Age-related microstructural changes quantified using myelin water imaging and advanced diffusion MRI

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Target Audience: Basic scientists and clinicians with an interest in diffusion MRI, neuroscience, neuroimaging and oncology.

Purpose: Age-related microstructural changes have been detected using diffusion tensor imaging (DTI)[1]. Whilst DTI is sensitive to the effects of aging, it is not specific to any underlying biological mechanism, including demyelination. Combining multi-exponential T2 relaxation (MET2) and multi-shell diffusion magnetic resonance imaging (dMRI) techniques may elucidate such processes. This study therefore aimed to characterise how advanced dMRI and MET2 parameters evolve during adulthood.

Methods: Multi-shell dMRI (b700 x 25d, b1000 x 45d, b2800 x 75d) and MET2 data were acquired on 59 healthy adults aged 17-70 years (3T Philips). Whole brain and regional age-associated correlations of multiple dMRI measures (DTI, diffusion kurtosis imaging[2] (DKI), neurite orientation dispersion and density imaging[3] (NODDI)) and myelin sensitive MET2[4] metrics were assessed using both region-of-interest (JHU atlas labels) and voxel-based analysis (custom-made white matter template and lateral ventricle exclusion mask).

Results: DTI and NODDI revealed widespread increases in measures of isotropic diffusivity with increasing age, with the most significant changes located at the cortical white matter boundary and in the fornix. In frontal white matter, fractional anisotropy (FA) linearly decreased with age, paralleled by increased 'neurite' dispersion (Orientation Dispersion Index). Myelin water fraction (MWF) remained stable, with minimal increases in deep WM. DKI measures related more to MET2 metrics than to DTI measures.

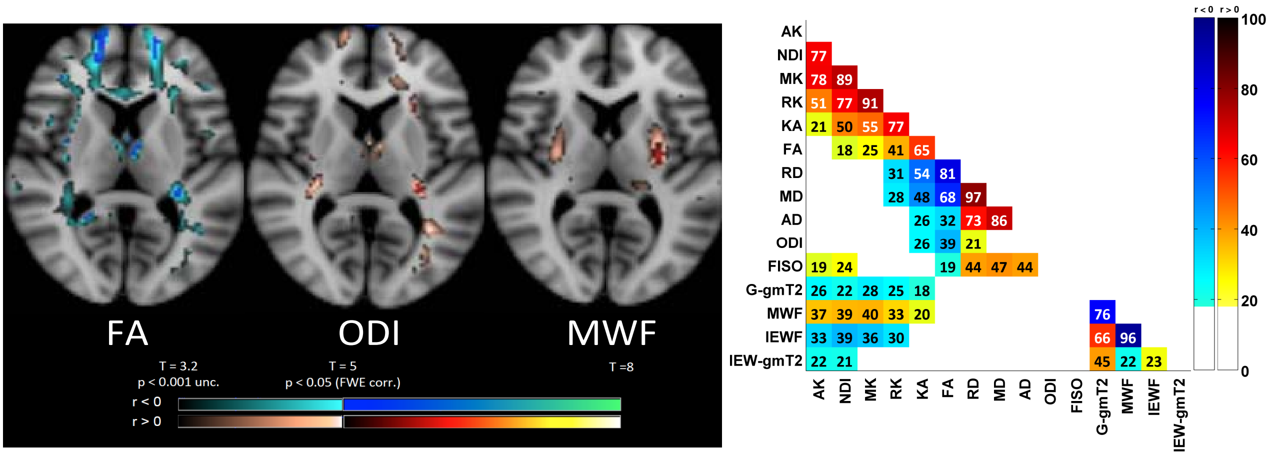

Fig. 1 (left) Significant voxel-wise correlations with age on axial T1 slice. Results for clusters surviving FWE correction thresholds at p=0.001(unc) and pFWE=0.05 are shown. The decrease in frontal FA was not paralleled by a change in MWF but by an increase in ODI, reflecting axonal dispersion. (Right) Percentage shared variance between all parameters. DKI metrics correlated most strongly with MET2 metrics. Red scale = positive, blue = negative correlation.

Conclusion: DTI estimates remain among the most sensitive markers for age-related alterations in white matter. NODDI, DKI and MET2 indicate that the initial decrease in frontal FA in late adulthood (50-60 years) may be due to increased axonal dispersion rather than demyelination. These findiings confirm the added value of combining multiparametric microstructural imaging measures to assess human aging *in vivo*.

References:[1] Sullivan, E.V. and A. Pfefferbaum, Neuroscience and Biobehavioral Reviews, 2006. **30**(6): p. 749-61. [2] Jensen, J.H. and J.A. Helpern, NMR in biomedicine, 2010. **23**(7): p. 698-710. [3] Zhang, H., et al., Neuroimage, 2012. **61**(4): p. 1000-16. [4] MacKay, A., et al., Magnetic resonance imaging, 2006. **24**(4): p. 515-25.