Cerebellar Peduncles Intrinsic Damage in Multiple Sclerosis: Association With Clinical Disabilty

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Introduction. The cerebellum and cerebellar peduncles (CP) are regions frequently affected by demyelinating and neurodegenerative processes in multiple sclerosis (MS). The assessment of microstructural damage in the might contribute to explain permanent clinical disability of the disease.

Objectives. To apply a voxel-wise analysis to metrics from diffusion tensor (DT) MRI tractography and T2 lesions of the middle (M) and superior (S) CP to quantify their structural damage in MS patients, and to assess the relationship between CP damage *vs*. global clinical disability, impairment in cerebellar (C) and brainstem (B) functional systems (FS) and in ambulation.

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 CFS and BFS (impaired: FS≥1, unimpaired: FS=0), EDSS (ambulatory impaired: EDSS≥4.0, fully ambulatory: EDSS<4.0) and AI (impaired: AI≥1, unimpaired: AI=0). Using DT MRI tractography, probability maps of the SCP and MCP were produced. Voxel-wise analysis was used to assess the topographical distribution of damage along these tracts.

Results. Compared to HC, MS patients showed widespread increase of mean (MD), axial (AD), radial (RD) and decreased fractional anisotropy (FA) in both tracts. According to the predefined criteria for impairment, impaired patients were significantly older and had a longer disease duration. Diffusivity abnormalities were more pronounced in patients with EDSS≥4.0, CFS≥1 (**Figure 1**), BFS≥1 and AI≥1. Patients with EDSS≥4.0 had a higher probability of having T2 lesions in the MCP bilaterally, partially overlapping with diffusivity abnormalities, patients with BFS≥1 showed a higher probability of having T2 lesions in one small cluster in the left SCP, while no differences were found for the other comparisons.

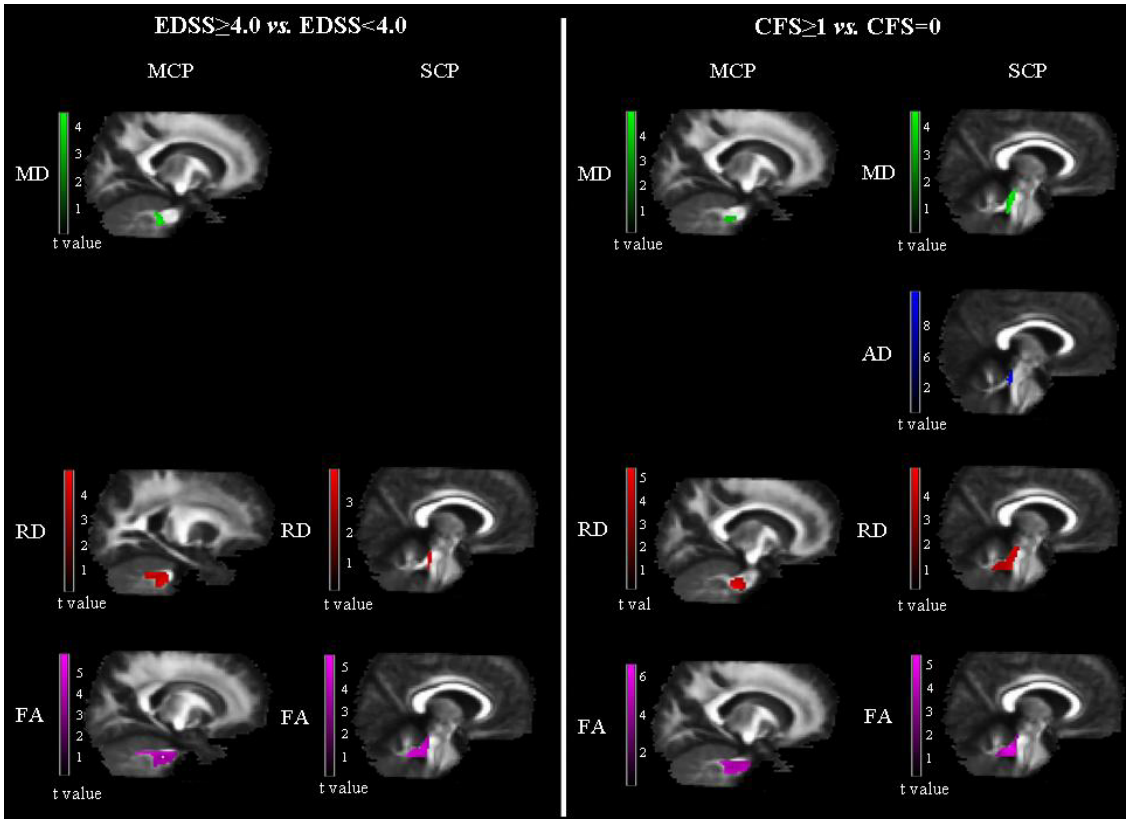

Figure 1.
Left column: Statistical parametric mapping (SPM) analysis (color-coded for t values) of clusters with increased MD (green), RD (red) and decreased FA (violet) in the MCPs and SCPs of MS patients with EDSS≥4.0 *vs.* MS patients with EDSS<4.0.
Right column: SPM analysis (color-coded for t values) of clusters with increased MD (green), AD (blue), RD (red), and decreased FA (violet) in the MCPs and SCPs of MS patients CFS≥1.0 *vs.* patients with CFS=0. P <0.05, corrected for multiple comparisons. Images are in neurological convention.

Conclusions. The assessment of MCP and SCP damage in terms both of local inflammation (presence of T2 focal lesions), and diffuse normal appearing white matter tract injury (Wallerian degeneration), might contribute to explain global clinical impairment as well as impairment at single FS in MS.