MEAN DIFFUSIVITY AND FRACTIONAL ANISOTROPY HISTOGRAM ANALYSIS OF THE CERVICAL CORD IN PATIENTS WITH MULTIPLE SCLEROSIS.

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Introduction

The spinal cord is frequently involved in MS and because it contains important sensory and motor tracts, spinal cord damage may cause important disability in patients with MS[1]. Diffusion-tensor imaging (DTI) provides quantitative information about the structural and orientational features of the nervous system, and it is an invaluable tool for detecting MS-related subtle damage. In this study, we obtained mean diffusivity (MD) and fractional anisotropy (FA) histograms of the cervical cord from a large cohort of MS patients, in order to investigate whether diffusion histogram-derived metrics are significantly different between controls and patients and among different MS phenotypes, and whether cord damage, measured using this technique, is correlated with brain dual-echo lesion load and patient's disability.

Patients and methods

We studied 45 patients with clinically definite MS (12 men, 33 women: mean age=38.6 years, range=25-61 years; median disease duration=10.5 years, range=1-37 years; median EDSS=4.0, range=1.0-7.5). Twenty-two patients had a relapsing remitting (RR) and 23 a secondary progressive (SP) disease course. Twenty-one sex- and age-matched volunteers served as controls.

Using a 1.5 T scanner a SENSE-EPI sequence[2] was obtained from all subjects to calculate the DT images of the cervical cord. During the same session, a dual-echo sequence of the brain was also acquired.

The DT was calculated for each voxel, and quantitative indexes of diffusion (MD and FA) were derived from it. Then, the cervical cord from C1 to C5 was segmented from FA and MD maps, using a semi-automated segmentation technique, and normalized intensity histograms were produced. Finally, average histogram MD and FA, MD and FA histogram peak height, and MD and FA histogram peak position were derived. A Student t test for non-paired data was used to compare MD and FA histogram-derived indexes between controls and MS patients and between controls and the different MS phenotypes. Univariate correlations between histogram-derived metrics and conventional MRI and clinical parameters were assessed using the Spearman Rank correlation coefficient.

Results

In the Table, MD and FA histogram-derived metrics of MS patients and controls are reported.

	Control Subjects	All MS Patients	RRMS	SPMS
Average MD (SD) [$mm^{-2}s^{-1}x10^{-3}$]	1.214 (0.08)	1.279 (0.12)	1.256 (0.10)	1.304 (0.14)
MD Peak Height (SD)	107.6 (18.5)	106.0 (21.8)	110.7 (19.2)	101.8 (22.3)
MD Peak Location (SD) [$mm^{-2}s^{-1}x10^{-3}$]	1.15 (0.09)	1.23 (0.12)	1.19 (0.11)	1.27 (0.13)
Average FA (SD) [%]	0.43 (0.03)	0.36 (0.06)	0.38 (0.05)	0.34 (0.05)
FA Peak Height (SD)	63.7 (16)	65.3 (13.4)	66.2 (11.4)	65.2 (15.1)
FA Peak Location (SD) [%]	0.47 (0.076)	0.38 (0.075)	0.40 (0.077)	0.37 (0.07)

Compared to controls, MS patients had significantly higher average MD and MD histogram peak location ($p=0.01$ for both the comparisons) and lower average FA and FA histogram peak location ($p<0.0001$ for both the comparisons). The differences in FA histograms metrics between patients and controls remained significant even when considering the two subgroups of MS patients, separately. SPMS patients had also significantly higher average MD and MD histogram peak location ($p=0.01$ for both the comparisons) than controls and lower average FA than RRMS patients ($p=0.009$).

In MS patients, significant correlations were found between: a) cord average FA and EDSS score ($r=-0.63$, $p<0.0001$) and b) cord average MD value and the EDSS score ($r=0.49$, $p=0.003$). No correlations were found between cord DT MRI metrics and brain dual-echo lesion load.

Discussion

These data show that DT histogram-derived metrics of the spinal cord are significantly different between MS patients and controls and that MS pathology in the cervical cord is greater in the progressive forms of the disease. The correlations found between DT metrics of cervical cord damage and clinical disability suggests that an accurate assessment of cervical cord damage in MS provides information that might be useful to explain the clinical manifestations of the disease, and which is largely independent of brain tissue damage.

References

1. Tartaglino LM, Friedman DP, Flanders AE, et al. Radiology 1995;195:725-732.
2. Cercignani M, Horsfield M, Agosta F, et al. AJNR Am J Neuroradiol 2003;24:1254-1256.