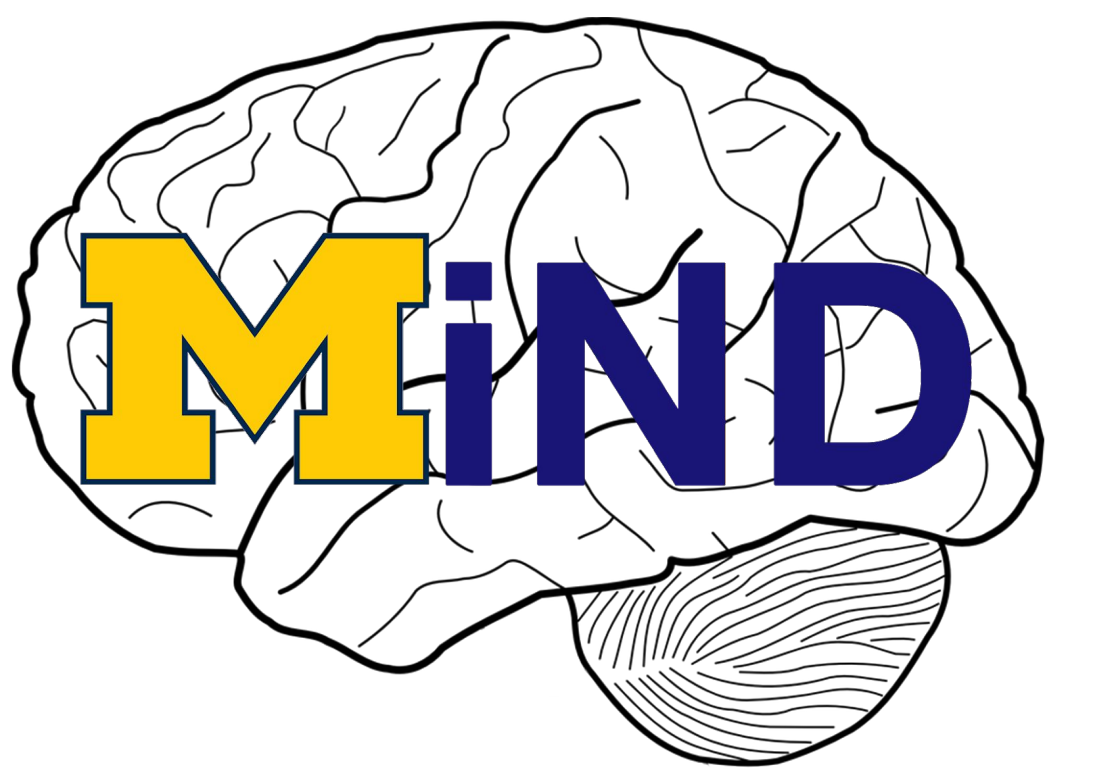




# Age-related differences in white matter: Comparing fixel-based and tensor-based analyses



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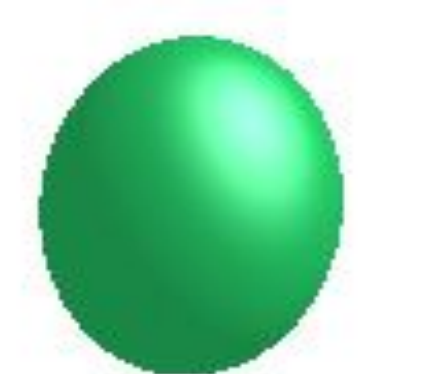
## Background

- Age-related changes in white matter (WM) have been hypothesized to play a role in some behavioral declines
- Most prior studies of WM and aging have used diffusion tensor imaging (DTI) and measured fractional anisotropy (FA)
- FA is influenced by multiple biological factors and DTI aging studies have produced varied results
- Recent results also suggest that FA is strongly influenced by multifiber complexity (CX: the relative size of primary vs. non-primary fibers in a voxel)
- Fixel-Based analysis (FBA) makes it possible to distinguish microstructural (e.g., fiber density, fiber cross-section) and macrostructural factors (e.g., crossing fibers) that underlie DTI results

## Aims

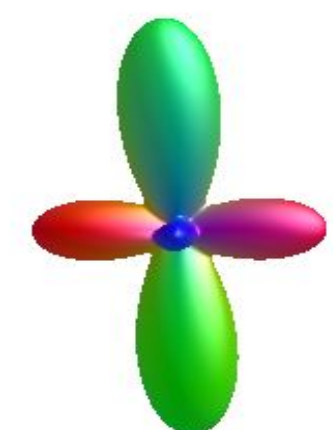
- Investigate relationship between FA and CX in a group of younger and older adults
- Explore effect of fiber organization, fiber density, and fiber cross-section on age group differences in FA using CX and FBA

## Tensor, Complexity and Fixels



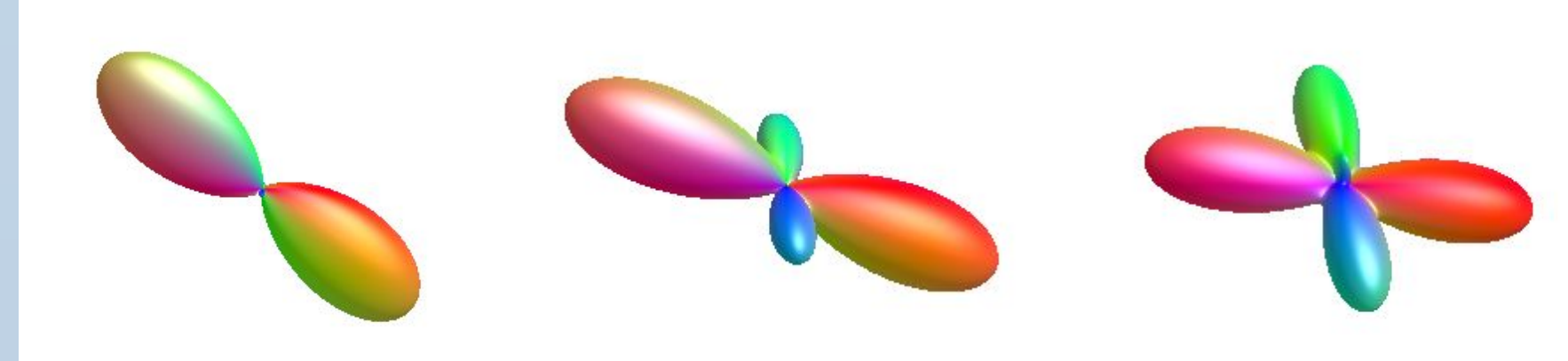
### Tensor

- Models diffusion as a three-dimensional zero-mean Gaussian distribution
- Cannot model crossing fibers
- Sensitive to fiber cohesion, diameter and packing density, as well as extent of myelination



### Fixel

- Spherical harmonic representation of diffusion that can more readily represent complex multi-fiber geometry
- Utilizes constrained spherical deconvolution to estimate fiber orientation distribution functions within each voxel



Increasing Complexity

## Methods

Participants - Healthy and free of significant cognitive impairment

- n = 25 younger adults (mean age 23.32)
- n = 45 older adults (mean age 70.69)

Imaging Acquisition

- 3T MRI
- 32 directions, b = 1000 s/mm<sup>2</sup>

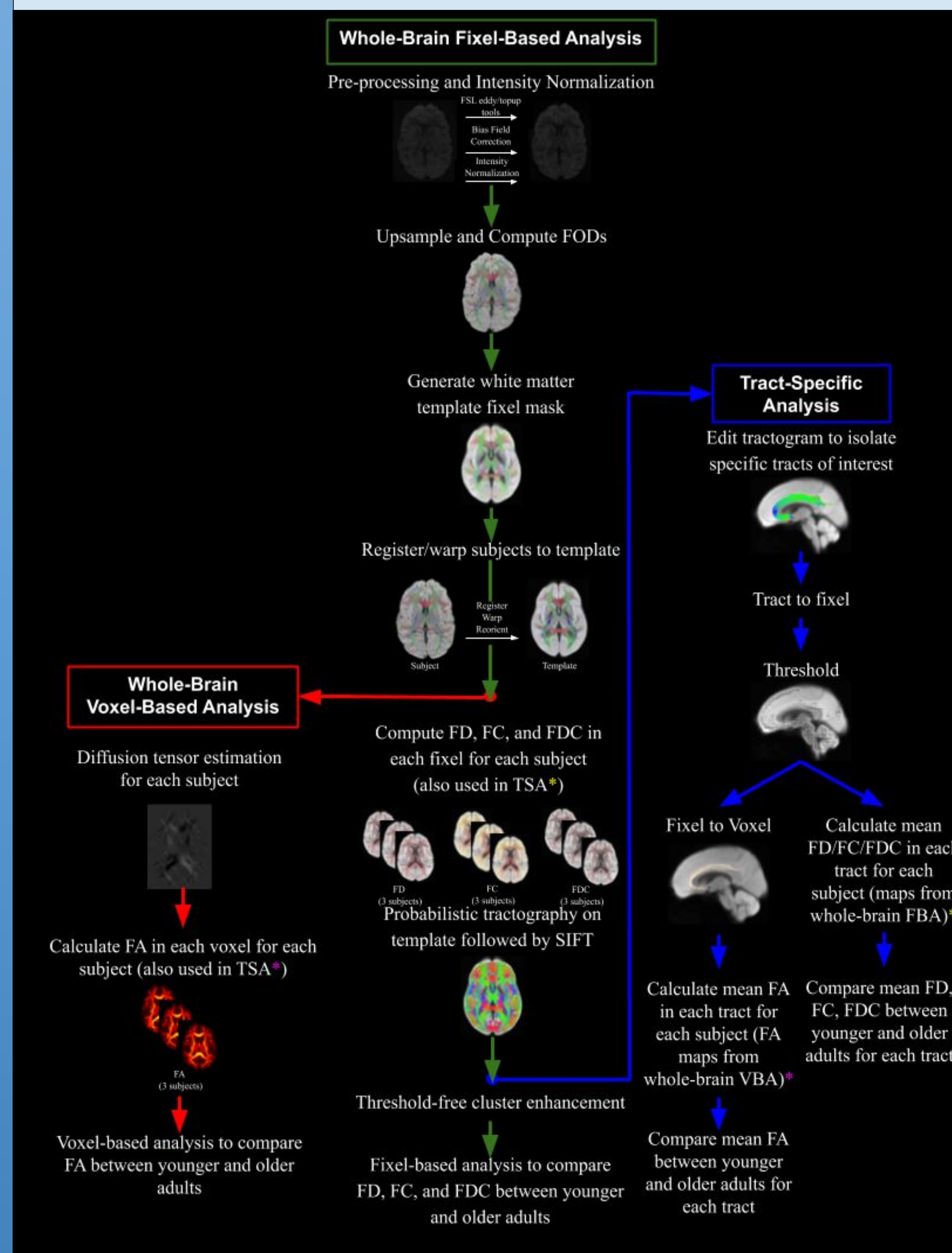
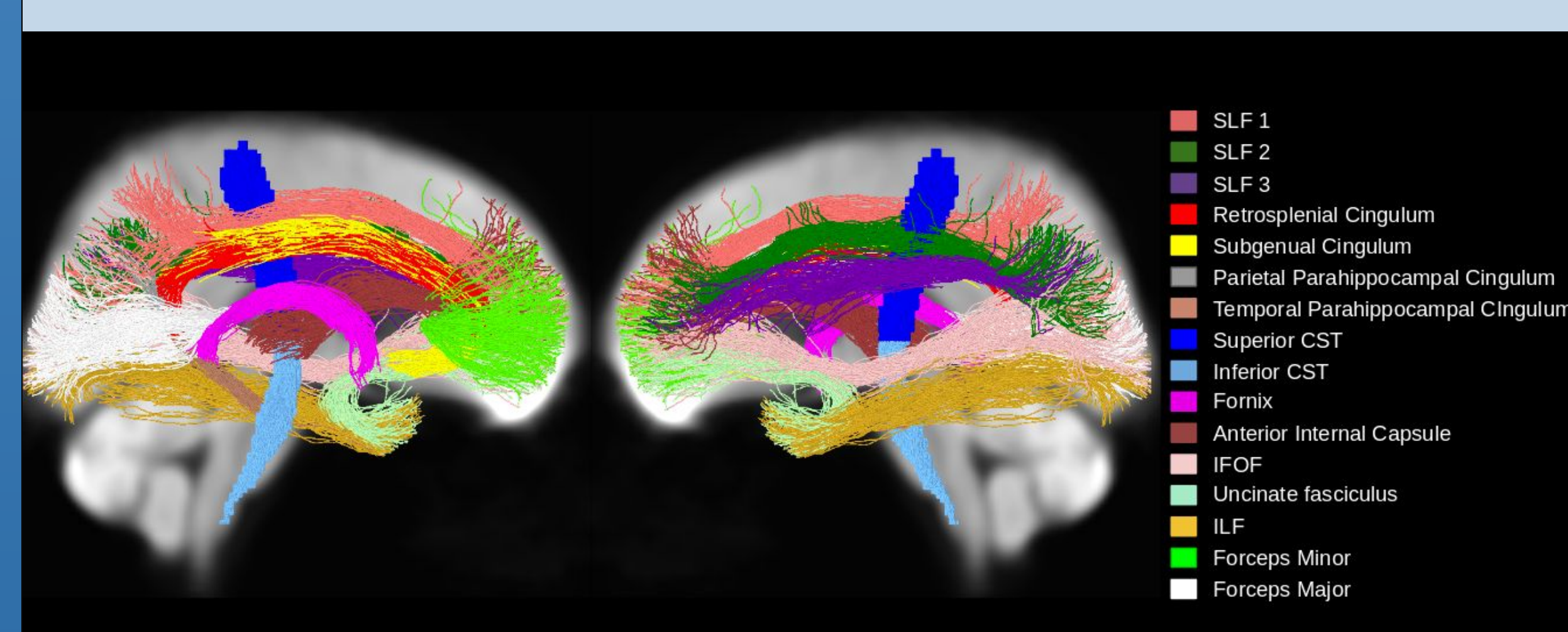
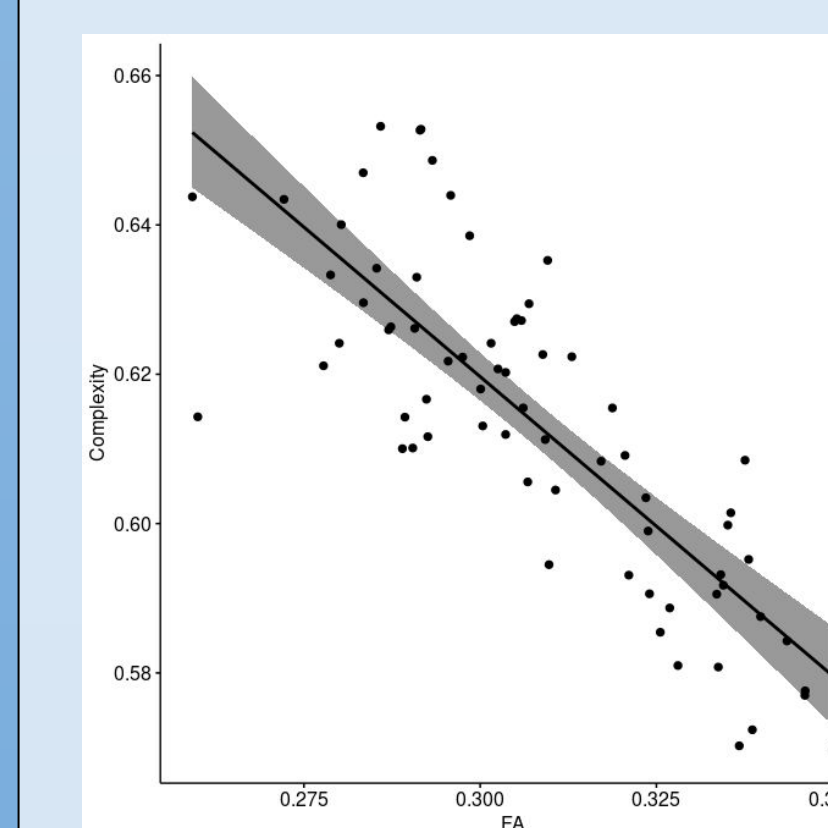


Diagram displaying the workflow for the different analyses conducted in the current study.



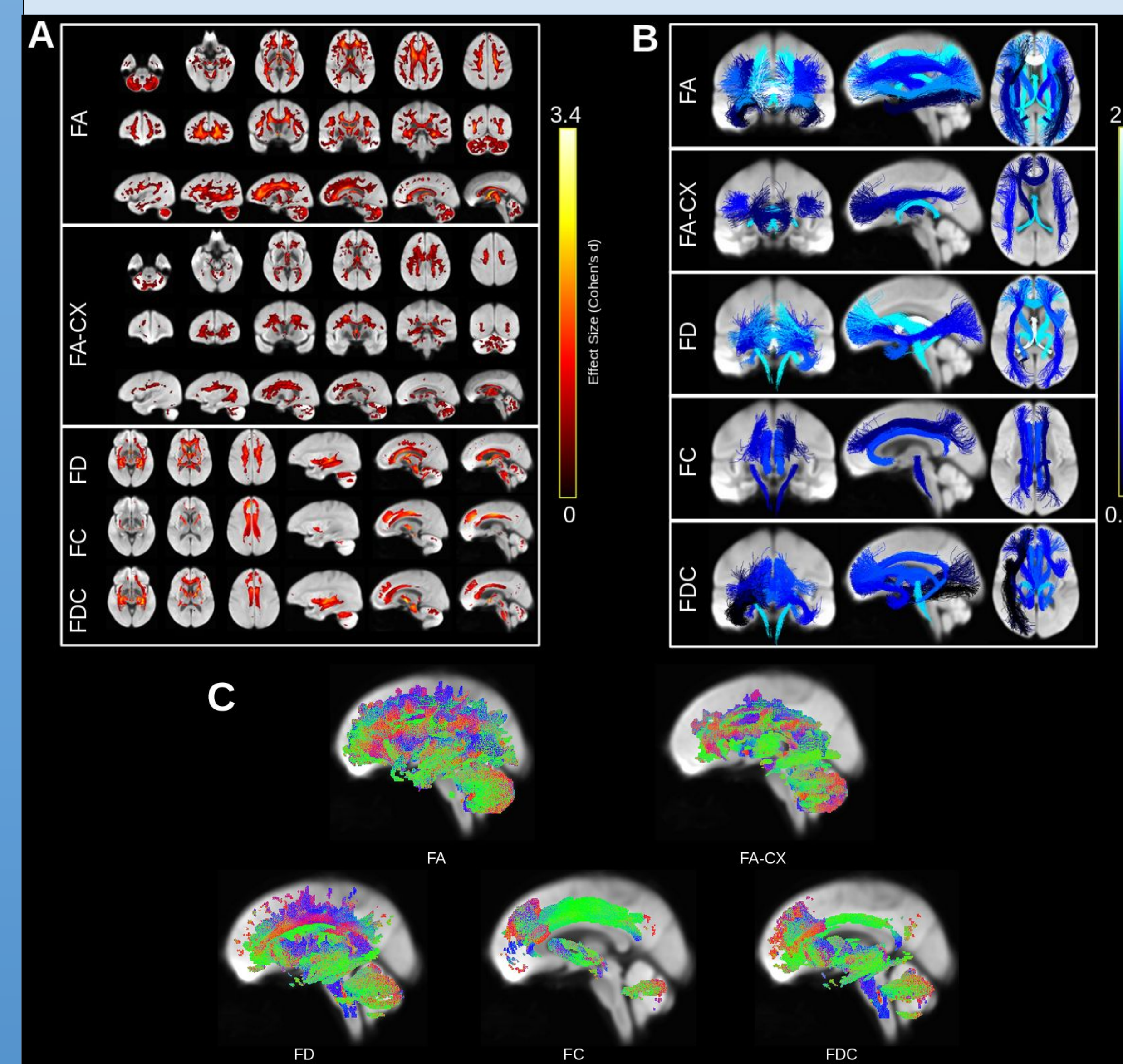
The 16 tracts that were included in the tract-specific analyses, displayed on the white matter population template.

## Results



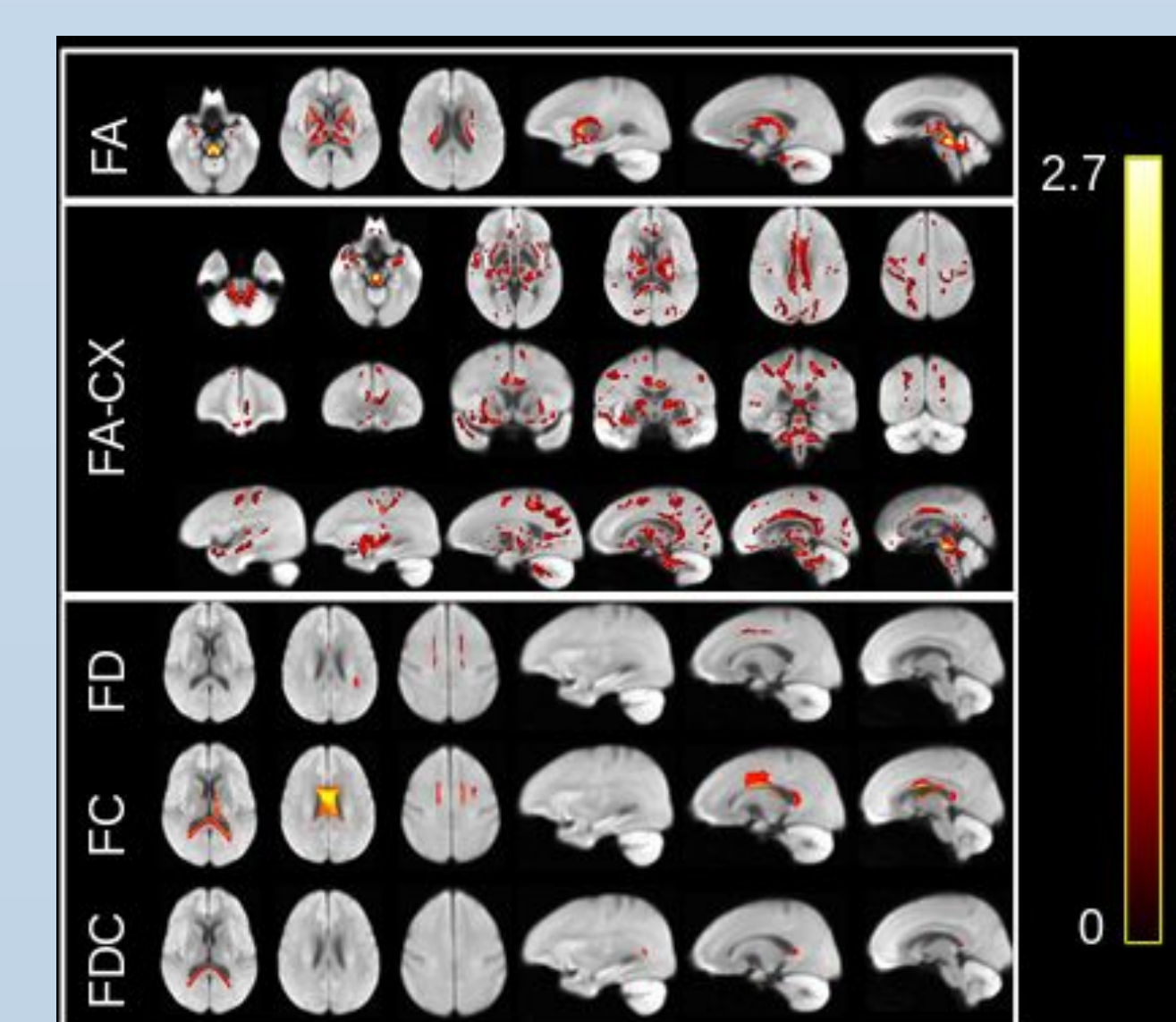
Plot of mean CX and FA for each subject in all voxels identified as significantly different between age groups in DTI analysis. There is a highly significant negative correlation ( $r=-0.81$ ,  $p<0.001$ ).

Young > Old



Voxel-based and fixel-based results using whole-brain and tract specific analysis. All results are displayed on the group template. (A) Significantly ( $p < 0.05$ ) greater FA, FA corrected for CX, FD, FC and FDC from whole-brain analysis, colored by effect size. (B) Significantly ( $p < 0.05$ ) greater FA, FA corrected for CX, FD, FC and FDC from tract specific analysis, colored by effect size. (C) Glass brain view of significantly greater ( $p < 0.05$ ) greater FA, FA corrected for CX, FD, FC and FDC from whole-brain analysis, colored by fiber orientation.

Old > Young



Voxel-based and fixel-based results using whole-brain analysis. All results are displayed on the group template. Significantly ( $p < 0.05$ ) greater FA, FA corrected for CX, FD, FC and FDC from whole-brain analysis, colored by effect size.

## Discussion

- Some but not all age differences in FA are influenced by local multi-fiber geometry within individual voxels.
- Fixel-based analyses afford new insight into the micro- and macro-structural nature of age differences in white matter pathways
- DTI and fixel-based findings reveal a more heterogeneous pattern of age differences than are commonly reported, independent of crossing fibers.
- The fixel-based analysis confirmed age differences across many canonical white matter tracts previously implicated in cognitive aging.
- There was a significant anterior-posterior gradient in the FBA results (particularly the FDC results), with greater age differences in more anterior regions relative to more posterior regions.
- Limitations: Cross-sectional study, highly-educated older adults, b=1000 s/mm<sup>2</sup> single shell data

## References

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