FUNCTIONAL AND STRUCTURAL DISRUPTION OF THE PRECUNEUS CONTRIBUTES TO COGNITIVE IMPAIRMENT IN PEDIATRIC MULTIPLE SCLEROSIS

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Purpose. Cognitive impairment affects more than 40% of pediatric patients with multiple sclerosis (MS) (1). In this study, we combined structural and functional magnetic resonance imaging (MRI) techniques to improve our understanding of the mechanisms responsible for the presence and severity of cognitive impairment in patients with pediatric MS.

Methods. Using a 3.0 Tesla scanner, brain dual-echo, diffusion tensor (DT), 3D T1-weighted fast field echo (FFE) and resting state (RS) fMRI scans were acquired from 35 pediatric MS patients and 16 sex- and age-matched healthy controls (HC). All patients underwent neurological and neuropsychological assessment. Patients with abnormalities in ≥ 2 neuropsychological tests were classified as cognitively impaired (CI). T2 and T1 lesion volumes (LV) were calculated using Jim5 software and lesion probability maps (LPMs) were produced. After refilling of white matter (WM) T1-hypointense lesions on the 3D FFE scans, voxel-based morphometry (VBM) was performed using SPM8 and DARTEL software and atrophy distribution in the WM and gray matter (GM) evaluated (2). Microstructural damage to the WM was assessed on DT MRI scans using tract based spatial statistics (TBSS) analysis and FMRIB's Diffusion Toolbox. Functional connectivity (FC) analysis of the default mode network (DMN) was measured using an independent component analysis (ICA) with the GIFT software.

Results. Forty-five% of patients were CI. Compared to cognitively preserved (CP) patients, CI patients had an increased probability to harbor lesions in the right (R) thalamus, bilateral cingulum, R precuneus and bilateral parieto-occipital WM. Compared to CP, CI patients had atrophy of the R precuneus and left (L) middle temporal gyrus. They also had atrophy of the splenium of the CC, posterior cingulum, WM in the vicinity of the precuneus, and R superior longitudinal fasciculus (Figure 1a). Significant reduced DMN RS FC of the precuneus was found in CI patients (Figure 1b), whereas CP patients showed an increased RS FC of the anterior cingulate cortex. MRI findings correlated with the number of abnormal neuropsychological tests and performance at spatial, verbal memory and attention tests (r: 0.42 to 0.70, $p<0.001$).

Figure 1a: regional strucutural damage in cognitively impaired (CI) vs. cognitively preserved (CP) pediatric MS patients and healthy controls

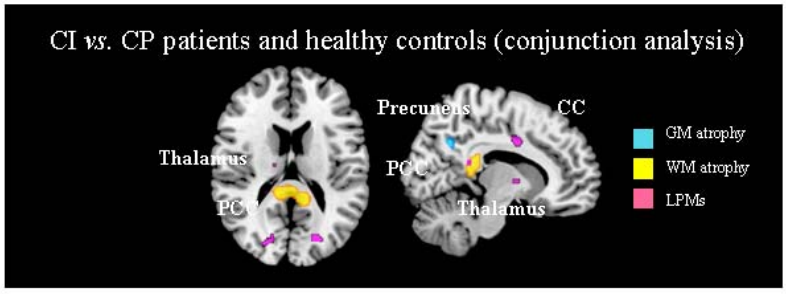
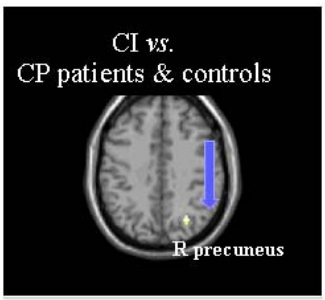


Figure 1b: reduced DMN FC in CI vs. CP pediatric MS patients and healthy controls



Discussion and conclusions. In pediatric MS patients, cognitive dysfunction is associated to structural and functional abnormalities of core regions of the DMN located in posterior regions of the brain, particularly the precuneus. Increased RS FC of regions located in the frontal lobe might counteract such a dysfunction and contribute to cognitive preservation.

References.

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