REGIONAL BRAIN ATROPHY EVOLVES DIFFERENTLY IN MS PATIENTS ACCORDING TO THEIR CLINICAL PHENOTYPES

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Introduction

The progressive development of brain atrophy is a well-known feature of MS[1] and it is viewed as a potential marker of irreversible tissue damage.[1] Although the magnitude of brain atrophy seems to be greater in patients with progressive MS than in those in the relapsing-remitting (RR) phase, recent studies have demonstrated considerable tissue loss also in patients in the early, RR phase of the disease[2] and in patients with clinically isolated syndromes suggestive of MS.[3] Cross-sectional and longitudinal studies have shown that measurements of brain atrophy correlate better with clinical disability and neuropsychological functioning than other conventional MR metrics, including T2- and T1-lesion volumes.[1]

In this study, we used the Structural Image Evaluation using Normalization of Atrophy (SIENA) software[4] to spatially characterize the evolution of brain atrophy in MS patients with different disease phenotypes in order to investigate whether regional brain atrophy development might be one additional factor characterizing the phenotypical variation of the disease.

Patients and methods

We studied 70 patients with clinically definite MS (26 men, 44 women; mean age=49.9 years, range=25-68 years; median disease duration=10 years, range=0-34 years; median EDSS=5.0, range=0.0-8.0). Twenty patients had a RRMS, 19 a secondary progressive (SP) MS, and 31 a primary progressive (PP) disease course. In each subject, brain MRI scans were obtained at study entry and after 15 months using the same 1.5 Tesla scanner on a regular course of maintenance. During each session, a dual-echo turbo spin echo and a T1-weighted conventional spin echo sequence were acquired. At follow-up, patients were carefully repositioned following published guidelines.[5] Changes in regional atrophy were assessed on T1-weighted scans using the SIENA[4] software. The method calculates boundary movement between time points, after a skull-based coregistration between them. In the results, negative values reflect local volume reduction, while positive values reflect local volume increase. After standardization to the Talairach space, between-group differences were assessed using statistical parametric mapping (SPM99).

Results

During the follow-up, RRMS patients developed significant atrophy around the ventricular system (including the lateral, third, aqueduct and fourth ventricles). The putamen, the corpus callosum, the cingulate sulcus, the hippocampus, the parieto-occipital fissure, the lateral fissure and several regions of the frontal, parietal and occipital lobes, bilaterally, were also involved. They also developed significant atrophy of the pericerebellar spaces and along the tentorium of the cerebellum, the right middle temporal gyrus and the left insula. In these patients, the enlargement of the ventricular system was significantly correlated with changes in T2 (r ranging from -0.72 to -0.81) and in T1 (r ranging from -0.69 to -0.76) lesion volumes during the follow-up. Changes in EDSS scores during the study period were significantly correlated with development of atrophy of the lateral ventricles (r ranging from -0.69 to -0.73), the left superior parietal gyrus (r=-0.82), the left calcarine sulcus (r=-0.79), the left lingual gyrus (r=-0.71), the left pericerebellar spaces (r=-0.80) and the right lateral fissure (r=-0.71). During the follow-up, SPMS patients developed significant atrophy of the left cingulate sulcus, the pulvinar, bilaterally, the head and the tail of the left caudate nucleus, the tail of the right caudate nucleus, the anterior orbital gyrus, bilaterally, the left middle temporal gyrus, the left insula, the left mammillary body, the right inferior portion of the lateral fissure, the right fourth ventricle and several regions of the frontal, parietal and occipital lobes. In these patients, change in T2 lesion volumes during the follow-up was significantly correlated with development of atrophy of the left cingulate sulcus (r=-0.74), the left inferior frontal gyrus (r=-0.71), the left orbital gyrus (r=-0.75), the left insula (r=-0.71), and the right inferior portion of the lateral fissure (r=-0.76). Changes in EDSS scores during the study period were significantly correlated with development of atrophy of the intra-occipital gyrus, bilaterally (r=-0.86); the right supramarginal gyrus (r=-0.83), the right superior frontal gyrus (r=-0.70), the left cingulate sulcus (r=-0.70) and the tail of the left caudate nucleus (r=-0.73). During the follow-up, PPMS patients developed significant atrophy of the central sulcus, bilaterally, the head of the left caudate nucleus, the insula, bilaterally, the middle temporal gyrus, bilaterally, the middle occipital gyrus, bilaterally, the parahippocampal gyrus, bilaterally, the prepontine and quadrigeminal cisterns, several regions of the frontal and parietal lobes, the right lateral ventricle and the right lateral fissure. In these patients, change in T1 lesion volume during the follow-up was significantly correlated with development of atrophy of the central sulcus, bilaterally (r ranging from -0.58 to -0.65), the left angular gyrus (r=-0.69) and the head of the left caudate nucleus (r=-0.61). Changes in EDSS scores during the study period were significantly correlated with development of atrophy of the right middle frontal gyrus (r=-0.59), the right lateral fissure (r=-0.57), the left angular gyrus (r=-0.60), and the prepontine cistern (r=-0.57).

Discussion

These data suggest that, in MS, brain atrophy develops involving different structures in the different phases of the disease. While ventricular enlargement is predominant in the RR forms, cortical atrophy seems to be more important in the progressive forms of MS. In addition, measures of regional brain atrophy correlated significantly with disability, suggesting that the application of such an approach to the study of MS patients is a promising tool to bridge the gap between clinical and MRI findings in MS.

References

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