P8.13

NODDI and Curvature-based Investigation of Superficial White Matter in Young-Onset Alzheimer's Disease

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Introduction

- Superficial white matter (SWM) lies just below the cortex and consists of short, dispersing and crossing fibres that may contain the majority of fibres in WM[1,2].
- Short and thin fibres, characteristic of SWM, harbour unique properties that may make it particularly vulnerable to Alzheimer's disease (AD)[3,4].
- However, SWM's proximity to the curving cortex and complex organisational structure means extracting reliable metrics *in-vivo* is challenging.
- To overcome these methodological limitations, we used Neurite Orientation Dispersion and Density Imaging (NODDI) in combination with curvature-based segmentations of the cortex to determine how SWM is affected in young-onset Alzheimer's disease (YOAD).

Methods

Sample

Group	Control	YOAD
N	22	29
F/M	12/10	16/13
Age (SD)	60.5 (5.7)	61.7 (4.6)
Age at Onset (SD)	NA	56.6 (4.2)
MMSE (SD)	29.4 (0.7)*	20.7 (5.4)*
Cortical Thickness (SD)	2.60 (0.08)*	2.49 (0.12)*

Figure 1) Demographics of young-onset AD (YOAD) cohort used for analysis (comprising of 18 with typical AD and 11 posterior cortical atrophy). Stars indicate significant differences between groups ($p < 0.001$). Cortical thickness is averaged across 15 regions of interest (ROI), see below.

SWM Processing

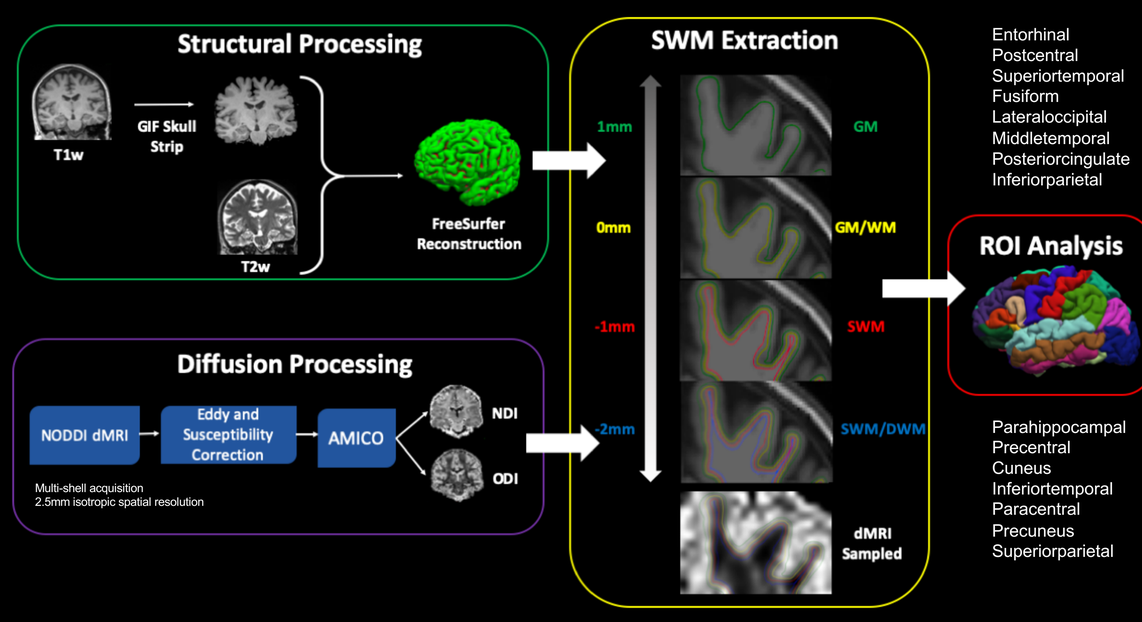
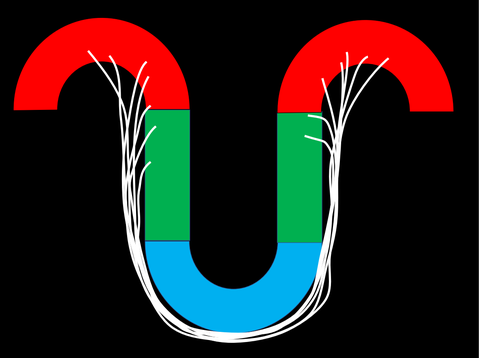


Figure 2) Diagram depicting preprocessing for SWM extraction. NODDI metrics representing neurite density index (NDI) and orientation dispersion index (ODI) were sampled at various distances from the GM/WM boundary and 15 region of interest (ROI) measures extracted. Change in NODDI metrics across the GM/WM boundary, for each ROI, were modelled using a linear mixed effect models.

Curvature-Based Sub-Regions

Figure 3) ROIs consist of many gyri and sulci with distinct SWM organisational properties. Splitting ROIs into curvature-based subregions may improve measures of AD-related change in SWM.



Curvature Processing

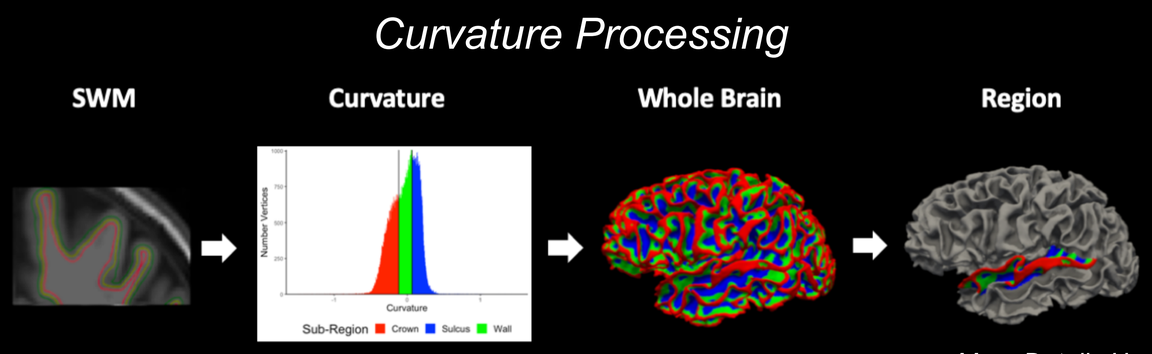


Figure 4) In a separate analysis, NODDI metrics at 1mm below the GM/WM boundary within 4 ROIs were split into sub-regions based on curvature values (gyral crowns < 33rd percentile; sulcal wall 33rd >= and =< 66th percentile; sulcal fundi > 66th percentile)[5]. Mixed models were used to determine if NODDI metrics varied by group across sub-regions in ROIs.

https://git.io/JvKyq

NODDI Changes from GM to SWM

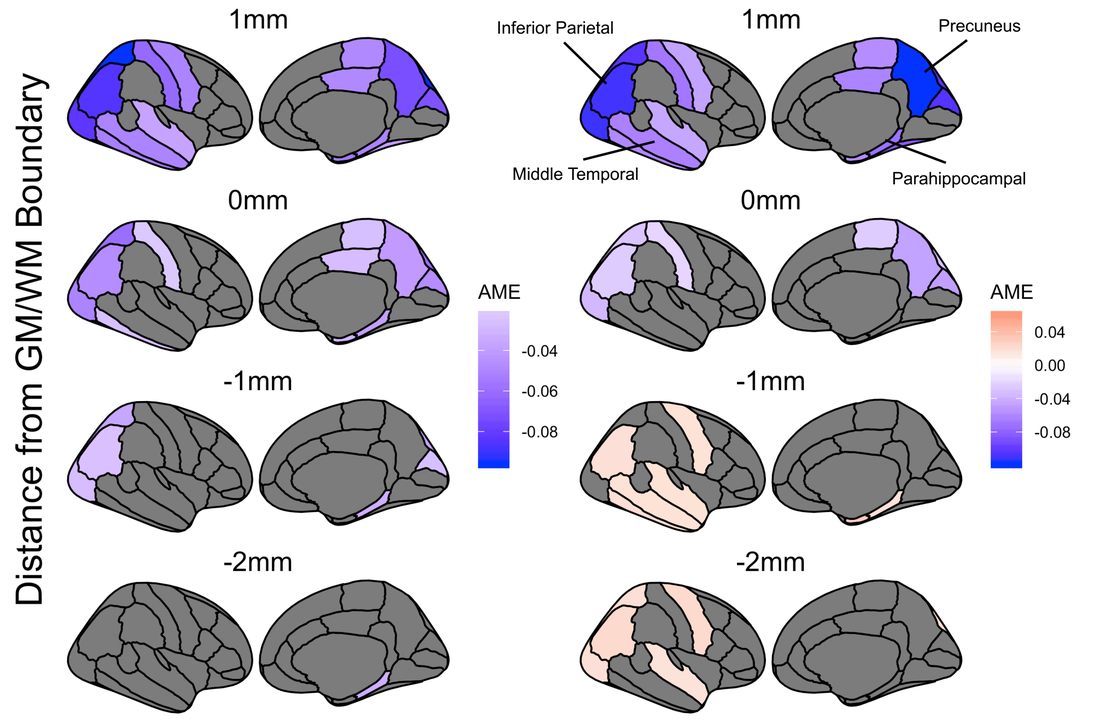


Figure 5) Average Marginal Effects (AME) from linear mixed effect models represent change in NODDI metric in YOAD group, compared to controls, while keeping covariates (i.e. cortical thickness) constant. Most group differences occur in GM (1mm), but YOAD individuals showed reduced NDI from GM (1mm) into SWM (-2mm) (blue/purple). Those with YOAD had decreased ODI (blue/purple) in the GM but increased ODI when moving into SWM (cream/peach). AMEs are statistically significant (pFDR < 0.05).

SWM Metrics Vary with Curvature

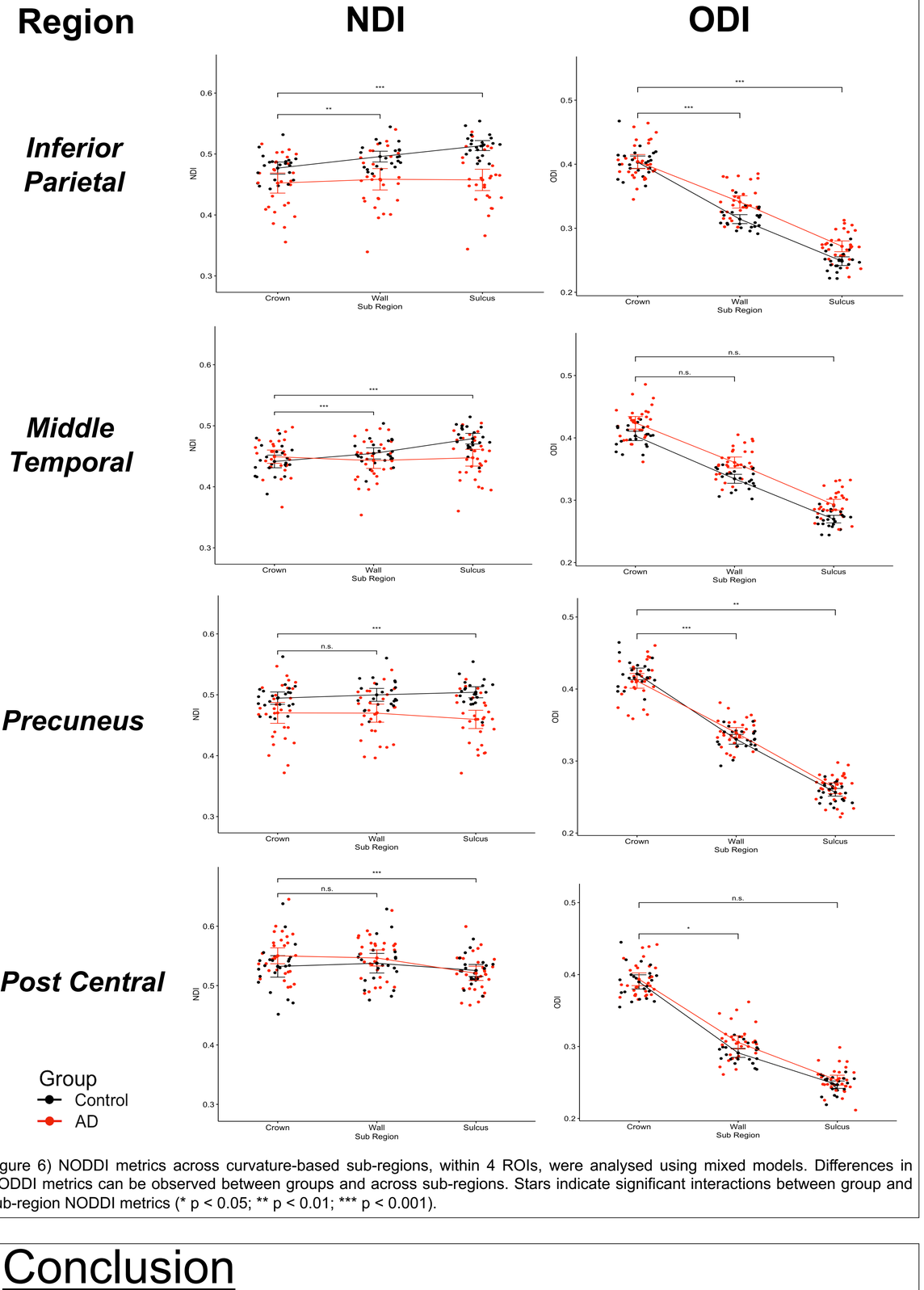


Figure 6) NODDI metrics across curvature-based sub-regions, within 4 ROIs, were analysed using mixed models. Differences in NODDI metrics can be observed between groups and across sub-regions. Stars indicate significant interactions between group and sub-region NODDI metrics (* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$).

Conclusion

- YOAD individuals have reduced NDI and increased ODI in SWM which persist when taking organisational changes into account using NODDI.
- NODDI SWM measures are influenced by cortical morphology and influence healthy age-matched controls and YOAD individuals in different ways.
- These novel NODDI SWM measures may uncover unseen WM changes in AD.

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