SHORT-TERM EVOLUTION OF BRAIN TISSUE DAMAGE IN PATIENTS WITH PROGRESSIVE MULTIPLE SCLEROSIS: AN IN VIVO STUDY USING DIFFUSION TENSOR MRI

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Introduction

The mechanisms underlying the progressive course of multiple sclerosis (MS) are still unclear. Diffusion tensor (DT) MRI can provide quantitative and accurate estimates of both conventional MRI-visible and MRI-occult tissue damage in the brain of MS patients (1, 2). The present study was performed: a) to assess the value of measures derived from DT-MRI of the brain for the *in vivo* investigation of the patterns of accumulation of irreversible tissue damage in patients with primary progressive (PP) MS; b) to compare the evolution of DT-MRI findings in patients with PP and secondary progressive (SP) MS; c) to investigate whether DT-MRI changes correlate with the clinical evolution of progressive MS over a short-term period.

Patients and Methods

Fifty-four patients with PPMS (mean age: 51.0 years) and 22 patients with SPMS (mean age: 48.3 years) were studied at baseline and after a mean follow-up of 15.0 months. Using a 1.5 T magnet, the following scans of the brain were acquired on both occasions: 1) dual-echo turbo spin echo (SE) (TR/TE/NEX=3300/16-98/1; number of slices: 24, contiguous, 5-mm thick); 2) pulsed-gradient spin–echo (PGSE) echo-planar (inter-echo spacing = 0.8, TE = 123; number of slices: 10, contiguous, 5-mm thick), with diffusion gradients applied in nine non-collinear directions; 3) T1-weighted SE (TR/TE/NEX=768/15/2; number of slices: 24, contiguous, 5-mm thick). The duration and maximum amplitude of the diffusion gradients were 25 msec and 21mTm^{-1}, giving a maximum b factor in each direction of 1044 s mm^{-2}. A local thresholding technique was used for MS lesion segmentation and brain total lesion volumes (LV) were measured. Percentage brain volume changes (PBVC) were computed using a fully-automated technique (SIENA) (3). After correction for eddy current-induced distortion, the diffusion tensor was estimated linearly for every voxel. Next, mean diffusivity (MD) and fractional anisotropy (FA) were derived for each voxel. FA and MD maps of the normal-appearing brain tissue were created by superimposing the lesion outlines and nulling out the corresponding regions. Normal-appearing white matter (NAWM) and grey matter (NAGM) were segmented using an automated technique based on statistical parametric mapping. NAWM and NAGM MD and FA histograms were produced and analyzed as previously described (4).

Results

In both patient groups, the average brain T2 and T1 LV did not change significantly over the study period, whereas a significant increase of average lesion MD ($p=0.01$) and of average NAGM MD ($p=0.007$), as well as a significant decrease of average NAGM FA ($p<0.001$) were found at follow-up. Average lesion MD was found to be significantly higher in SPMS than in PPMS patients ($p=0.02$). No significant differences between PPMS and SPMS patient groups were found as regards the on-study changes of any MRI-derived measure. No significant correlations were found between the percentage changes of DT MRI-derived measures and those of LV and PBVC. At follow-up, 10 PPMS patients (19%) and 5 SPMS patients (23%) showed a significant EDSS score increase. None of the changes of conventional and DT MRI-derived parameters significantly differed between the subgroups of patients with and without clinical worsening.

Conclusions

Over a short-term period of follow-up, DT MRI can detect subtle tissue changes occurring beyond the resolution of conventional MRI in the NAGM of PPMS and SPMS patients. The evolution of DT MRI-detectable gray matter damage does not seem to merely reflect the accumulation of T2-visible lesions or the progressive reduction of brain volume observed during the same period of time. DT MRI-derived measures of brain damage do not correlate with the worsening of patients' disability over a one-year period. Studies with longer follow-up durations, including an assessment of cognitive functions, are, therefore, warranted to clarify whether these measures may have any prognostic value for the clinical evolution of progressive MS.

References

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