A QUANTITATIVE STUDY OF WATER DIFFUSION IN MS LESIONS AND NAWM USING ECHO-PLANAR IMAGING

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Introduction

In multiple sclerosis (MS), diffusion-weighted imaging (DWI) is promising for overcoming some of the limitations of conventional magnetic resonance imaging (MRI), including the lack of specificity to the heterogeneous pathological substrates of MS lesions and the inability to detect subtle abnormalities occurring in the so-called normal-appearing white matter (NAWM) (1). DWI provides a unique form of MR contrast which enables diffusion of water molecules to be measured, and, as a consequence, pathological processes which modify tissue integrity, thus reducing «restricting» barriers, can result in increased apparent diffusion coefficient (ADC). Aims of this study were: a) to compare NAWM-ADC values from patients with those from white matter of controls; b) to evaluate whether lesions classified on the basis of their appearance on enhanced T1-weighted scans have different ADC values and c) to investigate the relationship between diffusion changes in lesions and NAWM to elucidate the nature of NAWM changes in MS.

Materials and methods

We studied 35 relapsing-remitting MS patients (median Expanded Disability Status Scale [EDSS] score 1.5, range=1.0-3.0) and 24 sex- and age-matched normal controls. Each subject underwent the following scans: dual-echo conventional spin echo (CSE) (TR = 3300, TE = 30-80); T1-weighted CSE (TR = 680, TE = 17) obtained 10 minutes after the injection of 0.1 mmol/kg of gadolinium-DTPA (this sequence was not obtained from controls). For these two scans, 24 contiguous, 5 mm-thick slices were acquired. A SE echo-planar pulse sequence (inter-echo spacing = 8000, TE = 160) was also obtained, collecting one T2-weighted and three DW images for each slice (total number of slices: 24, contiguous, slice thickness: 5mm) with identical diffusion-encoding waveforms, designed to give an attenuation dependent only on the trace of the diffusion tensor (Tr{**D**}) and a resulting b factor of 289 s mm^{-2}, in each of the read, phase-encode and slice-selection directions (isotropically-weighted imaging) (2). Lesions were identified on the proton-density (PD)-weighted scans and marked on the hard copies by two observers by agreement. Using post-contrast T1-weighted scans, these lesions were classified as enhancing or non-enhancing. Non-enhancing lesions were classified as T1-isointense or hypointense. DW images were then realigned to correct for misregistration due to eddy currents. An image of the ADC (= Tr{**D**}/3) was produced by performing the following calculation on a pixel-by-pixel basis: ADC = -(1/3b)ln (S_{av} /S_1), where S_{av} is the average DW signal intensity (to improve the signal-to-noise ratio) and S_1 is the T_2- weighted signal intensity (with b ≈ 0). Then, a single observer, unaware of lesion classification, displayed the dual-echo images on a computer screen and, using marked hardcopies as a reference, outlined these lesions on the PD-weighted images using a semi-automated segmentation technique based on local thresholding. The outlined regions of interest (ROI) were then mapped onto the co-registered ADC maps, and the areas and ADC of each lesion measured. Co-registration of images was performed using a surface-matching technique, based on mutual-information. ADC values of NAWM in different brain regions were also studied. The NAWM areas were selected on the dual-echo scans. They had not to have adjacent lesions either in the same slice and in the slices above and below. Square ROI of uniform size (3x3 pixels) were placed bilaterally in the white matter of the following areas: the pons, the cerebellar hemispheres, the internal capsules, the anterior and posterior portions of the corpus callosum, the temporal, parietal, occipital and frontal lobes (in regions far from ventricles and cortical gray matter). Two ROI were also placed close to the anterior and posterior parts of the body of the lateral ventricles and one close to the cortical gray matter of the frontal lobe. The outlined NAWM regions were then transferred on to the co-registered ADC maps. Using the same methodology, ADC of the same brain regions were measured from controls.

Results

Mean ADC value from the 747 NAWM areas from MS patients was 0.821 x 10^{-3} mm^2/sec (SD = 0.18 x 10^{-3} mm^2/sec) and was significantly higher ($p<0.0001$) than that from the 528 white matter areas of controls (0.727 x 10^{-3} mm^2/sec with a SD = 0.09 x 10^{-3} mm^2/sec). Mean ADC values from the NAWM of MS patients, for each of the anatomical regions studied, were significantly higher than those from controls (Table 1). A total of 173 hyperintense lesions were identified on the dual-echo scans from MS patients. The mean ADC value for these lesions was 1.085 x10^{-3} mm^2/sec (SD = 0.10 x10^{-3} mm^2/sec) and it was significantly higher ($p<0.0001$) than the mean ADC of NAWM. There was no significant correlation between the average ADC values in lesions and NAWM ($r=0.18$). No significant difference in ADC values was found between enhancing (n=20, mean ± SD = 1.039 ± 0.17 x 10^{-3} mm^2/sec) and non-enhancing lesions (n=153, mean ± SD = 1.040 ± 0.14 x 10^{-3} mm^2/sec), whilst the mean ADC value of T1-hypointense lesions (n=60, mean ± SD = 1.115 ± 0.13 x 10^{-3} mm^2/sec) was significantly higher ($p<0.0001$) than the mean ADC value of T1-isointense lesions (n=93, mean ± SD = 0.995 ± 0.13 x10^{-3} mm^2/sec).

Table 1. Mean ADC values (SD) in different white matter areas from controls and MS patients.
ADC values are expressed in 10^{-3} mm^2 /sec.

	Controls	MS	p
All areas	0.727 (0.08)	0.747 (0.18)	0.0001
Cerebellum	0.690 (0.21)	0.701 (0.26)	0.01
Pons	0.695 (0.12)	0.725 (0.43)	0.0001
Temporal lobe	0.700 (0.14)	0.762 (0.41)	0.0001
Occipital lobe	0.699 (0.12)	0.738 (0.37)	0.0001
Parietal lobe	0.701 (0.14)	0.754 (0.47)	0.0001
Frontal lobe	0.697 (0.14)	0.721 (0.31)	0.0001
Subcortical	0.751 (0.12)	0.916 (0.15)	0.0001
Posterior periventricular	0.795 (0.07)	0.939 (0.17)	0.0001
Anterior periventricular	0.716 (0.12)	0.813 (0.10)	0.0001
Corpus callosum	0.763 (0.13)	1.128 (0.33)	0.0001
Internal capsule	0.787 (0.09)	0.865 (0.09)	0.0001

Conclusions

This study shows that DWI is able to quantify the severity of tissue disruption in MS lesions. It also confirms the pathological heterogeneity of enhancing lesions (1) and that increased diffusion can be measured in the NAWM of different anatomical regions in the brain from MS patients. NAWM changes are likely to be independent of larger abnormalities, as suggested by the lack of correlation between lesion and NAWM ADC values.

References

1. Filippi, M., Neurology, 53, S18, 1999.
2. Cercignani, M., Horsfield, M.A., J Magn Res, 140, 58, 1999.