## Voxel-wise assessment of white matter architecture integrity in patients with relapsing remitting multiple sclerosis

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**Introduction.** Diffusion tensor (DT) magnetic resonance imaging (MRI) is sensitive to microstructural damage in multiple sclerosis (MS).

**Objective.** To investigate white matter (WM) integrity in a large sample of relapsing remitting (RR) MS patients using tract-based spatial statistics (TBSS), and the correlation between the distribution of WM damage and clinical quantities, as well as the presence of focal lesions.

**Methods.** Using a 3.0 Tesla scanner, brain T2, T1 and DT MRI scans were acquired from 81 RRMS patients and 88 sex- and age-matched healthy controls (HC). Expanded disability status scale (EDSS) score was assessed in all the patients, and 70 patients were evaluated with the Paced Auditory Serial Addition task (PASAT). TBSS (http://www.fmrib.ox.ac.uk/fsl/tbss/index.html) was applied for voxel-wise analysis of fractional anisotropy (FA) and mean diffusivity (MD) maps. Comparison with HC and correlations with EDSS, the PASAT score, disease duration and lesion load were assessed. We report differences at a threshold of 0.05, family-wise error corrected. Maps of correlation coefficients of FA and MD with clinical and MRI variables were calculated at each voxel of the WM skeleton.

**Results.** Compared to HC, RRMS patients had significant FA decrease and MD increase in the majority of skeleton voxels. FA decrease also involved the cerebellar WM. FA decrease in the optic radiations (OR) and the corpus callosum (CC) was significantly related ($-0.3<r<-0.5$) to disease duration. EDSS was significantly correlated ($0.3<r<0.6$) with FA and MD abnormalities in the CC, fornix and OR, while PASAT scores were related ($0.3<r<0.5$) to FA and MD abnormalities in the CC, fornix, bilateral inferior fronto-occipital fasciculus, and uncinate fasciculus. Relative high correlations ($0.3<r<0.8$) were found between T2- and T1-lesion volumes *vs*. DT MRI abnormalities in the majority of the WM tracts.

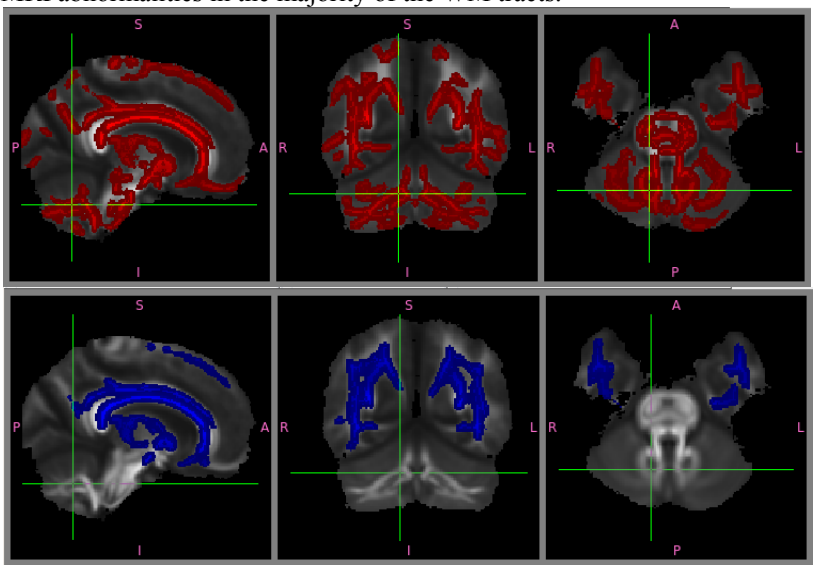


**Figure 1.** Clusters of significant FA (red) and MD (blue) difference between patients and healthy controls, overlaid on the FA atlas.

**Conclusion.** Diffuse WM microstructural abnormalities occur in RRMS patients and are largely related to focal lesion accumulation. The assessment of the regional distribution of these abnormalities might improve the understanding of disease clinical manifestations.

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