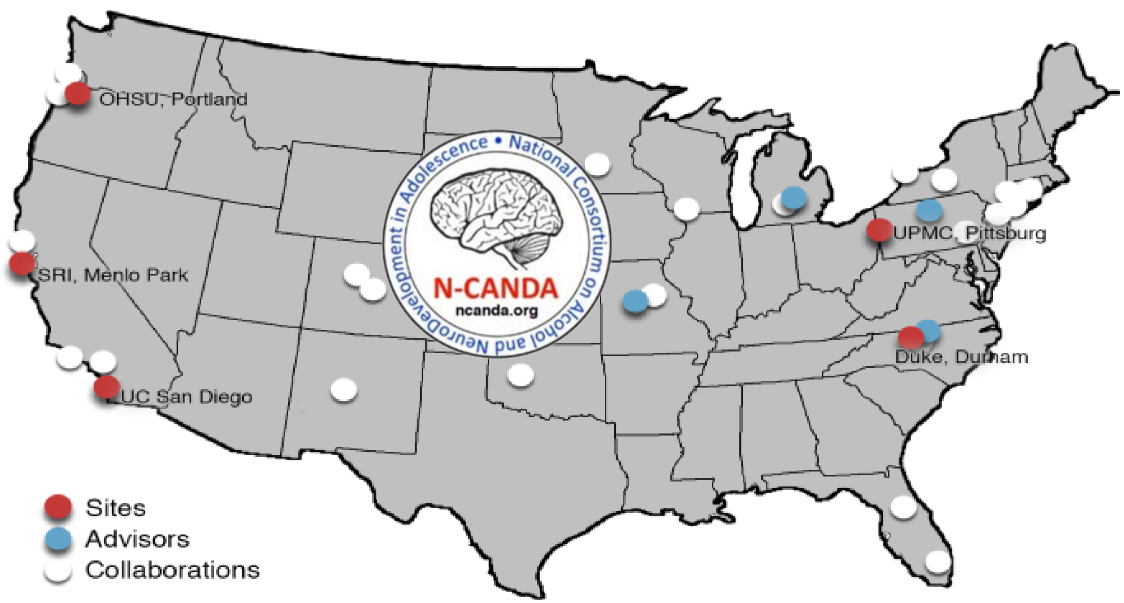


Overview

- **NCANDA Data Acquisition**
- **DWI Specific Processing**
- **Current Findings (N=671)**



Data Acquisition



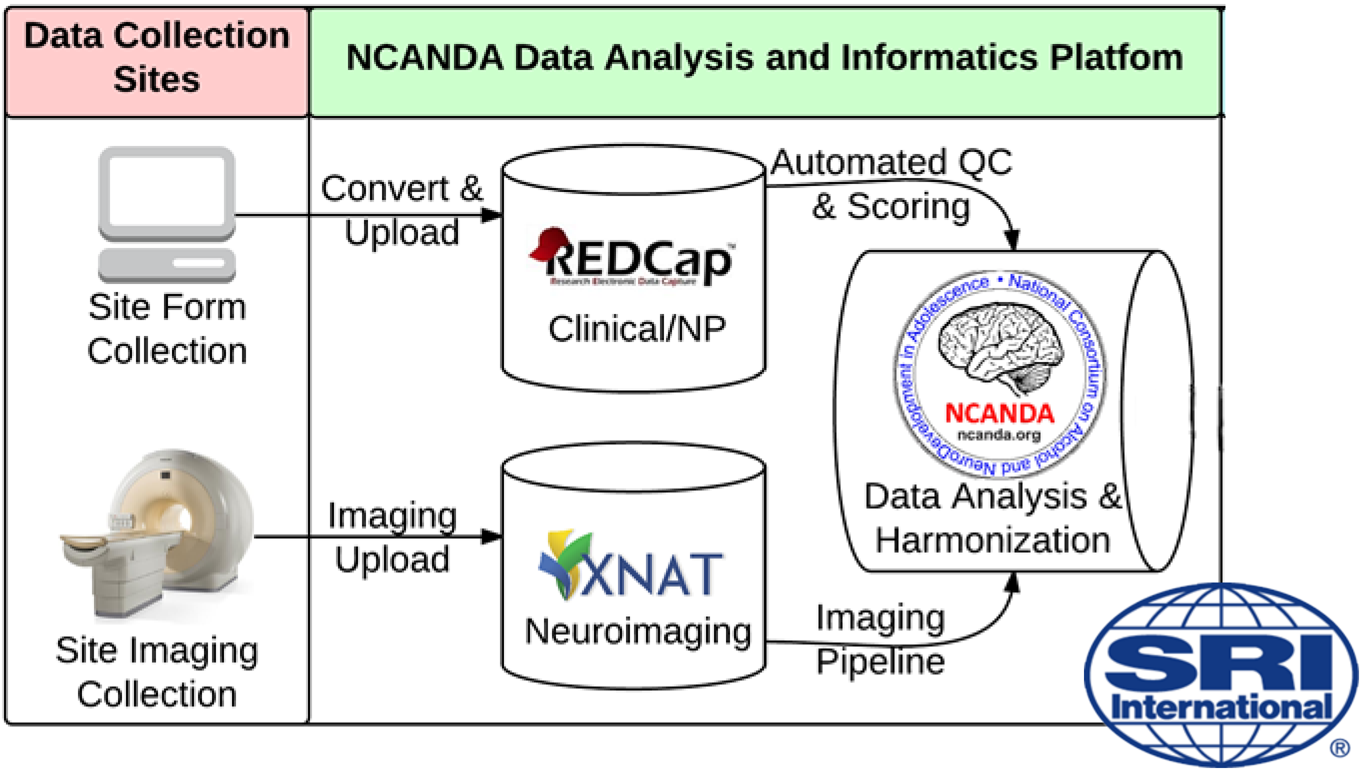
Monitoring brain development of 831 adolescence over a 5 year period across 5 sites

NCANDA Collection Sites

Sites collect:

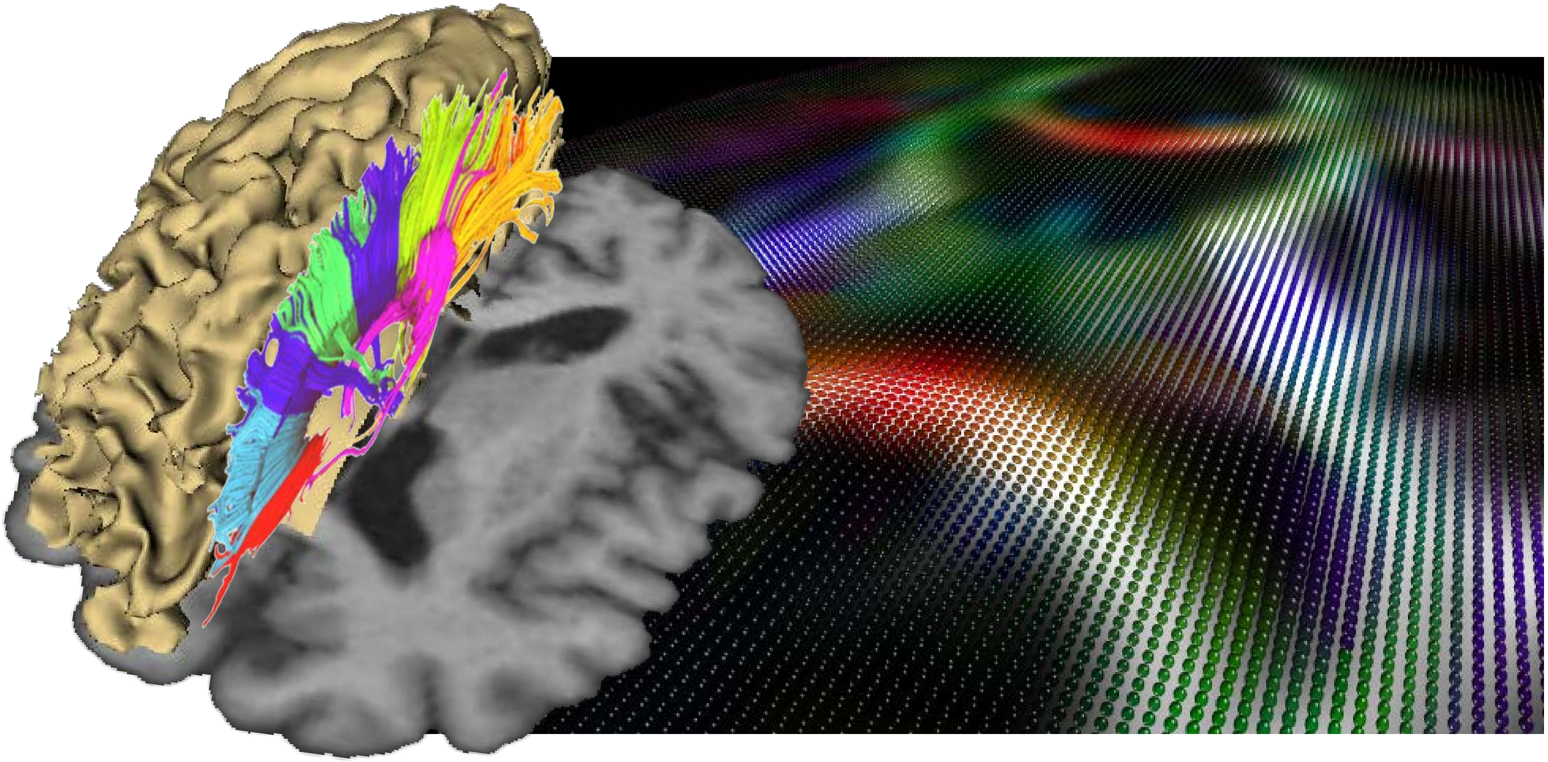
- Demographic Information
- Clinical Data
- Neuropsychological Test Scores
- MRI
  - Structural
  - Diffusion
  - Functional

NCANDA – Informatics Platform



Robustly and coherently fusing data across time, sites, and modalities

Diffusion Weighted Imaging

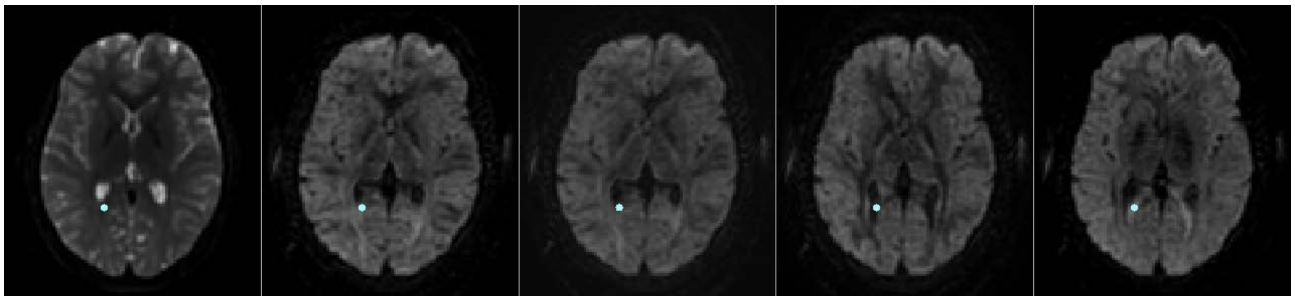


White matter contains axons that group together to bundles connecting gray matter regions

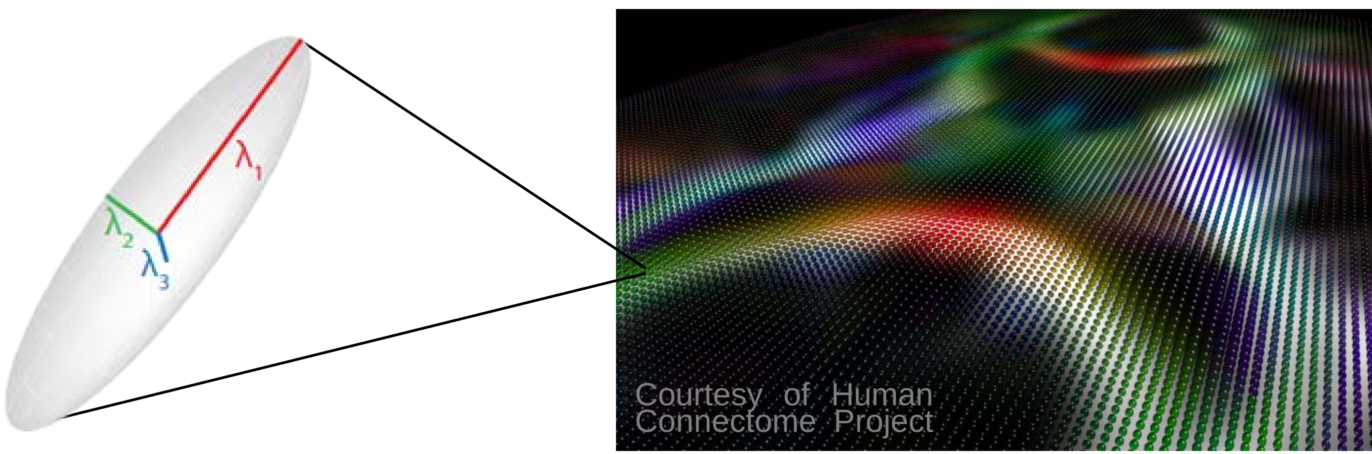
Fibers restrict diffusion of water molecules

Diffusion Weighted Imaging

Measure the rate of diffusion within white matter



by varying gradient direction of scanner’s magnetic field

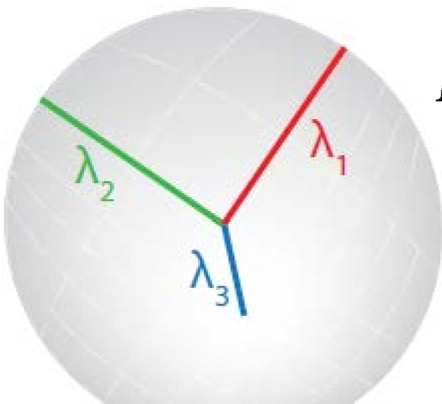


Ellipsoid represents diffusion direction at location

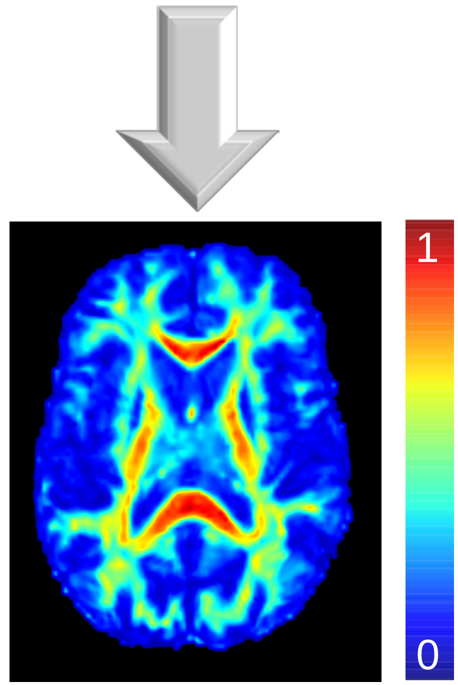
Diffusion Weighted Imaging

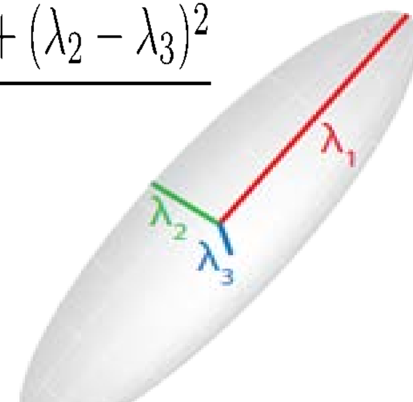
Summarize diffusion via Fractional Anisotropy (FA)

$$FA = \frac{1}{2}\frac{\sqrt{(\lambda_1-\lambda_2)^2+(\lambda_1-\lambda_3)^2+(\lambda_2-\lambda_3)^2}}{\lambda_1^2+\lambda_2^2+\lambda_3^2}$$



FA=0





FA=0.8

Acquisition

Acquire DWI of 831 subjects (12-22 years) on Siemens TIM TRIO and GE Discovery MR750:

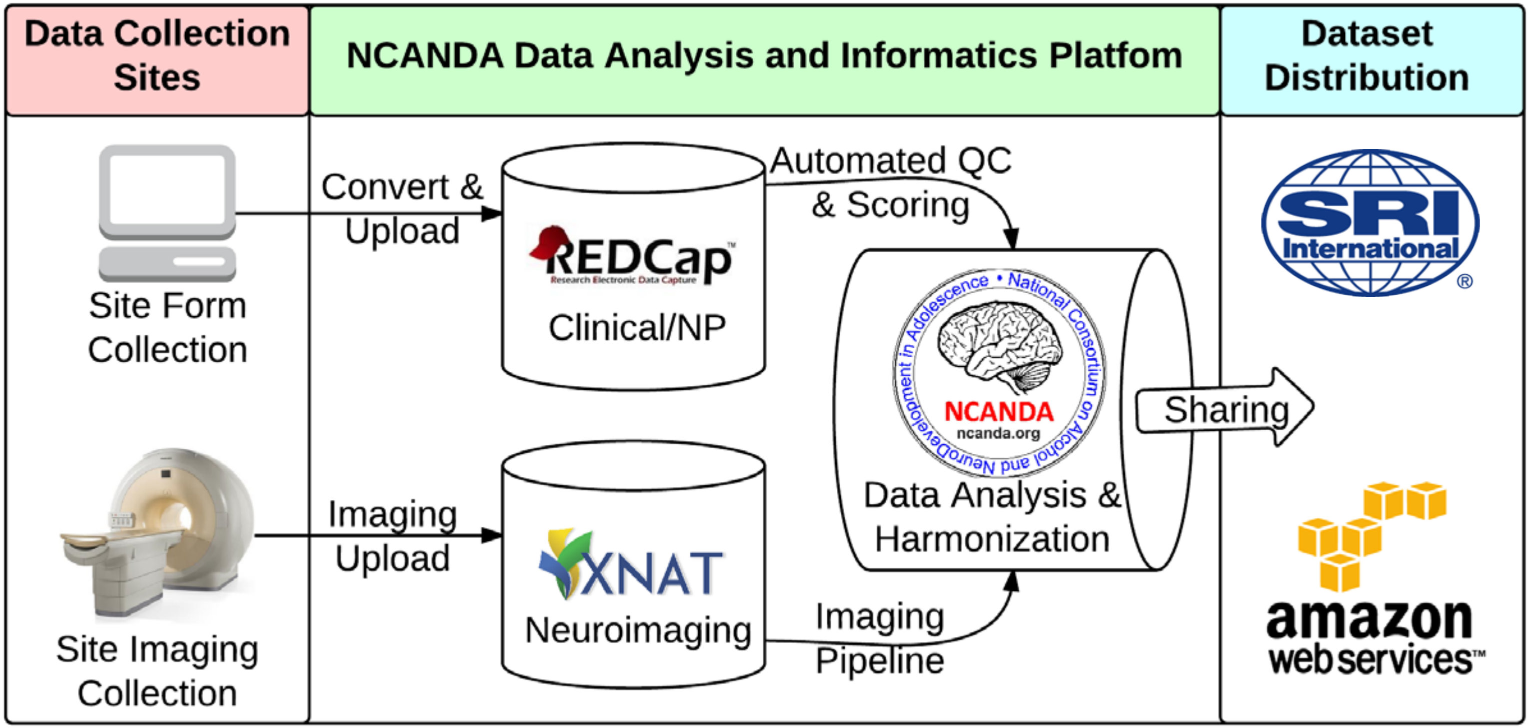
- **Reverse:**
  2D Axial Spin Echo Echo-Planar - b=0/500, 6 directions
  (TR=10,000, TE=85, Thick=2.5, Loc=65, FOV=240, xy_matrix=96x96, Phase = A/P, Partial k-space (48/64), Acceleration=2, Resolution=2.5x2.5x2.5 mm, Fat Sat=on)

  To correct for B0 field inhomogeneity spatial distortion

- **Forward:**
  2D Axial Spin Echo Echo-Planar - b=0/1000, 60 directions
  (TR=10,000, TE=85, Thick=2.5, Loc=65, FOV=240, xy_matrix=96x96, Phase = A/P, Partial k-space (48/64), Acceleration=2, Resolution=2.5x2.5x2.5 mm, Fat Sat=on)

  To compute FA Maps

Data Distribution and Archival



created by N. Nichols

Archive and share data via local it infrastructure and the Cloud

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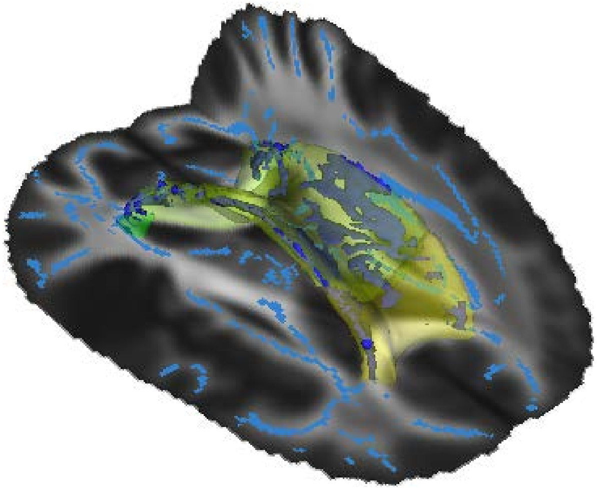
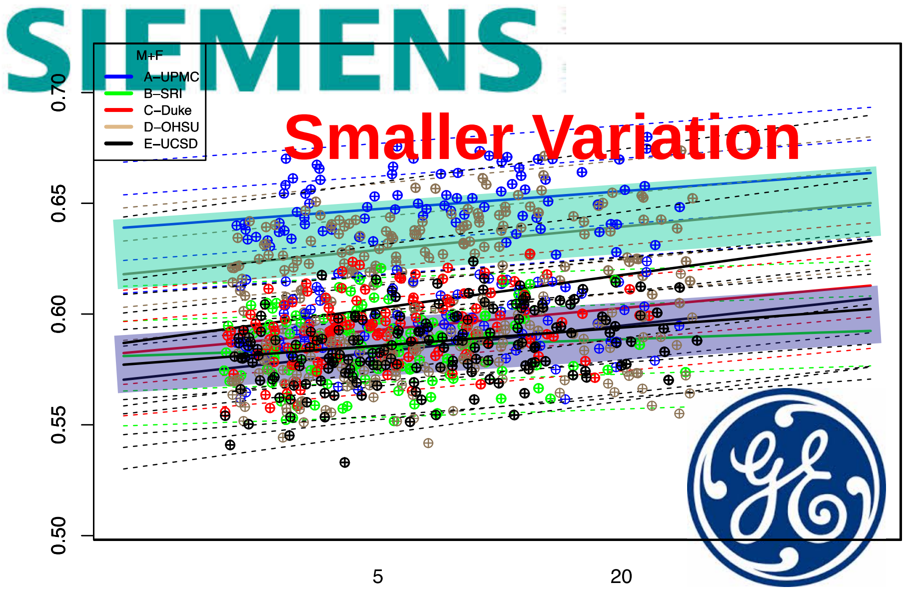


Correct for Manufacture Differences

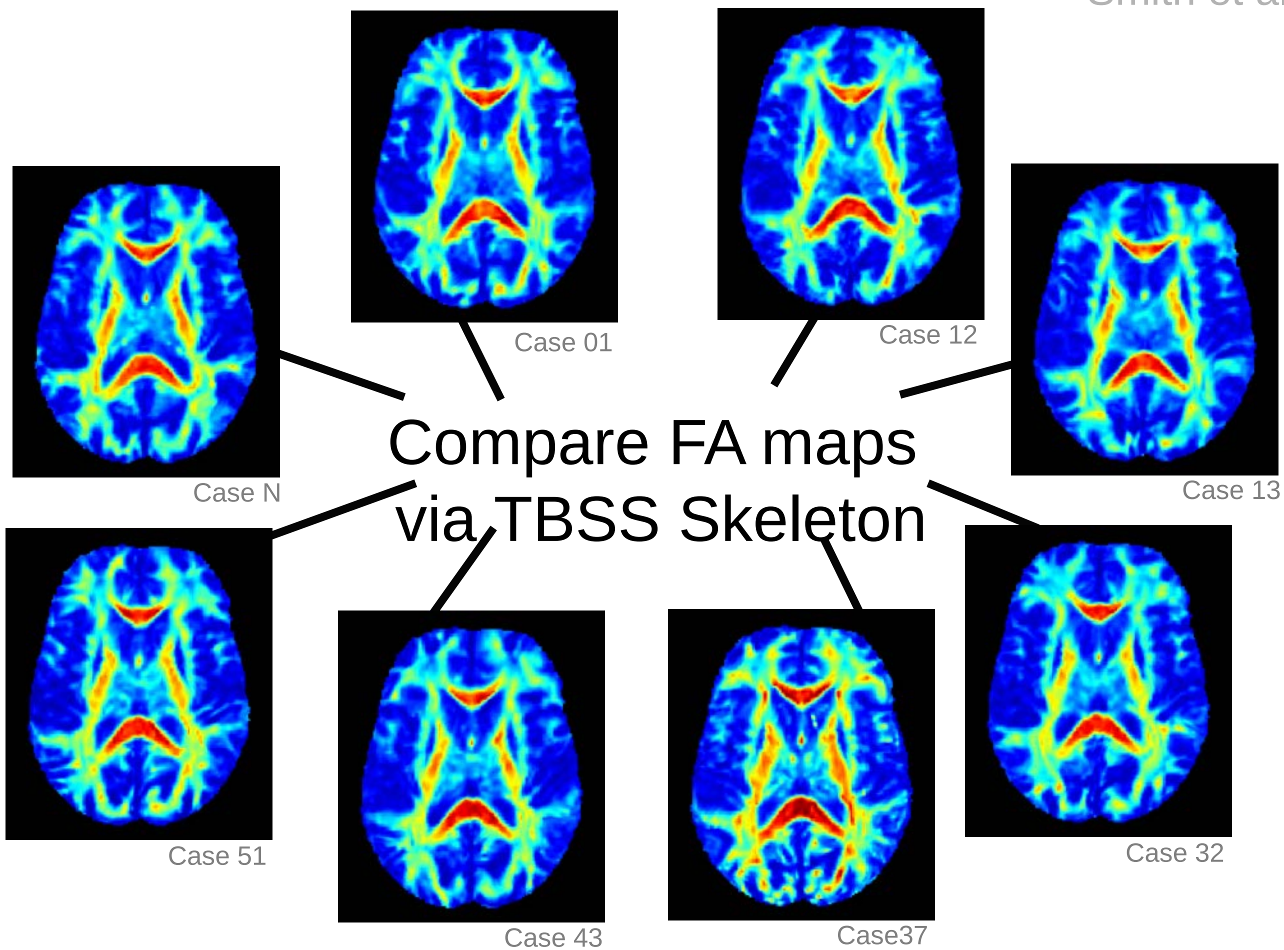


Normalize FA accounting for scanner differences:

- scan the same 3 human phantoms at all 5 sites
- compute ratio of mean FA value across scanner type
- apply ratio to FA maps

Tract-Based Spatial Statistics (TBSS)*

* Smith et al. 2006



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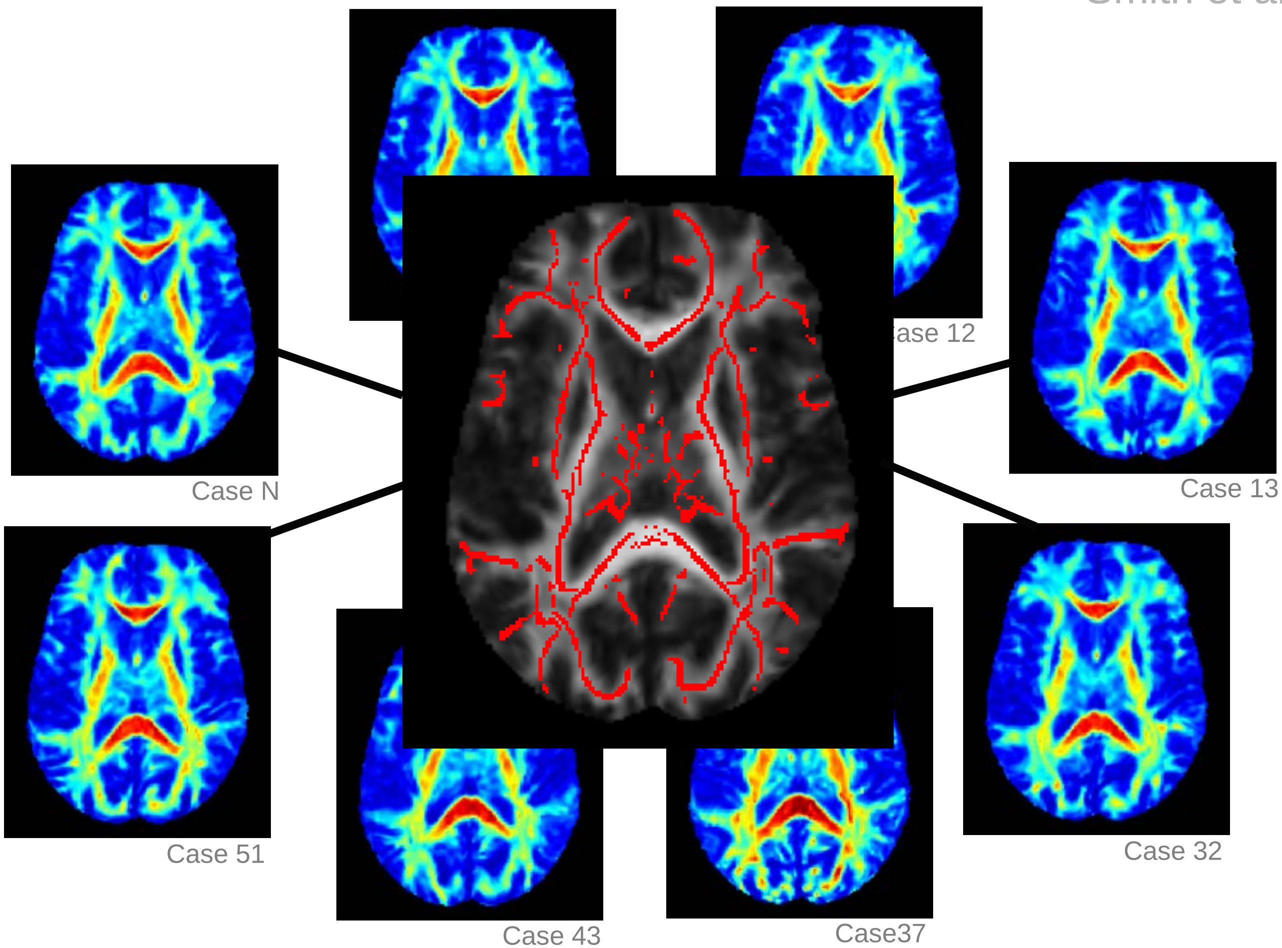
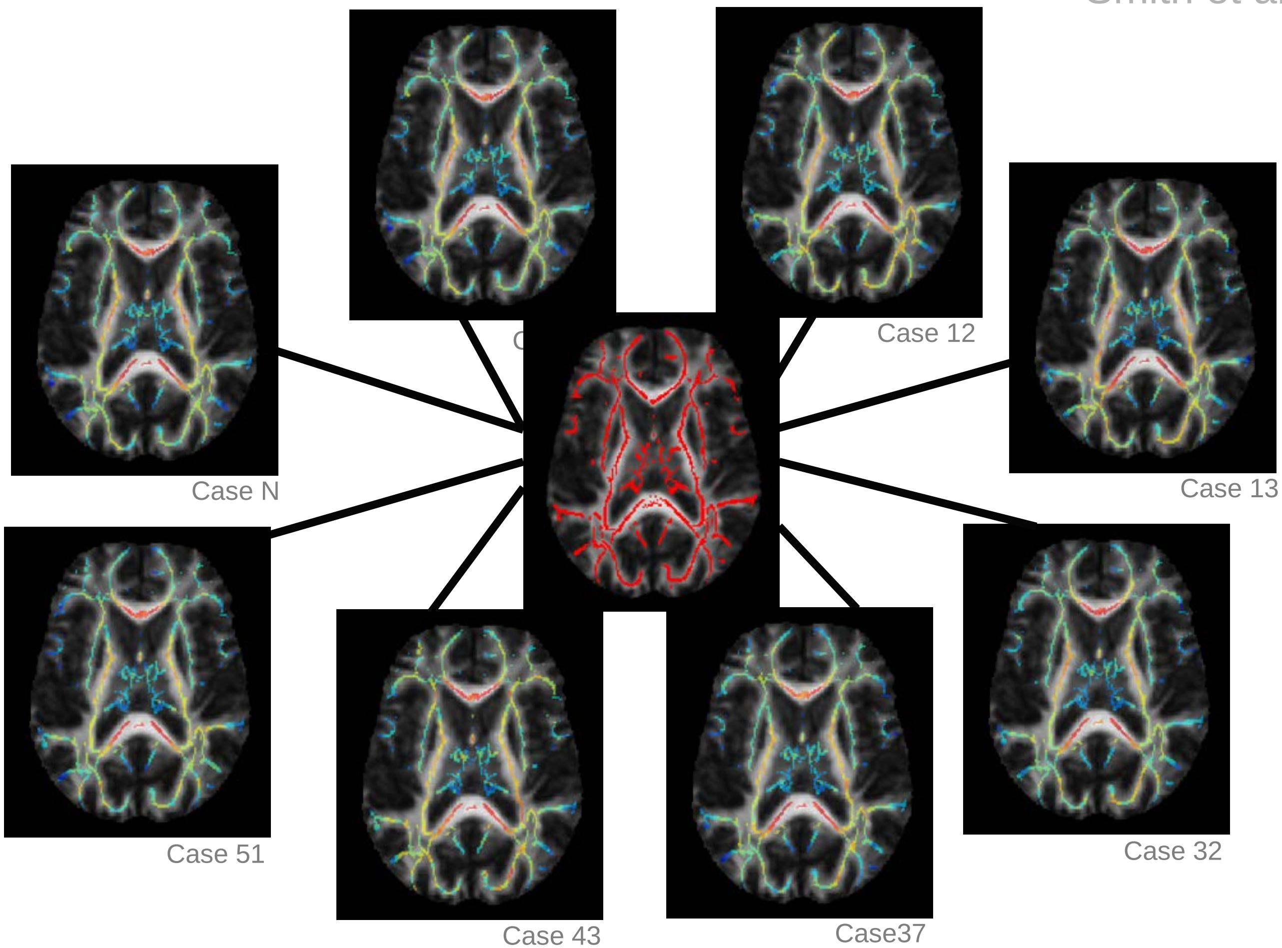


Compute Mean Skeleton

Tract-Based Spatial Statistics (TBSS)*

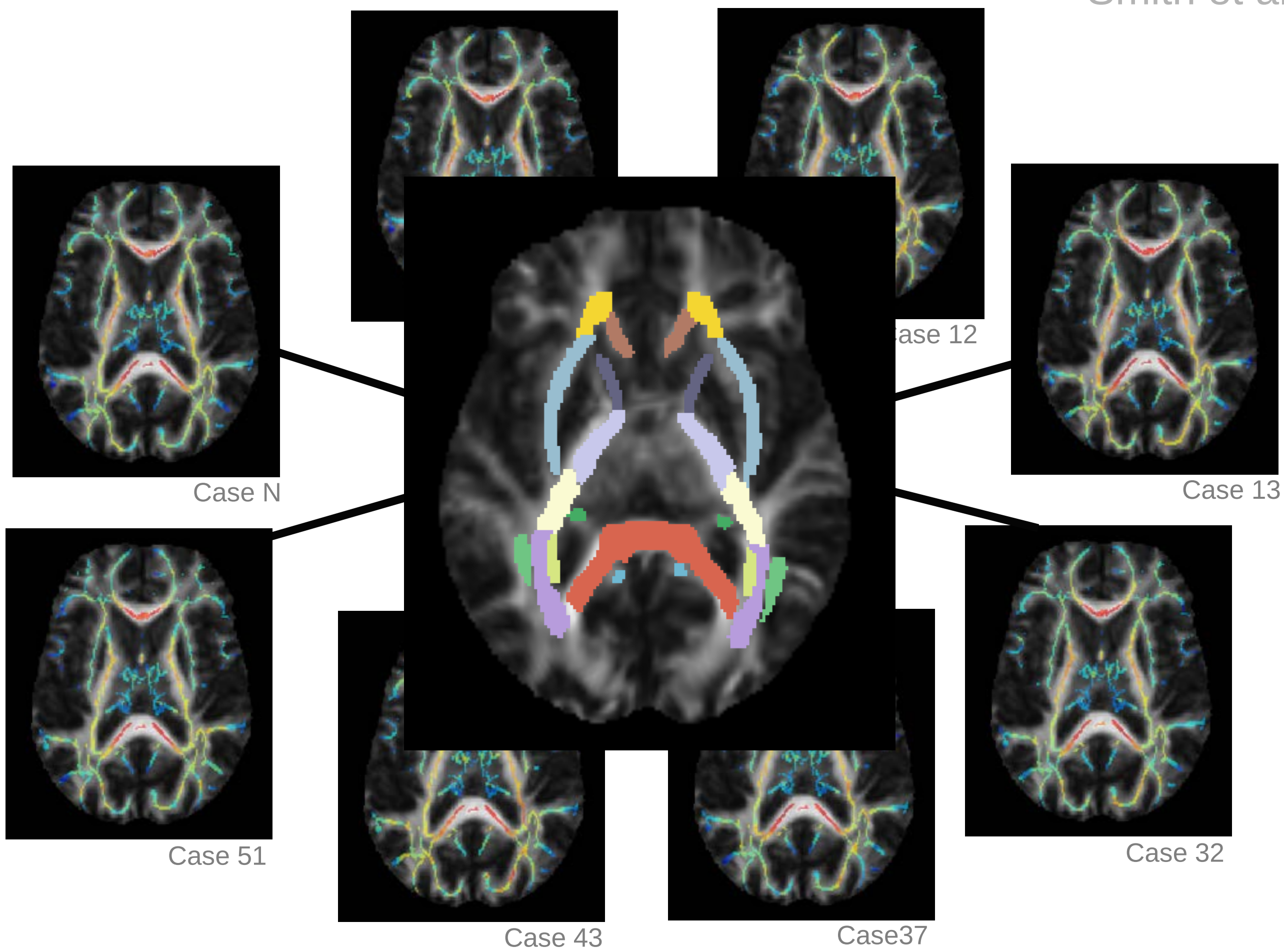
* Smith et al. 2006



Compute Subject Specific Skeleton

Compute Mean Skeleton FA for ROI

* Smith et al. 2006



ROIs are defined according to JHU DTI Atlas (Mori et al. 2005)

General Additive Model (GAM)

For each ROI of the atlas regress a thin plate spline with 3 control points to the mean skeleton FA values of that region ($meanFA_{ROI}$) of the 671 subjects with the subject's age being the predictor value and factors race, sex, and suptent supratentorium volume (svol):

GAM[$meanFA_{ROI}$ ~ s(age, bs = "ts", k = 3) + race + sex + svol]

Picture

P –value computations

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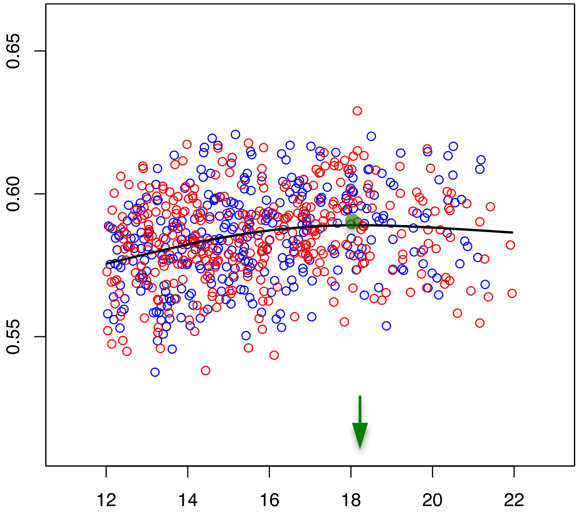
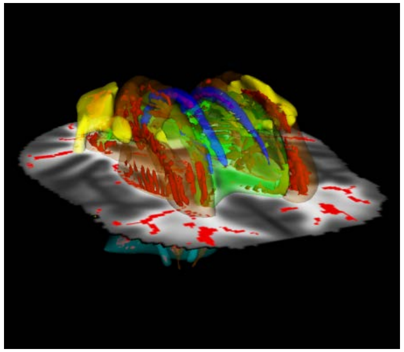
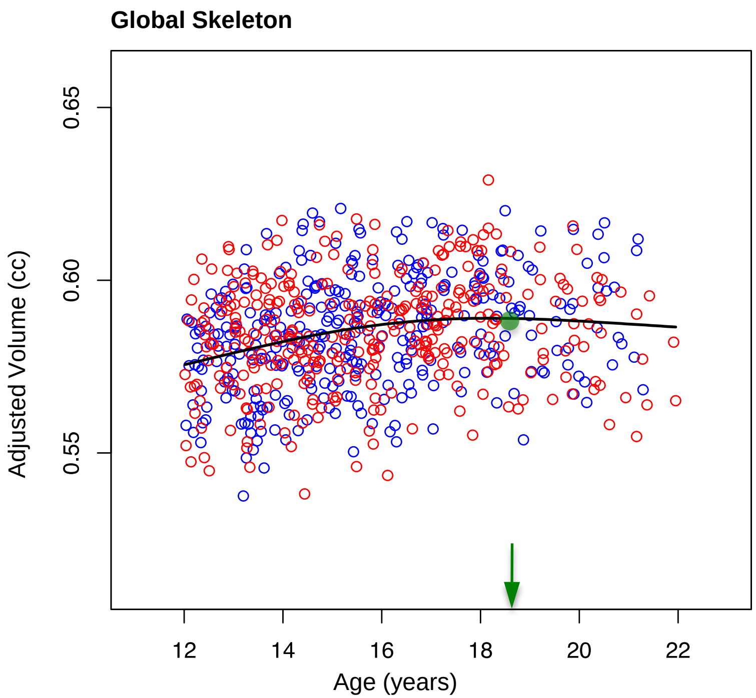
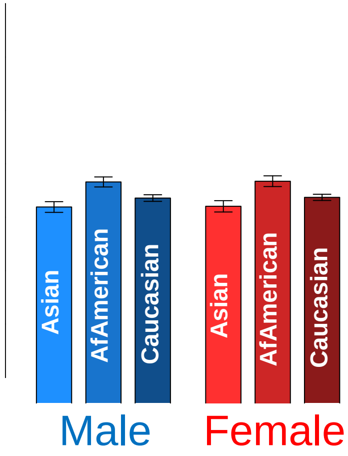


Global Skeleton



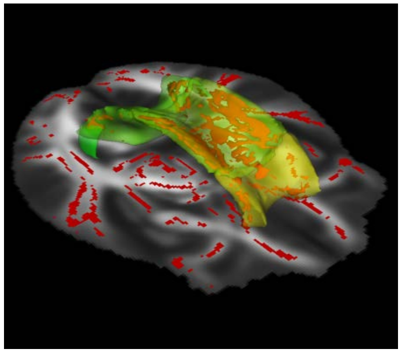


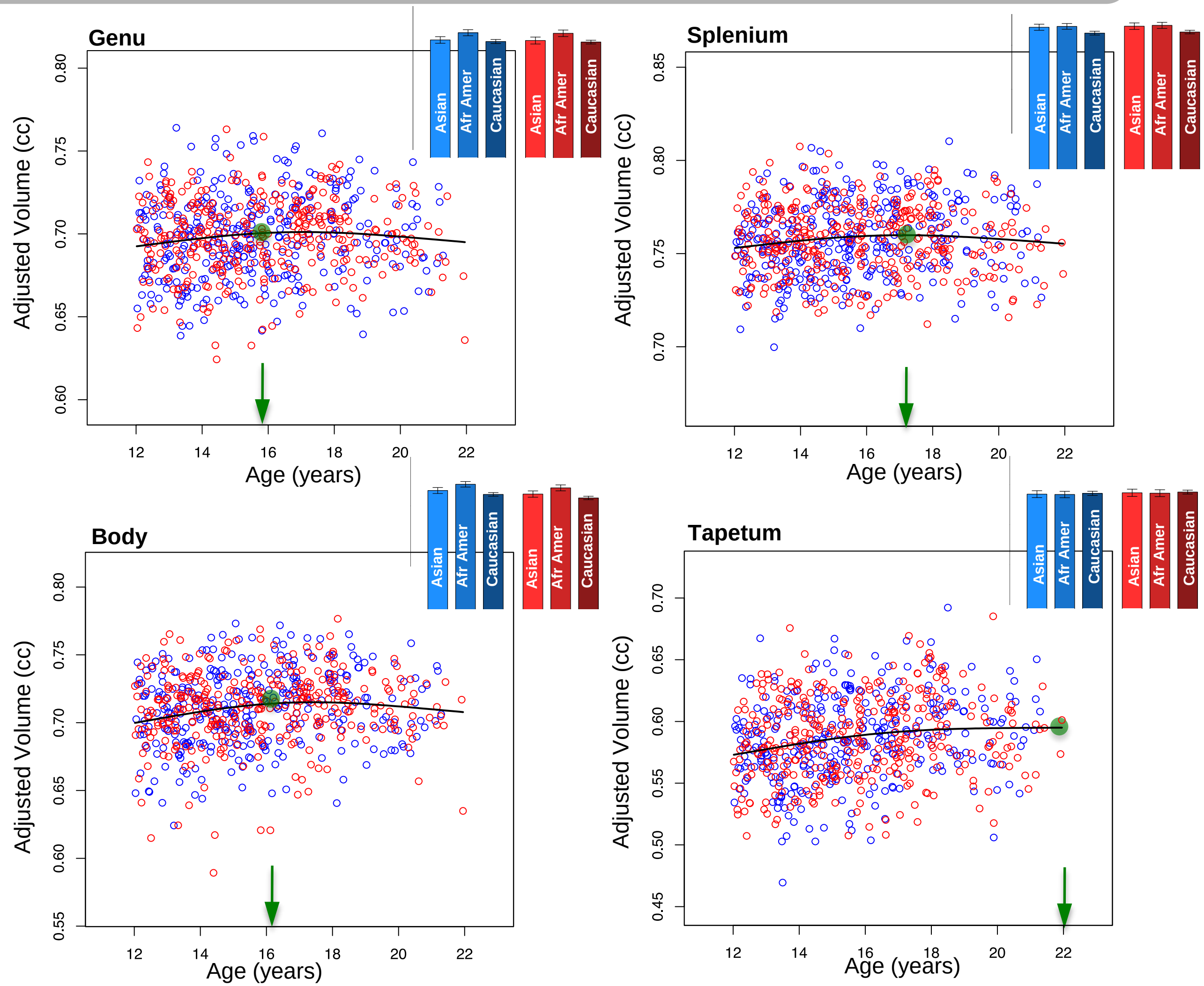


- Fiber organization peaks at 18.2 years
- African-Americans have higher and Asians have lower mean skeleton FA compared to Caucasians

P value of findin

Commissural Fibers





Development of white matter fiber systems is ROI specific

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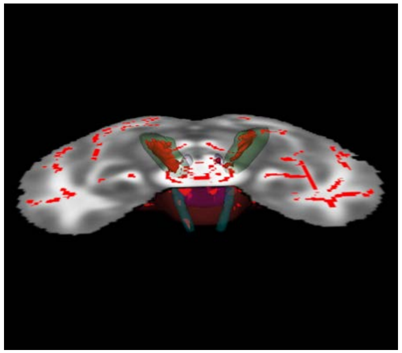
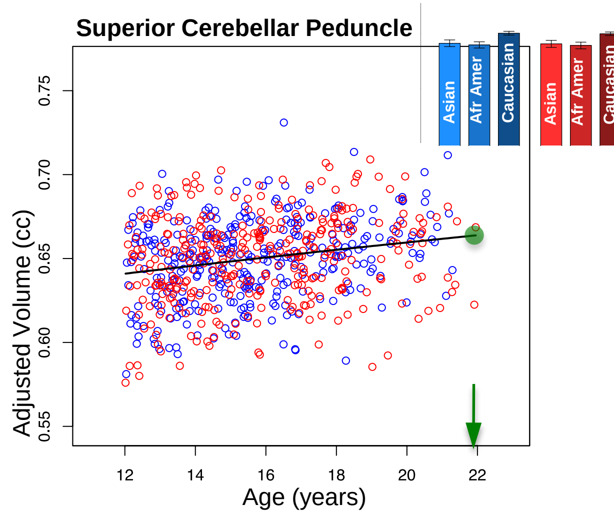
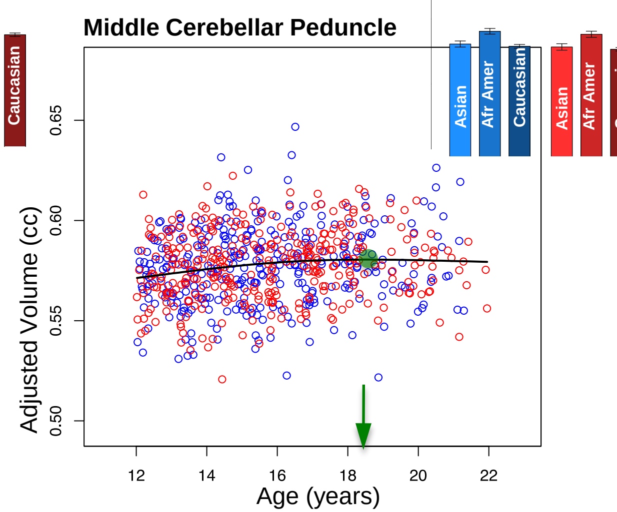
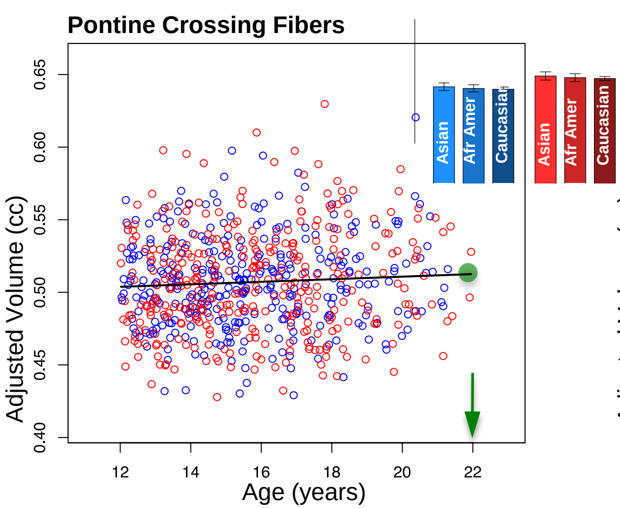
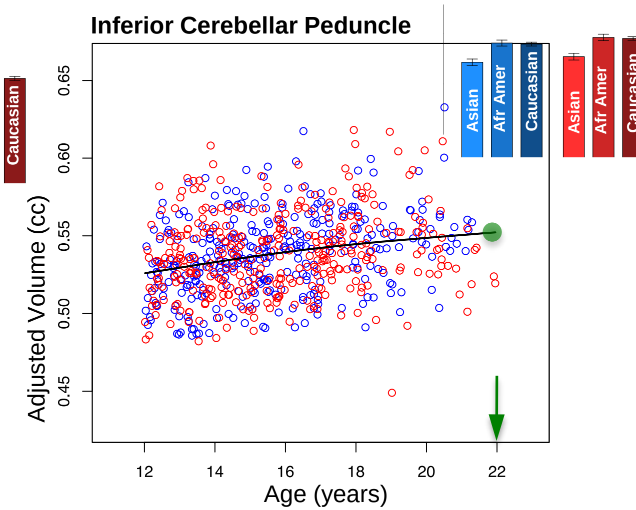
PROJECTION FIBERS: Brainstem Tracts

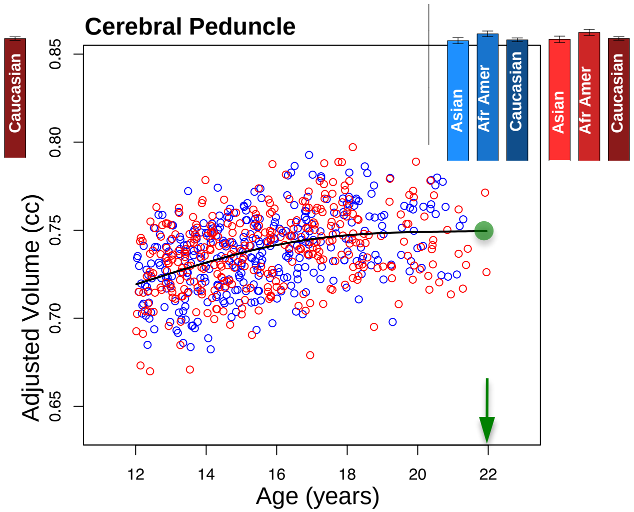












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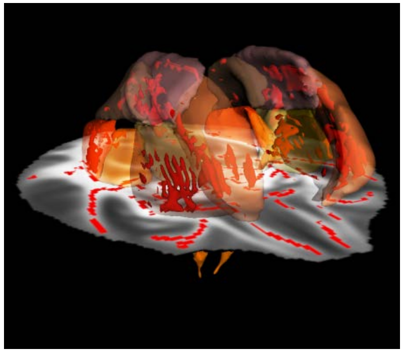
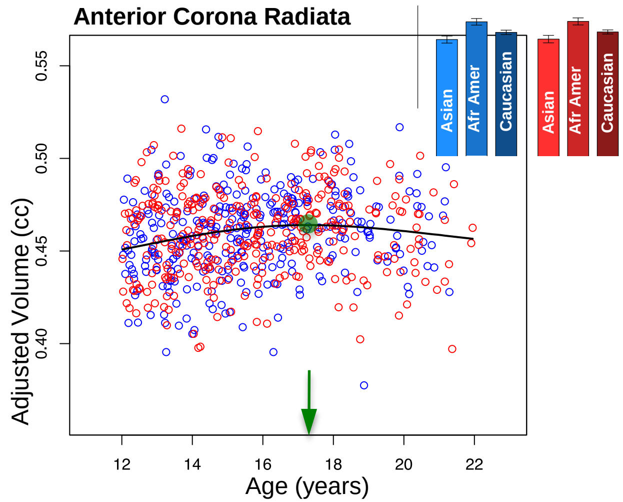
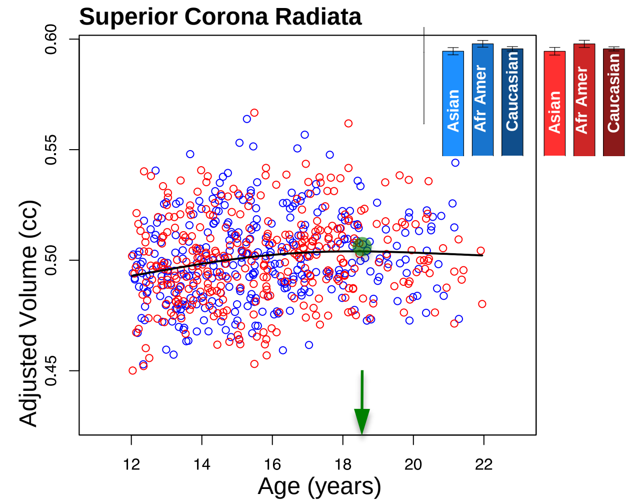
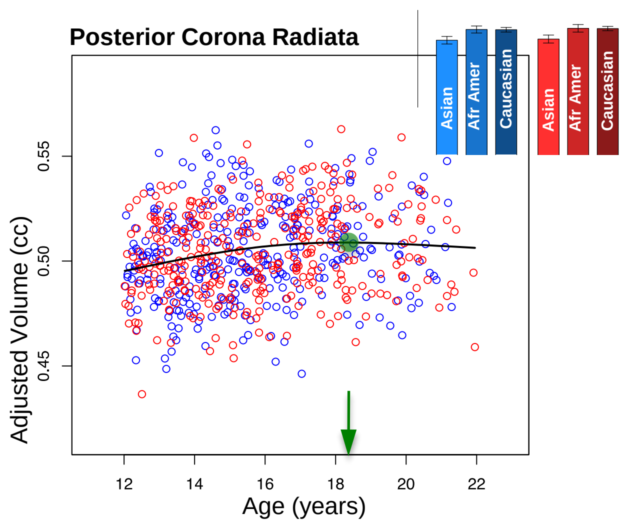
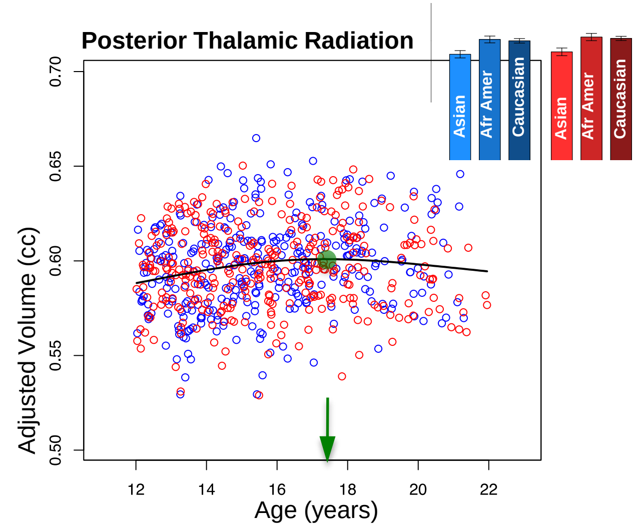
PROJECTION FIBERS: Corticospinal Tracts (Part 1)



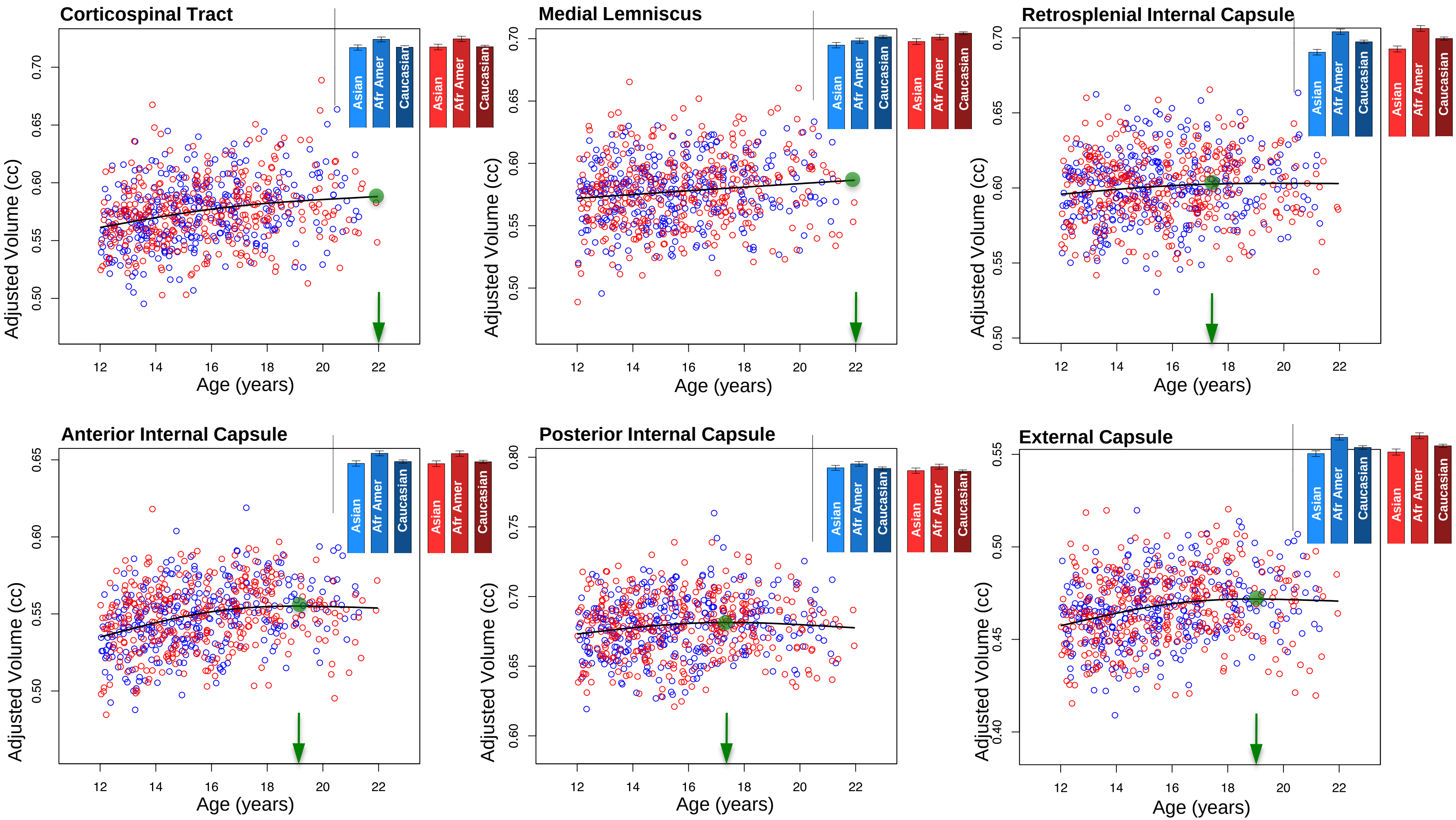








PROJECTION FIBERS: Corticospinal Tracts (Part 2)



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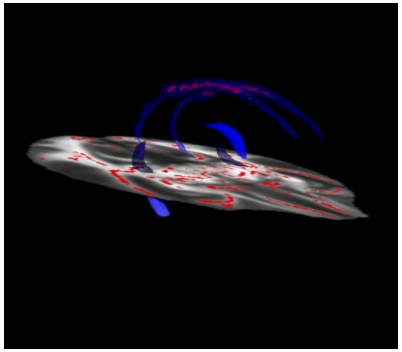
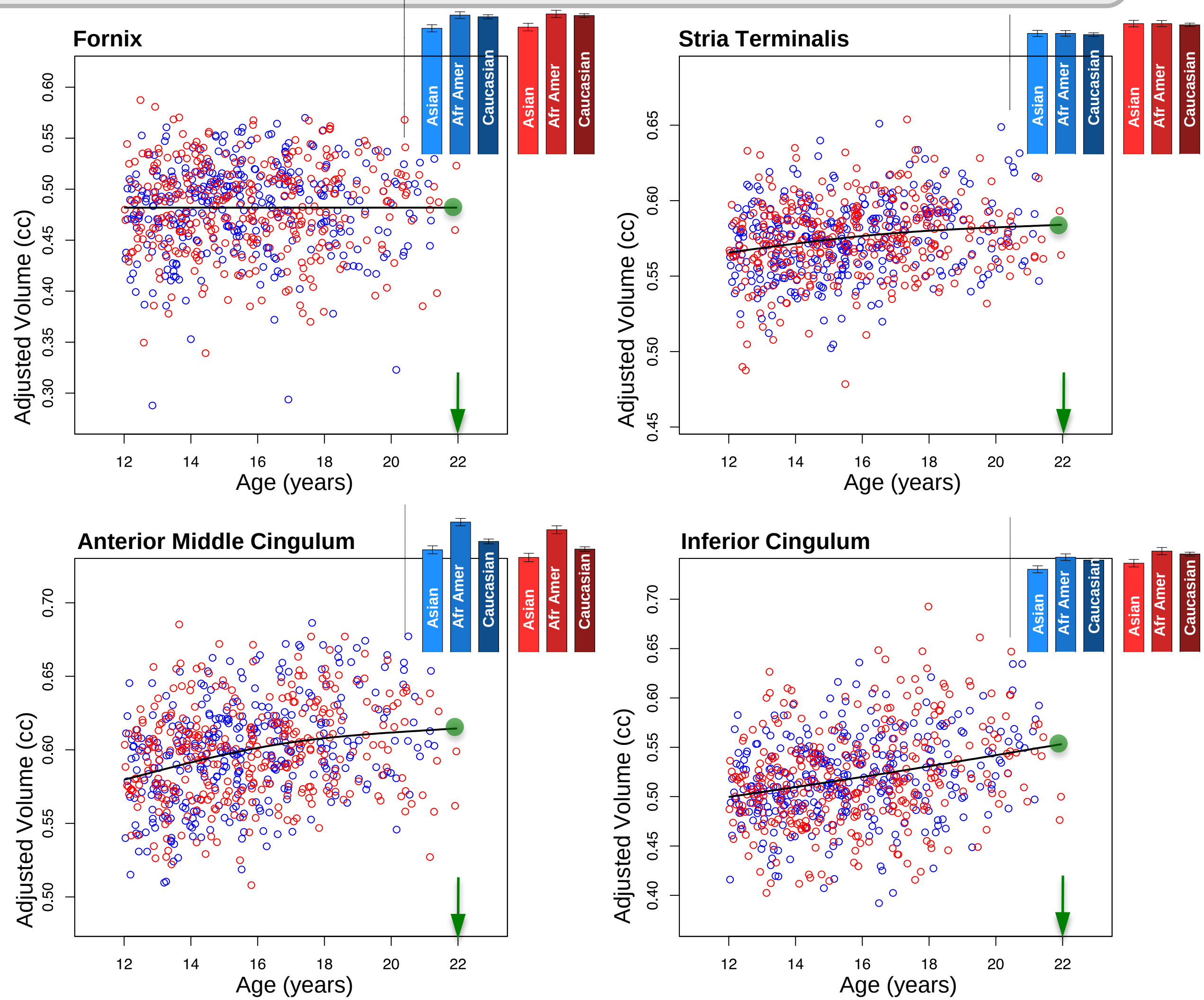
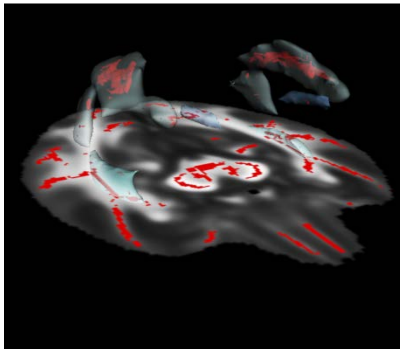
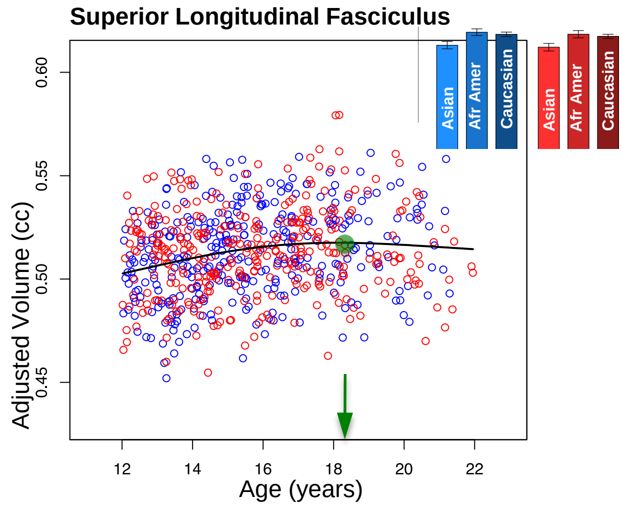
ASSOCIATION FIBERS: Limbic Tracts

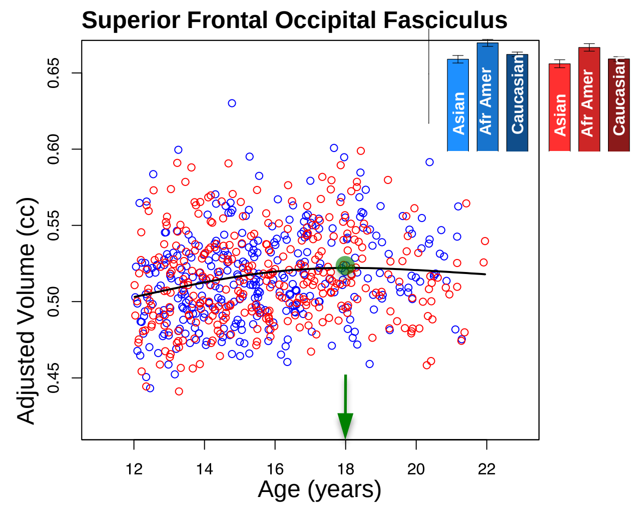


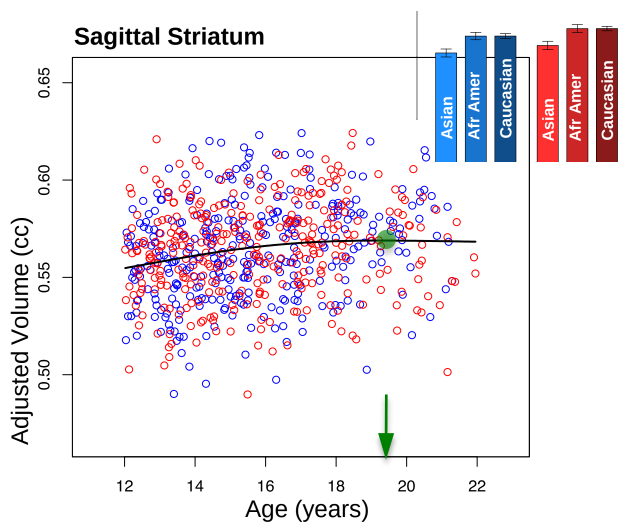


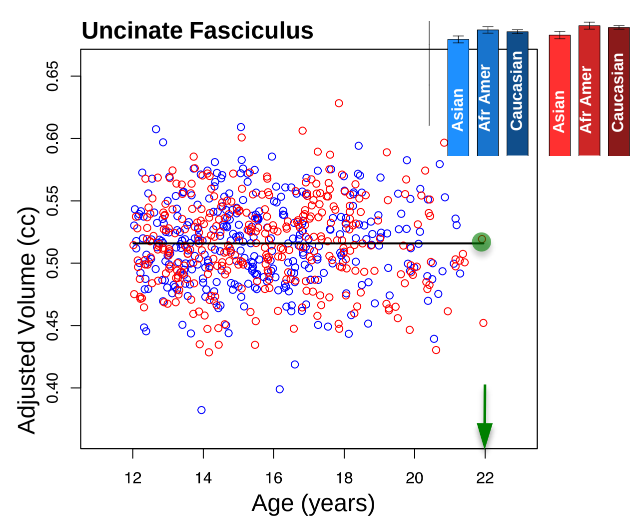
ASSOCIATION FIBERS: Fasciculi











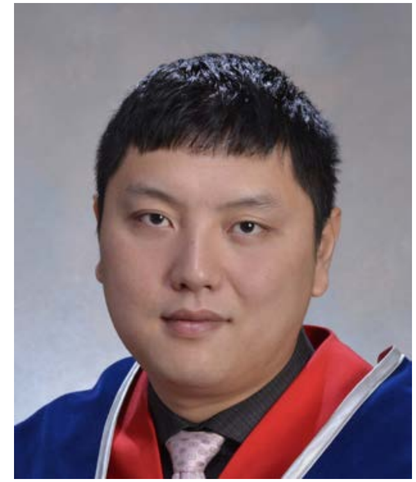
Conclusion

- Heterochronicity characterizes developmental patterns of white matter fiber systems in adolescence, e.g., commissural and selective projection systems reach peak fiber organization (assumed from FA) earlier than limbic association fibers.
- These patterns of age-related differences need confirmation with longitudinal examination.
- The continuing development of fiber bundles estimated from this cross-sectional analysis may render them vulnerable to environmental insult, including initiation of hazardous drinking.

Thank You

Dongjin Kwon, Ph.D.

Nolan Nichols, Ph.D.



Yong Zheng, Ph.D.

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