White matter abnormalities in early Relapsing-Remitting Multiple Sclerosis patients without cognitive impairment

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Objective

Cognitive impairment is a common and disabling clinical feature of Multiple Sclerosis (MS), and it has been related to white matter abnormalities. Diffusion tensor imaging (DTI) allows a microstructural assessment of the integrity of major bundles. In this study we aimed to explore macrostructural and microstructural integrity of brain tissue in patients with early Relapsing-Remitting MS (RRMS).

Materials and Methods

We enrolled 29 patients (12 female, 17 male; mean age 32.7 ± 7.7 years) with a diagnosis of RRMS (McDonald diagnostic criteria 2010) within two years of presentation and 28 age- and sex-matched healthy controls. Physical disability was assessed by the Expanded Disability Status Scale (EDSS, mean score 1.8 ± 0.5). All individuals underwent an extensive battery of neuropsychological tests and the same MRI scanning protocol by using a 3T Unit (MR-750 General Electrics), including whole-brain 3D T1-weighted and diffusion-weighted images.

Voxel-wise univariate comparisons of grey matter (GM) and white matter (WM) volumes, mean diffusivity (MD) and fractional anisotropy (FA) were performed in 'randomise', part of FSL. Statistical maps were corrected for multiple comparisons by implementing threshold-free cluster enhancement in which fully corrected P values < 0.05 were considered significant.

Results

All subjects of the two groups had normal cognitive performance. GM and WM volumes were not different between patients and controls. FA was reduced in early RRMS in the splenium of corpus callosum, in the right posterior thalamic radiation and in the sagittal stratum. (Fig. 1) MD was increased in patients in the posterior thalamic radiation and in the corona radiata bilaterally. (Fig 2)

Fig. 1

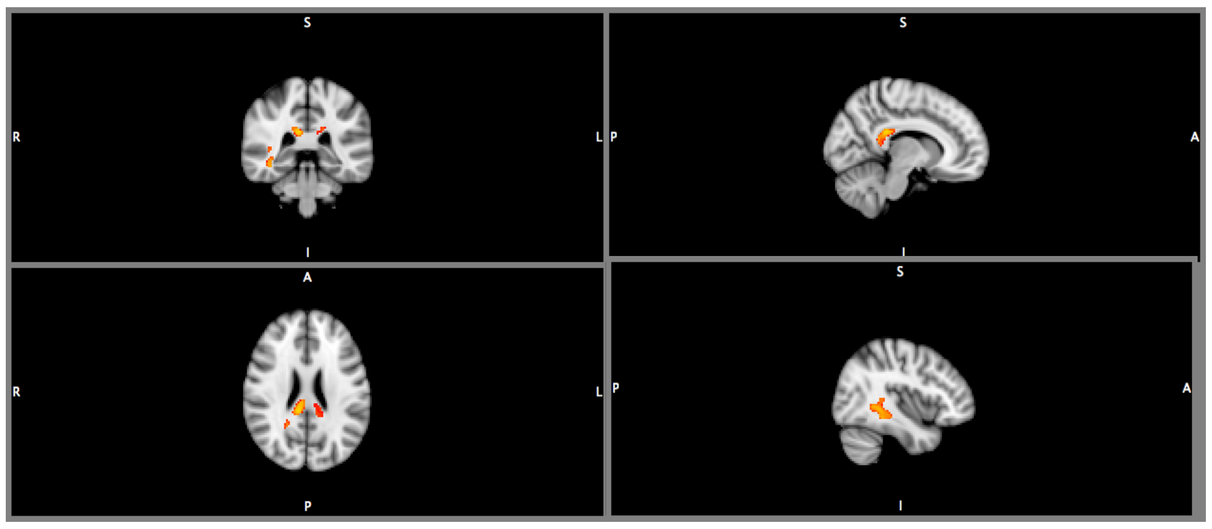
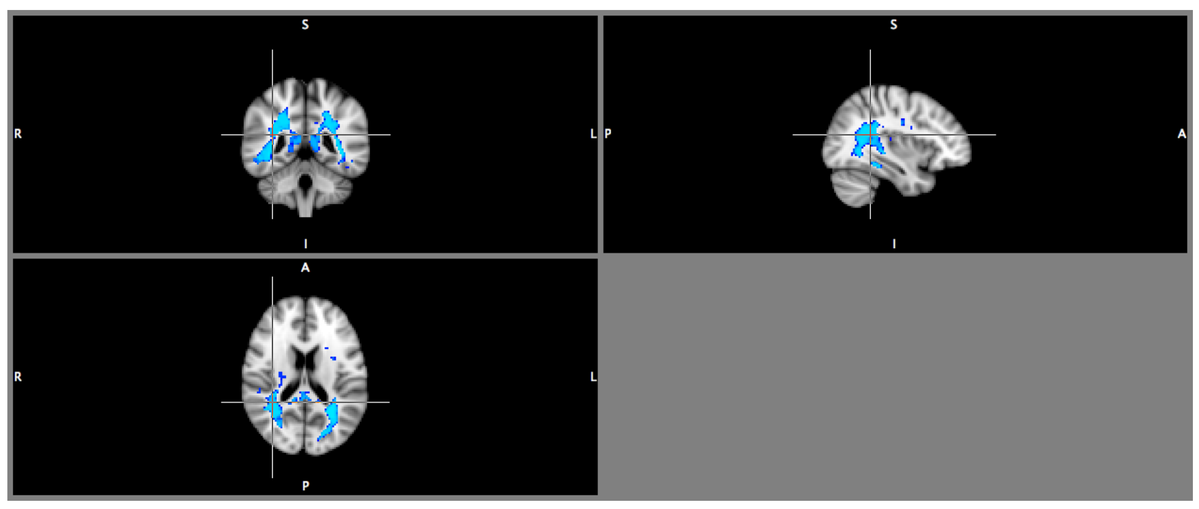


Fig. 2



Discussion & Conclusions

We found microstructural abnormalities in cognitively normal patients with early RRMS. These bundles are part of circuits related to executive functions, and have been found damaged in RRMS patients with cognitive impairment. Overall, our results suggest that MD and FA might play an important role in delineating mechanism underlying MS-associated cognitive impairment. In conclusion microstructural alterations in cognitive circuits may occur in a very early stage of RRMS. DTI metrics of white matter could be a preclinical marker of cognitive impairment in RRMS patients since the earliest stages of the disease.

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