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Background and Objectives

- Alzheimer's disease (AD) involves profound microstructural alterations beyond macro-atrophy.
- Diffusion MRI (DTI & NODDI) provides distinct biological markers: DTI-FA/MD (integrity/water diffusion) vs. NODDI-NDI/ODI/FWF (neurite density/dispersion/free water).
- The aims of this study were to:
- To compare the sensitivity of DTI vs. NODDI in detecting cross-sectional and longitudinal degeneration.
- To explore the spatial associations between gray matter (GM) and white matter (WM) degeneration.

Methods

- Participants:** We identified 226 participants from the Alzheimer's Disease Neuroimaging Initiative cohort and 110 participants from the Chinese Greater-Bay-Area Healthy Aging Brain Study (GHABS) who had concurrent multi-shell dMRI, β -amyloid (A β), and tau positron emission tomography (PET) scans.
- MRI processing:** DTI-based indicators (fractional anisotropy (FA), mean diffusivity (MD)) and NODDI-based indicators (neurite density index (NDI), orientation dispersion index (ODI), and free water fraction (FWF)) were extracted from the 68 Desikan-Killiany atlas regions in gray matter and from the ENIGMA-DTI FA atlas in white matter.
- PET processing:** A β PET was processed using a cortical summary composite standardized uptake value ratio (SUVR) and converted to the Centiloid units. Tau PET SUVR was extracted in the composite temporal-metaROI.
- Statistical analyses:** Linear mixed-effect (LME) models were applied to estimate slopes of dMRI measures in participants with follow-up data. Generalized linear models (GLMs) were used to compare baseline and slope values for dMRI indicators across cognitively unimpaired (CU), mild cognitive impairment (MCI), and dementia groups, adjusting for age and sex.

Acknowledgements

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Results

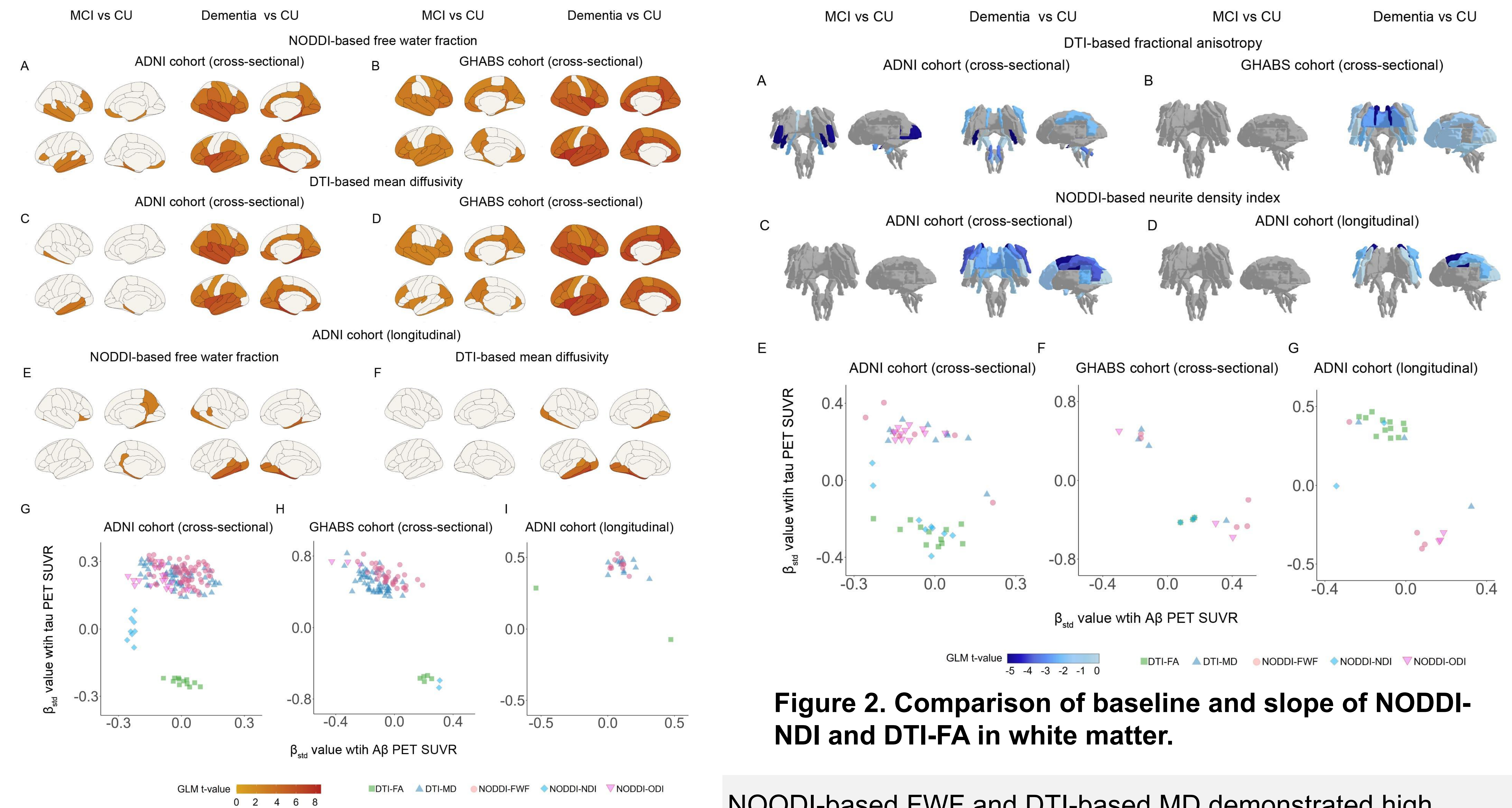


Figure 1. Comparison of baseline and slope of NODDI-FWF and DTI-MD in gray matter.

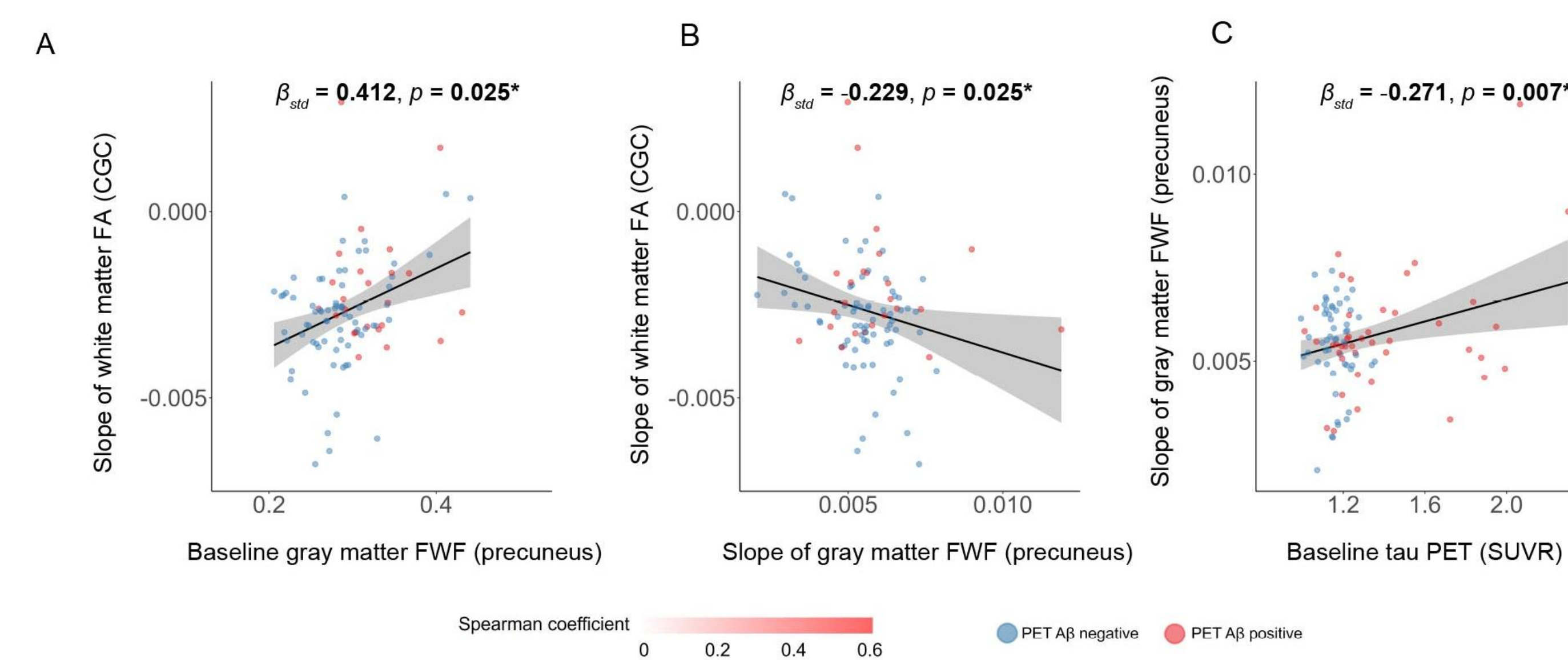


Figure 3. Spatial and temporal associations of gray matter NODDI-FWF and white matter DTI-FA

Figure 2. Comparison of baseline and slope of NODDI-NDI and DTI-FA in white matter.

NOODI-based FWF and DTI-based MD demonstrated high sensitivity for detecting cross-sectional and longitudinal alterations, particularly in gray matter (Figure 1). In white matter, NOODI-based NDI and DTI-based FA exhibited high sensitivity across multiple brain regions (Figure 2). Tau PET burden was associated with elevated FWF and MD in gray matter and with reduced NDI and FA in white matter, with relatively higher standardized β (β_{std}) values than A β PET SUVR. Additionally, cross-sectional and longitudinal gray matter FWF and white matter FA values were strongly correlated across multiple brain regions (Figure 3).

Discussions

The findings suggest that NOODI-based FWF is sensitive to detect microstructural degeneration in gray matter, while DTI-derived FA indicators show a much stronger association with microstructural alteration in white matter.