

Atrophy and diffusion tensor MRI metrics of brain fiber bundles. Application to primary progressive multiple sclerosis patients

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Introduction

Recent applications of diffusion tensor (DT) magnetic resonance imaging (MRI) in primary progressive (PP) multiple sclerosis (MS) patients have contributed to the understanding of the nature of the damage in the grey and white matter (WM) of the brain (1). Nevertheless, correlations with clinical disability are weak. Regional studies have shown promising results, when DT-derived metrics were averaged over clinically eloquent sites (2,3). Also, brain atrophy is a well-known feature of MS which is viewed as a potential marker of irreversible tissue damage (4).

In this study, we wished to examine whether the correlation of MRI measures with disability could improve when considering the tissue damage limited to the pyramidal tracts (PYT) and the corpus callosum (CC), instead of considering the whole brain. To this aim, an index of atrophy and DT derived metrics were obtained for the PYT and the CC.

Methods

We studied 47 PPMS patients (M/F: 21/26, age: 50.8±9.6 y, median EDSS score [range]: 5.5 [2.5-7.5]) and 16 healthy volunteers (M/F: 6/10 age: 40.9±11.0 y). The following brain scans were performed using a 1.5 Tesla scanner (Vision, Siemens, Erlangen, Germany):

- pulsed-gradient spin-echo (PGSE) echo-planar sequence (inter-echo spacing=0.8, TE=123), with diffusion-encoding gradients applied in 8 non collinear directions. Ten contiguous axial slices, with 5 mm slice thickness, 128x128 matrix and 250[mm]x250[mm] field of view.
- dual-echo turbo spin echo (TSE) (TR=3300, first echo TE=16, second echo TE=98, echo train length [ETL]=5). Twenty-four contiguous axial slices, with 5 mm slice thickness, 256x256 matrix and 250[mm]x250[mm] field of view.

DW images were first corrected for distortion induced by eddy currents; then the diffusion tensor was estimated by linear regression (5) and fractional anisotropy (FA) and mean diffusivity (MD) maps calculated (6). Subsequent steps consisted in the creation of tract probability maps from healthy volunteer data and their application to patient data as described in (3). Because of the presence of atrophy, a non linear deformation algorithm (7) was used in all steps requiring the normalization onto the standard space. Also, as a consequence of the augmented ability of the algorithm to compensate for local morphological differences, a new atlas was created using the same deformation algorithm and, to improve the overlay between WM fiber bundles, FA maps were used to drive the transformation. To this aim, an FA map was chosen as a temporary atlas and all other maps from healthy subjects were registered to the temporary atlas. The average of the registered FA maps was then re-sampled with the inverse of the average deformation field to achieve a morphological mean as well as an intensity mean of the group. The average map was again used as a target atlas during the next iterations of the process to reduce the effect of the first template chosen from a subject (8). Three iterations were used to create the final FA atlas.

The non-linear transformation between FA maps of all subjects and the atlas was then calculated; in controls it was applied to tracts obtained from tractography (3), before their average to produce tract probability maps; in patients it was used to transform MD and FA maps and to calculate the determinant of the jacobian (J) of the transformation. This last is a scalar summarizing the area change. The probability maps were then applied to the transformed MD and FA after exclusion of lesions and to J maps and average values obtained. The correlation of these variables with the expanded disability status scale (EDSS) scores (9) and the lesion load limited to the considered tracts were assessed. Also, two groups of patients were formed, according to the progression of disability after 1 year, and a two-sample t-test was performed to assess the significance of the difference of averages between groups. A p value<0.05 was considered significant.

Results

A positive correlation was found between the lesion load and the MD in the PYT and CC; this correlation was only weak with the index of atrophy in the CC (Table 1). No correlations were found with the EDSS score. Compared to patients without clinical disability progression, those who progressed had significantly higher atrophy (p=0.009) of the CC.

Table 1. Spearman correlation coefficients.

	PYT MD	PYT FA	PYT atrophy	CC MD	CC FA	CC atrophy
Lesion load	0.616	N.S.	N.S.	0.673	-0.520	-0.437

N.S. = not significant

Conclusions

With the approach described here we were able to characterize atrophy of the PYT and the CC. Also DT derived metrics were obtained within these fiber bundles. Results showed a strong influence of the lesion load on the MD values obtained within the tracts, suggesting that MD variations may reflect a damage caused by Wallerian degeneration. Atrophy of the CC was found able to predict disability progression, suggesting that this index may be a valuable measure of irreversible tissue damage.

References

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