PATHOLOGICAL DAMAGE IN MS ASSESSED BY DIFFUSION-WEIGHTED AND MAGNETIZATION TRANSFER MRI

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Introduction

In multiple sclerosis (MS), conventional magnetic resonance imaging (MRI) does not detect subtle abnormalities in the normal-appearing white matter (NAWM). Magnetization transfer imaging (MTI) and diffusion-weighted imaging (DWI), may go some way towards overcoming these limitations. MT and diffusion characteristics can be analyzed either on a region-of-interest (ROI) basis giving information about individual lesions and discrete areas of the NAWM, or on a more global basis using histograms[1], an approach that allows evaluation of large portions of the brain tissue, thus providing an assessment of both macro- and microscopic lesion burden in MS. The aims of this study were to examine both the MT and diffusion characteristics of individual lesions, and to assess the more subtle abnormalities seen using both techniques.

Materials and methods

We studied 35 patients with relapsing-remitting MS and 24 age- and sex-matched controls. The following scans were performed a) dual-echo conventional spin echo (TR = 3300, TE = 30-80; 24 contiguous, 5 mm-thick slices); b) 2D gradient-echo (GE) (TR = 600, TE = 12, flip angle = 20°; 20 contiguous, 5 mm-thick slices) with and without an off-resonance RF saturation pulse (offset frequency = 1.5 kHz, Gaussian envelope duration = 16.4 ms, flip angle = 850°) (this scan was not obtained from controls); c) spin-echo echo-planar (EP) pulse sequence[2] (inter-echo spacing = 0.8, TE = 160; 24 contiguous, 5 mm-thick slices), which collects one T2-weighted and three identical isotropically diffusion-weighted images for each slice, designed to give an attenuation dependent only on the mean diffusivity ($\overline{D}$) (the b factor was 289 s mm^{-2}, in each of the 3 directions). From the two GE images, with and without the saturation pulse, MTR images were derived pixel-by-pixel according to the following equation: $MTR=(M_0-M_S)/M_0\times100$ in which M_0 is the signal intensity without the saturation pulse and M_S is the signal intensity when the saturation pulse is applied. From the EP scans, an image of $\overline{D}$ was produced by performing the following calculation on a pixel-by-pixel basis: $\overline{D}=(-1/3b)\ln(S_{av}/S_1)$, where S_{av} is the average of the 3 DW signal intensity, and S_1 is the T_2-weighted signal intensity (with b≈0). From the co-registered MTR and $\overline{D}$ maps, 10 slices covering the brain tissue around the lateral ventricles were selected. Histograms of the MTR and $\overline{D}$ images were produced after manual removal of the extra-cerebral tissue and of cerebro-spinal fluid. For each histogram, the following measures were then derived: the relative peak height, the peak position and the mean brain MTR and $\overline{D}$. MTR and $\overline{D}$ values of MS lesions and NAWM (ROIs placed in 4 different brain areas, far from MS lesions) were also studied.

The Student t Test for non-paired data was used to compare a) $\overline{D}$ in the NAWM and histogram-derived metrics of patients with those of controls; b) MTR and $\overline{D}$ values in NAWM of patients with those in T2-visible lesions. The Spearman Rank Correlation Coefficient was used to evaluate the correlations between MTR, $\overline{D}$ and T2-visible lesions in patients.

Results

MS patients had significantly higher $\overline{D}$ in all the NAWM areas studied. Average lesion MTR was 37.7% (SD = 2.1%) and average lesion $\overline{D}$ was 1.085 (SD=0.1) $\times10^{-3}$mm^2 s^{-1}. The latter was significantly different from $\overline{D}$ in the NAWM ($p<0.001$) The $\overline{D}$ histogram-derived metrics from the controls and the MS patients are reported in table 1, and average $\overline{D}$ histograms from patients and controls are presented in Figure 1. In MS patients, median T2 lesion volume was 8.7 ml (range=3.3-19.4 ml), average MTR from the histogram was 38.9% (SD=1.1%), mean histogram peak height was 117.7 (SD=16.9) and mean histogram peak position was 34.3% (SD=1.2%). In MS lesions, an inverse correlation between average lesion MTR and $\overline{D}$ ($r=-0.7$, $p<0.0001$) was found. When considering regional NAWM ROIs, a moderate inverse correlation ($r=-0.4$, $p=0.001$) between MTR and $\overline{D}$ was found only for the ROIs located in the posterior periventricular white matter. No correlation was found for any of the other brain regions studied or for average MTR and $\overline{D}$ values taken from the histograms.

Table 1. Three properties of the histograms of the mean diffusivity ($\overline{D}$) are shown for patients and controls.

	Controls	MS patients	p*
Average $\overline{D}$ (SD) [$\times10^{-3}$ mm^2 s^{-1}]	0.907 (0.021)	0.950 (0.038)	<0.001
$\overline{D}$ peak height (SD)	19.01 (1.70)	18.00 (1.27)	0.01
$\overline{D}$ peak position (SD) [$\times10^{-3}$ mm^2 s^{-1}]	0.854 (0.018)	0.877 (0.038)	0.003

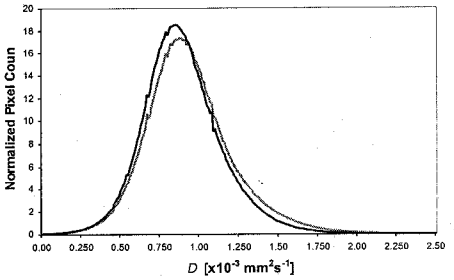

Fig 1. Mean diffusivity ($\overline{D}$) ($\times10^{-3}$ mm^2 s^{-1}) histograms from patients (gray line) and controls (black line).

Conclusions

DWI and MTI are able to detect the widespread subtle changes occurring in the NAWM of MS patients. Tissue loss can increase $\overline{D}$ and decrease MTR, while gliosis or inflammatory processes can act as "restricting" barriers thus resulting in a decreased diffusivity, but still determining decreased MTR values. In MS lesions, the observation that the MTR and $\overline{D}$ are strongly inversely correlated suggests that, inside lesions, the increase of water diffusivity is related to the degree of demyelination and axonal loss.

References

1. Van Buchem M.A. et al, Magn. Reson. Med. 36, 632-9 (1996).
2. Cercignani M: et al, J. Magn. Reson. 140, 58-68 (1999).