White matter microstructural changes in sporadic and genetic FTD using neurite orientation dispersion and density imaging

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Background

Frontotemporal dementia (FTD) is characterized by abnormal white matter (WM) integrity measured with conventional diffusion tensor imaging techniques. No study has yet investigated the microstructural WM changes across different FTD forms using the novel neurite orientation dispersion and density imaging (NODDI) (**Figure 1**). Here, we focused the analyses on symptomatic individuals, investigating the difference between the sporadic and genetic origin within the same diagnostic group.

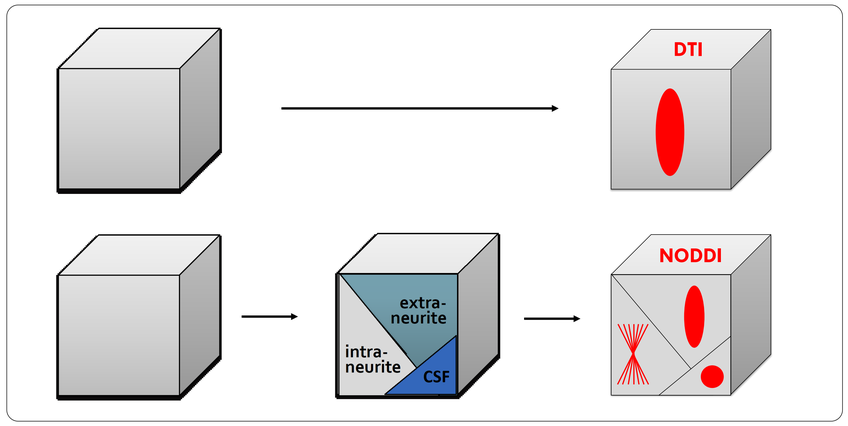

Figure 1. *Example in a voxel of models of diffusion tensor imaging (DTI) and neurite orientation dispersion and density imaging (NODDI) for diffusion-weighted MRI. Adapted from Slattery et al., Neurobiol Aging 2017.*

Methods

Neurite density index (NDI) and orientation dispersion index (ODI) were extracted from NODDI sequences, processed and corrected for tissue-weighted means [Parker *et al.*, NeuroImage 2021]. Images were acquired on a 3T MRI Siemens Prisma scanner from a cohort of participants seen in clinic at the National Hospital for Neurology and Neurosurgery, UCL (London, UK). Data were available for 27 individuals with behavioural variant FTD (bvFTD) and 27 with primary progressive aphasias (11 svPPA, 8 nfvPPA, 4 lvPPA, 4 PPA-NOS). 18 of these individuals (16 bvFTD and 2 PPA-NOS) carried an FTD-linked genetic mutation (6 *C9orf72*, 7 *MAPT*, 5 *GRN*). W-scores for NDI and ODI were computed from a regression model on 62 non-carrier healthy individuals, adjusting for their age, sex, and total intracranial volumes.

Results

The most abnormal values (<2.5th percentile of controls) were found in bvFTD (NDI: anterior corona radiata and left cingulum), lvPPA (NDI and ODI: left superior corona radiata; ODI: splenium of the corpus callosum) and PPA-NOS (NDI: left uncinate fasciculus) (**Figure 2**). Sporadic bvFTD and PPA-NOS showed more abnormal and widespread WM abnormalities compared to symptomatic mutation carriers.

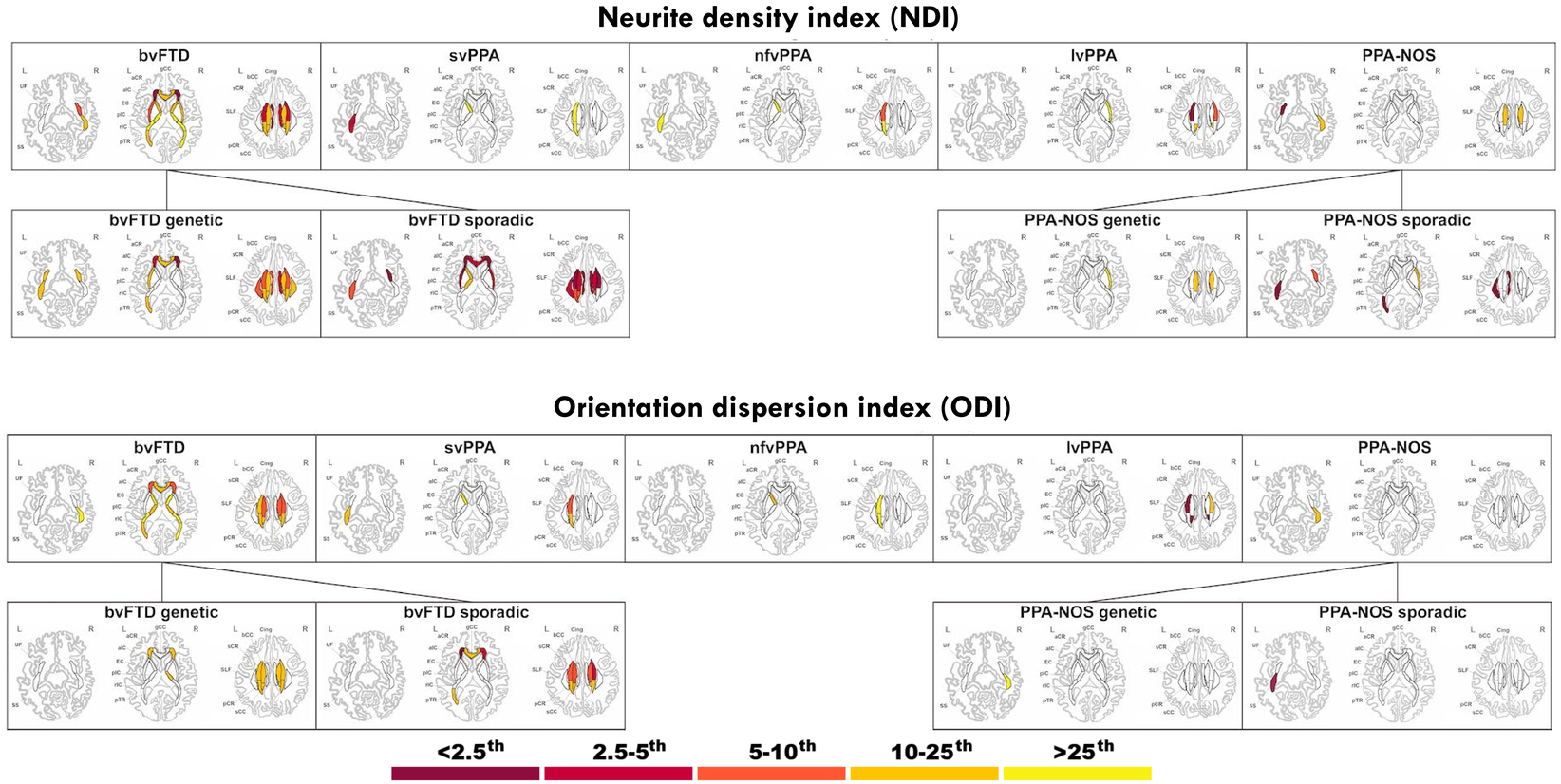

Figure 2. *Pattern of white matter involvement in the diagnostic groups, and the specific sporadic or genetic origin. The colour maps indicate the percentile corresponding to the mean w-scores in each group, when these were statistically abnormal (i.e., significantly different from 0) when compared to controls.*

Conclusions

Changes in WM structure in this cohort of patients with symptomatic FTD appear to be related primarily to a reduction in axonal density. Despite similar clinical features, sporadic forms tend to show more severe and widespread WM involvement than genetic cases.

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