

Atrophy and partial volume related bias in cortical region of interest NODDI metrics

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Background

Neurite Orientation Dispersion and Density Imaging (NODDI) provides *in-vivo* indices of neurite density (NDI) and orientation dispersion (ODI) within the tissue compartment of each voxel. However, NDI and ODI are treated equally when calculating region of interest (ROI) means, despite tissue fraction (TF) varying within regions undergoing neurodegeneration. Covariation between TF and cortical NODDI measures bias these conventional means and we recommend using tissue-weighted averages to address this.

Method

In this study, we included 22 healthy controls and 33 individuals affected by Young-Onset Alzheimer's disease (YOAD, see Table 1 for demographics) with suitable diffusion-weighted and T1-weighted 3T MR images. Diffusion data were corrected for eddy currents, motion and susceptibility artefacts before fitting the NODDI model to produce NDI, ODI, isotropic volume fraction (ISO) and TF maps (TF=1-ISO). T1w images were parcellated into cortical ROIs using Geodesic Information Flow (Cardoso et al., IEEE Trans.Med.Im.; 34:1976-1988, 2015). Five bilateral ROIs expected to undergo neurodegeneration were analysed (Precuneus, Fusiform Gyrus, Superior Parietal, Middle and Inferior Temporal cortex). ROIs were resampled into native diffusion space and two regional measures calculated: 1) conventional, unweighted NDI and ODI averages and 2) tissue-weighted averages using voxel TF as weights. Within-participant differences between conventional and tissue-weighted measures were calculated. Spearman's rank tested correlations and Wilcoxon tests evaluated within- and between-participant differences (Bonferroni adjusted for multiple comparisons).

Result

TF positively correlated with GM volume (r_s range=0.33-0.68, $p < 0.05$) in all ROIs except the left fusiform gyrus ($r_s=0.31$, $p=0.06$) (Figure 1). YOAD individuals had lower TF than healthy controls in all ROIs (Figure 2a), and lower volumes in all ROIs except the right fusiform gyrus ($W=475$, $p=0.27$) (Figure 2b). NDI showed small positive/negative biases in six of the ten ROIs (Figure 3a), while ODI showed significant positive biases across all ROIs (Figure 3b). Biases decreased as TF increased towards its maximum of one (Figure 4a-4b).

Conclusion

Lower cortical volumes in YOAD were associated with lower TF and higher bias, suggesting a greater risk for misestimation of cortical region NODDI metrics in studies involving neurodegenerative disease. We recommend tissue-weighted averages to account for varying intra-regional TF in NODDI measures.