COGNITIVE DYSFUNCTION IN BENIGN MS IS ASSOCIATED WITH INCREASED SEVERITY OF CORPUS CALLOSUM DAMAGE

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Introduction

In benign MS (BMS), cognitive dysfunction is associated with an increased severity of conventional MRI-occult white and grey matter damage. Based on the directional information provided by the proton self-diffusion measured with diffusion tensor (DT) MRI, we have developed a method (1,2) which enables us to track and investigate clinically eloquent pathways involved in cognitive performances, such as corpus callosum (CC). The aim of the present study is to investigate the relationship between the cognitive profile of BMS patients and the extent of tissue damage in the CC.

Methods

We studied 54 BMS patients, defined as having a disease duration of 15 years or more and an Expanded Disability Status Scale (EDSS) score of 3.0 or less, and 16 healthy volunteers. The following brain scans were performed using a 1.5 Tesla scanner(Vision, Siemens, Elangen, 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.

Neuropsychological tests (NPT) exploring memory, attention and frontal lobe cognitive domains were administered.

DW images were first corrected for distortion induced by eddy currents; then the diffusion tensor was estimated by linear regression (3) and fractional anisotropy (FA) and mean diffusivity (MD) maps calculated (4). Subsequent steps consisted in the creation of tract probability map of the CC from healthy volunteer data and its application to patient data as described in (1). Because of the presence of atrophy, a non linear deformation algorithm (5) was used in all steps requiring the normalization onto the standard space. Also, to improve the overlay between WM fibre bundles, a new atlas was created using the same deformation algorithm and 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 (6). 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 summarizes the point-wise volume changes produced by the deformation: values less than unity reflect atrophy, whereas values greater than unity reflect hypertrophy (2). 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 NPT and lesion load (LL) limited to the considered tract were assessed. Also, two groups of patients were formed, according to the cognitive impairment, and a Mann-Whitney-test was performed to assess the significance of the difference of averages between groups. A p value<0.05 was considered significant.

Results

Nine BMS patients (17%) had an abnormal performance in three or more NPT, thus fulfilling pre-defined criteria for cognitive impairment (CI). There was no differences in CC atrophy index between congnitively impaired and unimpaired BMS patients. Patients with CI had significantly higher CC lesion load, and more pronounced MD abnormalities, than those without. There were significant correlations between the results of NPT exploring executive functions (mainly the PASAT test), and measures of FA and MD features from the CC (r values ranged from 0.31 to 0.52).

Conclusions

In BMS, cognitive dysfunction is associated with an increased severity of CC damage, in terms of both discrete lesions and fiber bundle disrupiton. Assessing regional damage with DT MRI may represent a rewarding strategy for a better understanding of BMS profile.

References

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