

Clinical Impairment in Multiple Sclerosis Is Related to the Damage of Clinically Eloquent White Matter Tracts

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Introduction. Diffusion tensor (DT) MRI tractography studies showed that assessing damage in clinically eloquent pathways in multiple sclerosis (MS) might increase the clinical specificity of MRI.

Objective. To apply a voxel-wise analysis to metrics from DT MRI tractography and T2 lesions to assess whether measures of structural damage in the corticospinal tract (CST) and sensitive thalamocortical projections (sTCP) contribute to explain clinical disability and impairment at specific functional systems (FS) in MS.

Methods. Brain dual-echo and DT MRI sequences were collected from 172 MS patients and 46 matched healthy controls (HC). The Expanded Disability Status Scale (EDSS) score, the degree of impairment in the different EDSS FS and Ambulation Index (AI) were rated. Patients were dichotomized using pyramidal (P) and sensitive (S) FS (impaired: FS \geq 1, unimpaired: FS=0), EDSS (ambulatory impaired: EDSS \geq 4.0, fully ambulatory: EDSS<4.0) and AI (impaired: AI \geq 1, unimpaired: AI=0). Using DT MRI tractography, probability maps of the CST and sTCP were produced. Voxel-wise analysis was used to assess the topographical distribution of damage along these tracts.

Results. Compared to HC, MS patients had a diffuse increase of mean (MD), axial (AD), and radial (RD) diffusivities along the CSTs and sTCPs. Fractional anisotropy (FA) decrease was limited to the rostral part of the CSTs and sTCPs. Diffusivity abnormalities were more pronounced in patients with EDSS \geq 4.0, PFS \geq 1 and AI \geq 1 (**figure 1**). Patients with EDSS \geq 4.0 and those with PFS \geq 1 showed a higher probability of having T2 lesions in the CSTs and sTCPs, while patients with AI \geq 1 had a higher lesion occurrence in the left sTCP.

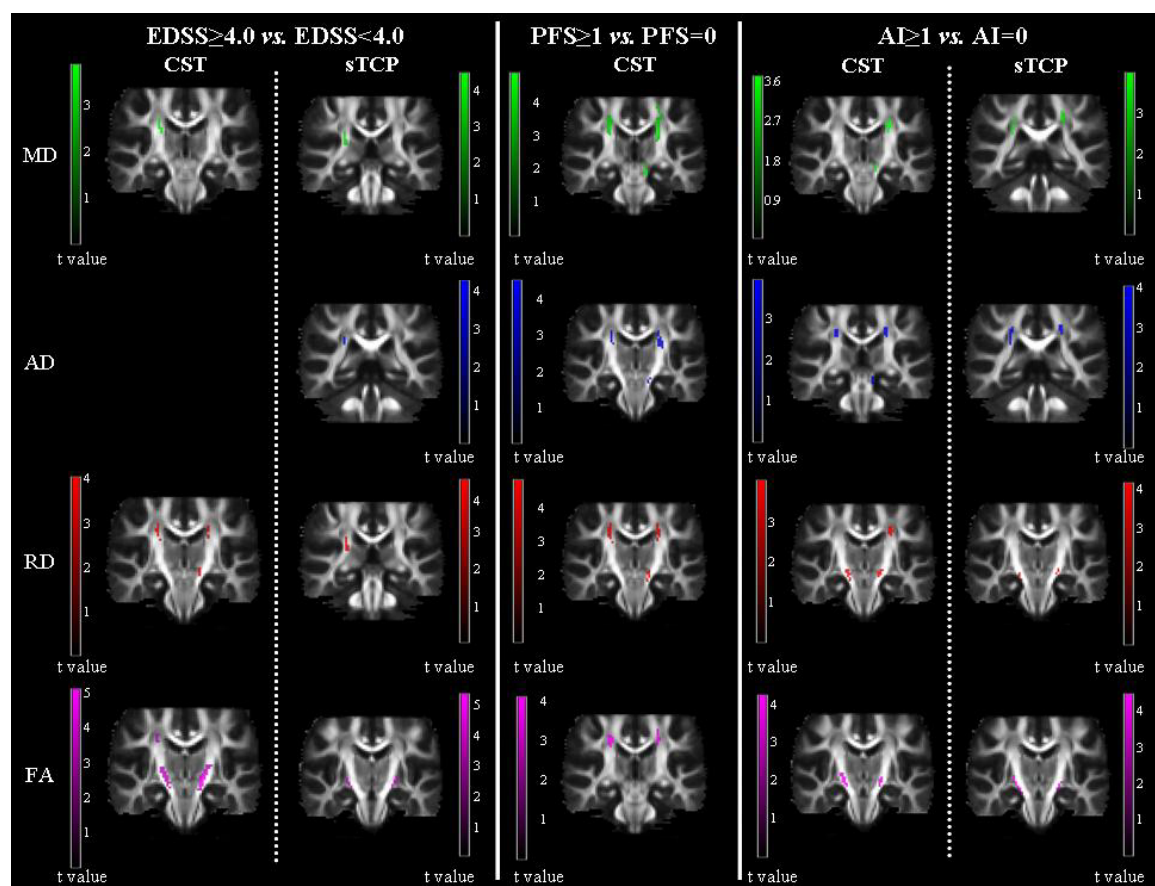


Figure 1. Statistical parametric mapping (SPM) analysis (color-coded for t values) of clusters with increased MD (green), AD (blue) and RD (red) and decreased FA in the corticospinal tract (CST) and sTCP in MS patients with EDSS \geq 4.0 vs. EDSS<4.0 (left column); in the CST of MS patients with PFS \geq 1 vs. PFS=0 (middle column); and in CST and sTCP in MS patients with AI \geq 1 vs. AI=0 (right column). P < 0.05, corrected for multiple comparisons. Images are in neurological convention.

Conclusions. Clinical impairment in MS is associated with the extent of CST and sTCP damage in terms of focal lesions and normal-appearing white matter tract injury. The assessment of the regional distribution of damage in MS contributes to improve the correlations between clinical and MRI findings.