

Regional gray and white matter atrophy are largely unrelated in relapsing remitting multiple sclerosis

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Introduction. Atrophy is a well-known feature of multiple sclerosis (MS). The patterns of regional distribution of atrophy in the white matter (WM) and gray matter (GM) in these patients deserve further investigations.

Objective. To apply voxel-based morphometry (VBM) to investigate the regional distribution of GM and WM atrophy in a large sample of relapsing remitting (RR) MS patients and their relationship with focal lesions and clinical disability.

Methods. Using a 3.0 Tesla scanner, dual-echo turbo spin echo and three-dimensional (3D) T₁-weighted images were acquired from 78 RRMS patients and 88 sex- and age-matched healthy controls (HC). Expanded disability status scale (EDSS) score was assessed in all the patients, and 67 patients were evaluated with the Paced Auditory Serial Addition task (PASAT). T2 hyperintense and T1 hypointense lesions were semi-automatically segmented using Jim5 (www.xinapse.com). Then, since VBM is biased by the presence of lesions, T1-hypointense lesions were refilled with values randomly extracted from a gaussian distribution with mean and standard deviation estimated from the normal appearing WM, as previously described (1). Using SPM8 and DARTEL (2), VBM (3) was performed for the GM and the WM. A two sample t-test was used to assess between-group differences at a voxel level. A regression analysis was used to investigate the correlations between atrophy and lesion load, EDSS and the PASAT test. We report results at a threshold of 0.05, family-wise error corrected.

Results. Compared to HC, RRMS patients had GM atrophy in the deep GM nuclei, bilaterally, and in several regions mainly located in the fronto-parietal lobes, including the cingulum (Figure 1A). WM atrophy mainly involved posterior regions in the brain (i.e. cerebellar peduncles, temporo-occipital lobes), the corpus callosum and the corona radiate (Figure 1B). T2 and T1 lesion volumes were correlated with GM loss in the basal ganglia and the cingulum, as well as with WM loss in the temporal regions and the corpus callosum. PASAT score correlated with GM loss in the parietal lobes, posterior cingulum, caudate, insula, and in the cerebellum, as well as with WM loss in the fronto-parietal-temporal lobes and the middle cerebellar peduncles. No significant correlations were found with the EDSS score at the chosen threshold.

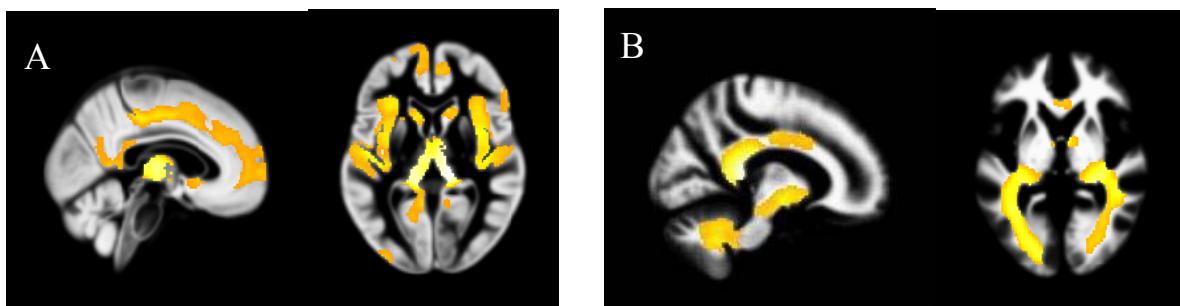


Figure 1. Clusters of significant atrophy (in yellow) in the GM (A) and the WM (B).

Conclusions. In patients with RRMS, GM and WM atrophy tends to have distinct patterns of regional distribution, with a prominent involvement of anterior areas of the brain for the GM and posterior regions for the WM. The correlation between atrophy and PASAT performance supports the theory of an anterior-posterior rather than an interhemispheric disconnection syndrome.

References.

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Acknowledgments. The study was partially supported by a grant from FISM/2008/R/13.