Increased Fractional Anisotropy in cortical lesions in multiple sclerosis

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INTRODUCTION. Diffusion tensor imaging (DTI) of cortical lesions in multiple sclerosis (MS) can potentially provide important insights into their microstructural environment and underlying pathology. These lesions typically elude detection by conventional magnetic resonance imaging (MRI) (1). As a result, all DTI studies in the cortex to date have focused on the normal-appearing gray matter (NAGM) instead (2,3). However, a direct probe of the cortical lesions would be more informative. In this work, we identify cortical lesions using a combination of double inversion recovery (DIR) (4) and phase-sensitive inversion recovery (PSIR) (5,6), and overlay them on DTI maps in order to perform the first direct focal analyses of cortical lesions in MS.

METHODS. MRI was performed on seven MS subjects and eight normal controls using a Philips 3T Intera scanner with a SENSE-compatible head coil. The scan protocol included axial DIR, PSIR, and single-shot EPI diffusion tensor imaging with 21 directions using an icosahedral scheme (7). Each scan had 44 slices of 3 mm thickness and reconstructed image matrix of 256x256 over a 24 cm square FOV. Inversion times were 325/3400 ms for DIR and 400 ms for PSIR. Diffusion-weighted images were first corrected for eddy-current distortions using a Philips PRIDE workstation, and subsequently registered to the DIR images using a non-linear model from the AIR software package (8). Fractional anisotropy (FA) and mean diffusivity (MD) maps were then computed from the post-registered DTI data. For each patient, cortical lesions were identified on DIR and PSIR as described elsewhere (5,6). An ROI was placed on each lesion on the DIR image and the mean FA and MD values for that ROI were recorded from the DTI overlay. For comparison, corresponding ROIs of equal size were also drawn in the contralateral NAGM for each lesion, and ROIs were also placed in normal gray matter of control subjects. To avoid CSF contamination or misregistration artifacts, a cortical ROI was excluded from the analysis if MD > 0.002 mm^2/sec or FA > 0.2. Statistical analysis of the mean FA and MD for each group (lesion, contralateral, and control) was performed with Bonferroni corrections for multiple comparisons.

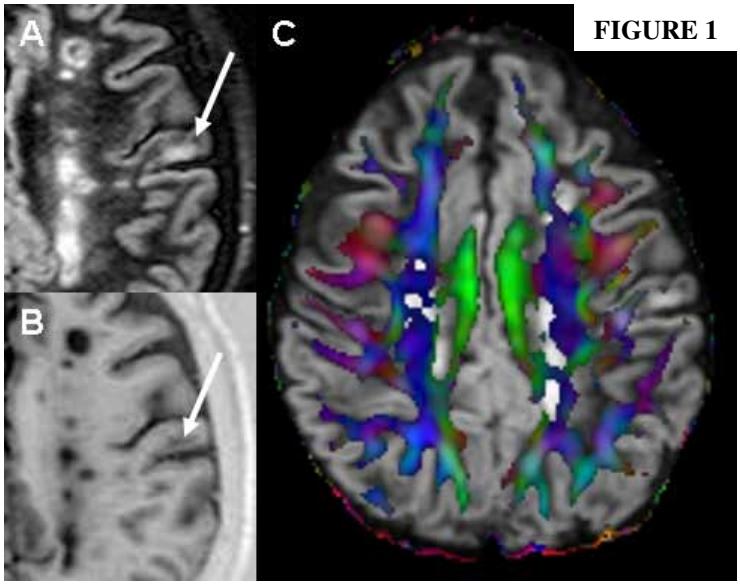

FIGURE 1

RESULTS. An example of a cortical lesion is shown in Figure 1 (white arrows). The lesion is hyperintense on DIR (a) and is hypointense on PSIR (b), with the latter providing localization within the cortical ribbon. A color-coded FA map overlay (c) shows the co-registration of major white-matter tracts to the DIR image. The red, green, and blue colors indicate R/L, A/P, and S/I directions, respectively. The mean DTI measurements for each group are summarized in Table 1. In cortical lesions, MD and FA were significantly higher relative to controls ($p < 0.0001$). The lesion FA values were also significantly higher than in the contralateral NAGM ($p < 0.0001$). MD and FA were also significantly elevated for contralateral NAGM relative to controls ($p = 0.0005$). An overall increasing trend in the DTI metric values from normal control GM to contralateral NAGM to cortical lesions was observed.

TABLE 1	MD (mm^2/sec)	FA
Normal controls	0.0009 ± 0.0001	0.08 ± 0.02
Contralateral NAGM	0.0010 ± 0.0002	0.09 ± 0.03
Cortical lesions	0.0010 ± 0.0002	0.13 ± 0.04

DISCUSSION. The primary finding of this study was that mean FA values of cortical lesions in MS were significantly higher relative to the contralateral NAGM or GM in normal controls. A possible mechanism for the increased FA could be a loss of dendritic arborization, which is known to contribute to diffusion anisotropy in normal gray matter (9). There is histological evidence in the literature for targeted transection of neurites, as well (10).

CONCLUSION. Focal analysis of cortical lesions in MS using DTI reveals that the mean FA increases relative to contralateral NAGM and normal controls.

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