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

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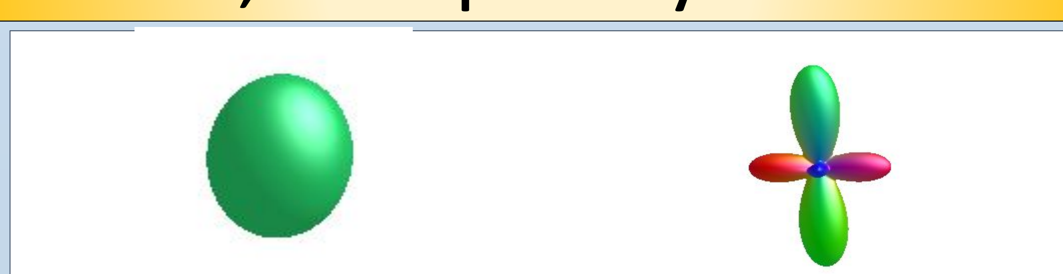
Background

- 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

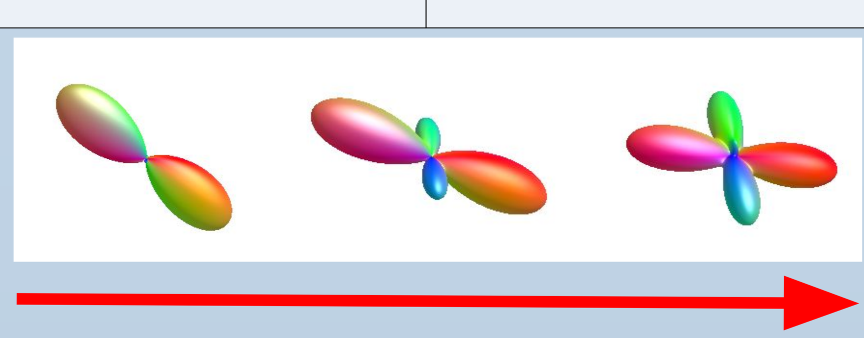
Aims

- 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	Fixel
• 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	• 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/mm²

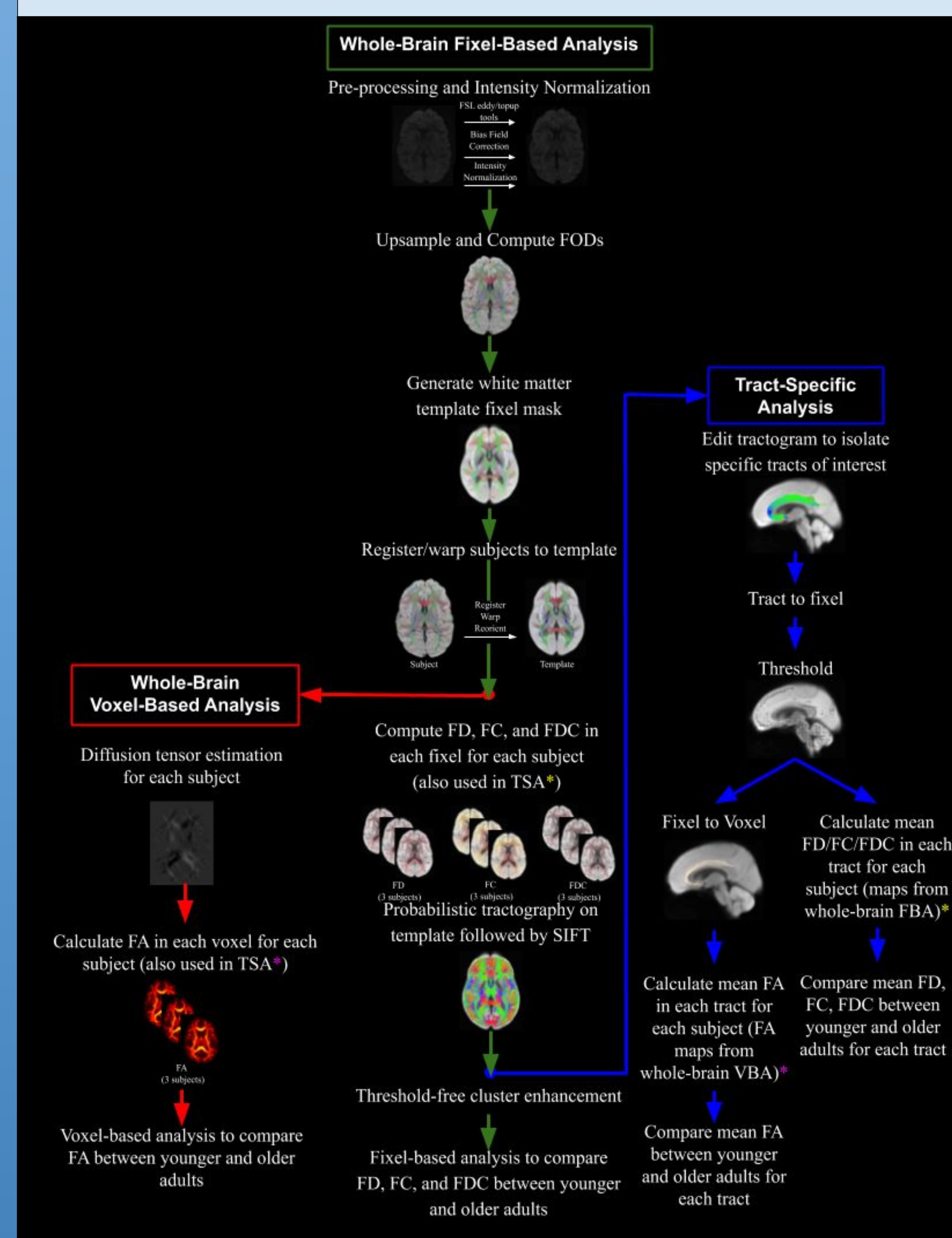
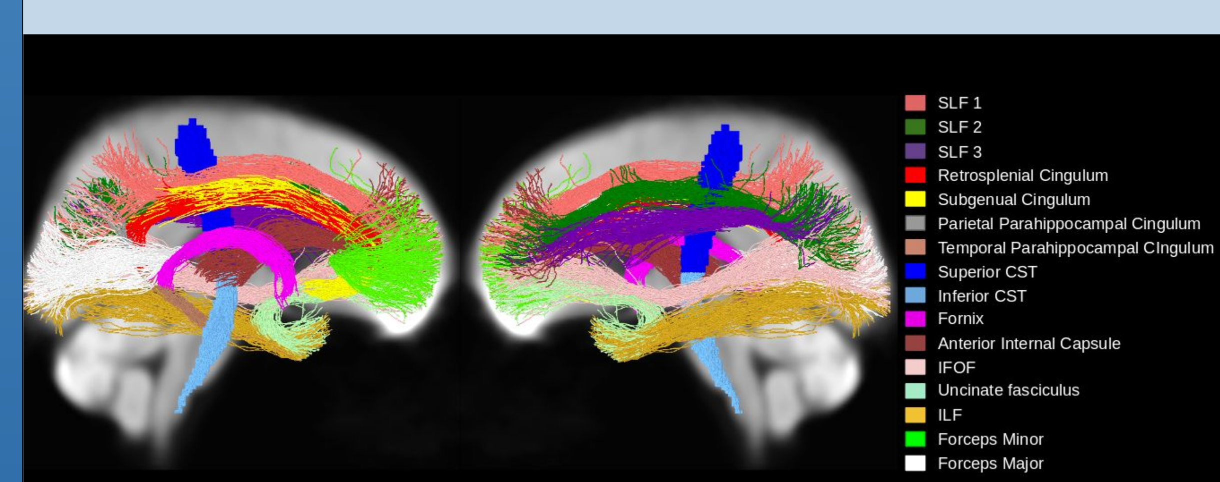
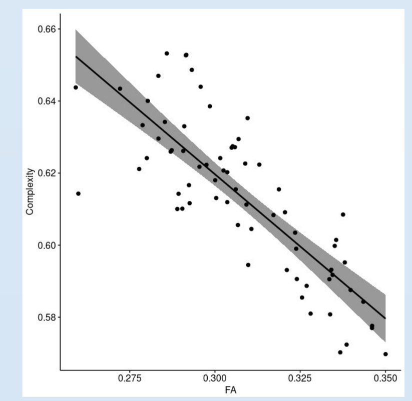


Diagram displaying the workflow for the different analyses conducted in the current study.



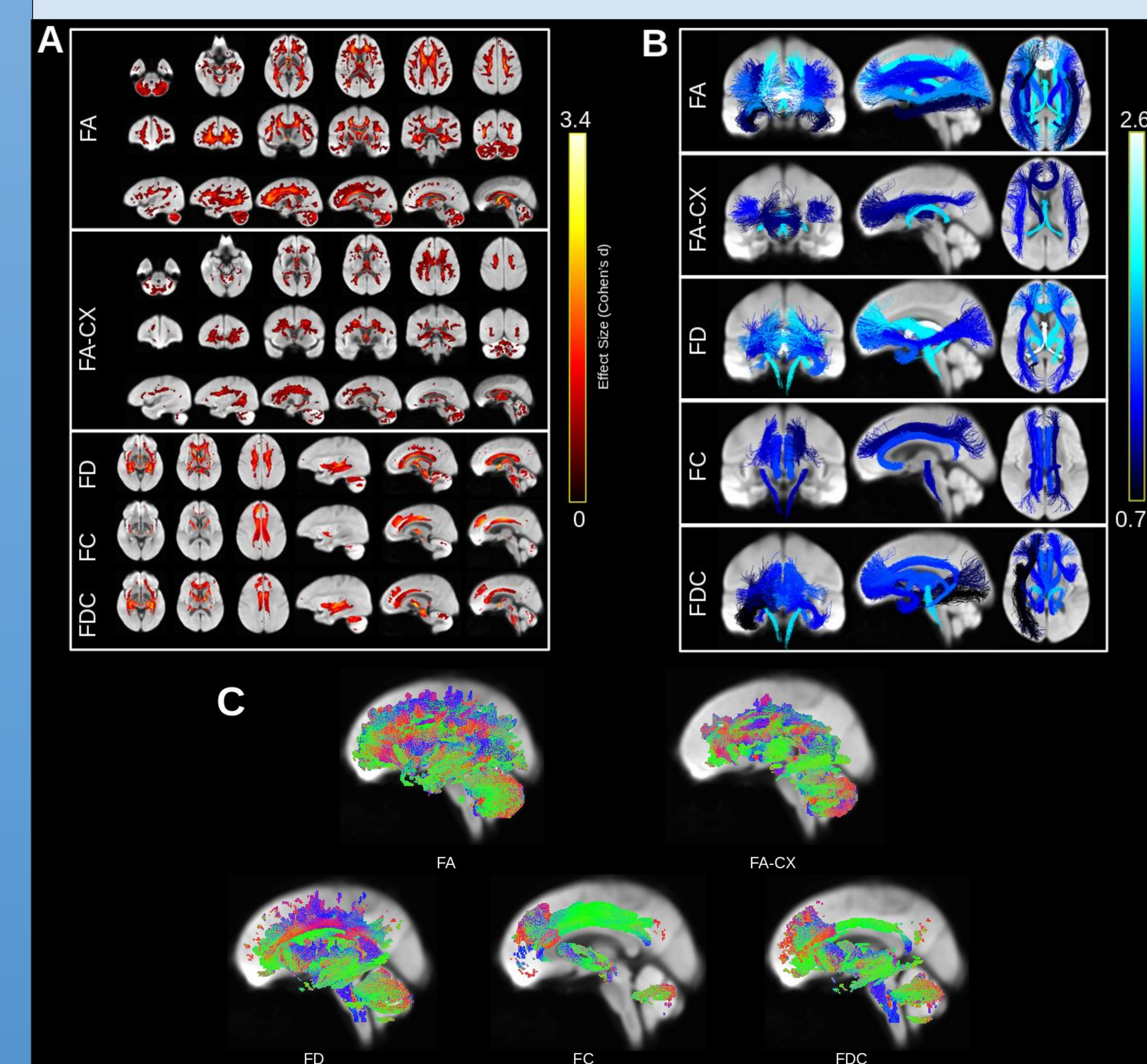
The 16 tracts that were included in the tract-specific analyses, displayed on the white matter population template.

Results



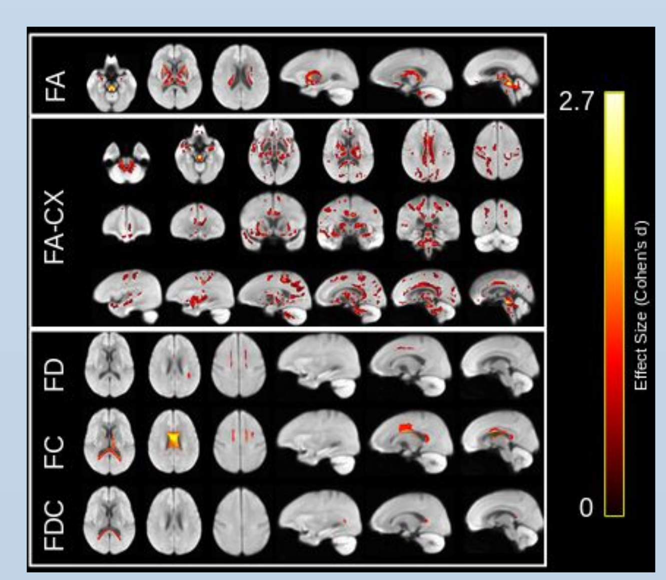
Plot of mean CX and FA for each subject in all voxels identified as significantly different between age groups in DTI analysis. There is a highly significant negative correlation (r=-0.81, p<0.001).

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 significanlty greater ($p < 0.05$) greater FA, FA corrected for CX, FD, FC and FDC from whole-brain analysis, colred 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/mm² single shell data

References

Grazioplene, R. G., Bearden, C. E., Subotnik, K. L., Ventura, J., Haut, K., Nuechterlein, K. H., & Cannon, T. D. (2018). Connectivity-enhanced diffusion analysis reveals white matter density disruptions in first episode and chronic schizophrenia. *NeuroImage: Clinical*, *18*, 608–616. doi: 10.1016/j.nicl.2018.02.015

Riffert, T. W., Schreiber, J., Anwander, A., & Knösche, T. R. (2014). Beyond fractional anisotropy: Extraction of bundle-specific structural metrics from crossing fiber models. *NeuroImage*, *100*, 176–191. doi: 10.1016/j.neuroimage.2014.06.015

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