STRUCTURAL MRI CORRELATES OF BENIGN MULTIPLE SCLEROSIS. A VOXEL-BASED MORPHOMETRY STUDY OF REGIONAL GREY MATTER ATROPHY

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Introduction

Using voxel-based morphometry (VBM), previous studies have shown grey matter (GM) atrophy in several cortical and subcortical structures in patients with multiple sclerosis (MS). The regional distribution of GM atrophy in patients with benign MS (BMS) has not been investigated yet. The aim of the present study is to determine the patterns of regional distribution of GM atrophy in BMS and secondary progressive MS (SPMS) patients, in order to better clarify the mechanisms underlying the presence or absence of irreversible locomotor and cognitive impairment.

Methods

Using a 1.5 Tesla scanner, the following sequences of the brain were obtained from 60 patients with BMS, 35 with SPMS and 21 age-matched healthy controls: a) dual-echo turbo spin-echo (TSE): TR/TE = 3300/16-98 ms, ETL = 5, slice thickness = 5 mm, matrix size = 256x256, FOV = 250x250 mm, 24 contiguous axial slices; b) 3D T1-Weighted MP-RAGE sequence: TR/TE = 11.4/4.4 ms, TI= 300 ms, flip angle = 15°, matrix size = 256x256, FOV = 256x256 mm; slab thickness = 160 mm, voxel size 1x1x1 mm. Neuropsychological tests exploring memory, attention and frontal lobe cognitive domains were administered in BMS patients. Total lesion volume (TLV) was measured on PD-weighted scans using a local thresholding segmentation technique (1). On MP-RAGE images, normalized brain volume (NBV) and total intracranial volume (ICV) were measured using the SIENAx software (2). An optimized version of for VBM analysis (3) was used to assess between-group differences in GM volumes on MP-RAGE scans, using SPM2 (4). A customized GM template was created from MP-RAGE scans of both healthy controls and MS patients, then segmented GM images were normalized onto the GM template and modulated to retain pre-normalization volume information. Prior to statistical analysis, images were smoothed with a 12 mm gaussian kernel. An Ancova model, with age, sex and ICV as nuisance covariates, was used to compare GM volumes between groups. SPM maps were thresholded at p=0.05, corrected for multiple comparisons.

Results

Twelve BMS patients (20%) had an abnormal performance in three or more neuropsychological tests, thus fulfilling pre-defined criteria for cognitive impairment. Compared to HV, SPMS patients showed a pattern of widespread GM atrophy, while BMS had reduced GM volume in the subcortical and frontoparietal regions. In comparison with BMS patients, those with SPMS had significant GM loss in the both cerebellar hemispheres, as well as in the right nucleus dentatus. There was no differences in the pattern of regional GM atrophy between BMS patients with cognitive impairment and those without.

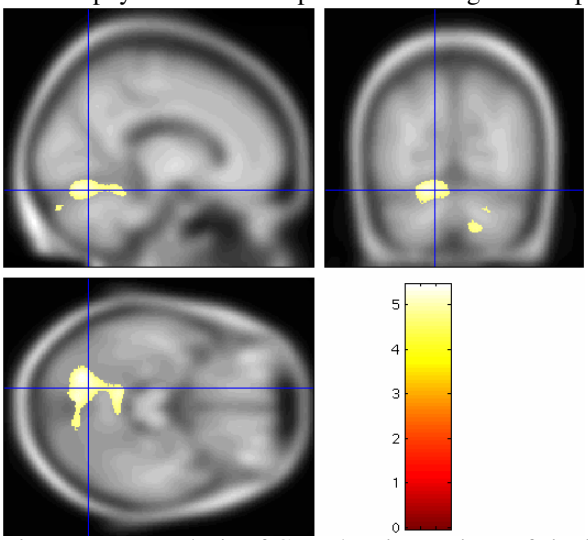

Figure.VBM analysis of GM, showing regions of significantly reduced GM volume in SPMS compared to BMS patients.

Conclusions

Cerebellar atrophy seems to be a major determinant of irreversible locomotor disability in MS.

References

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