

Corticospinal Tract Degeneration Correlates with Clinical Disability in Multiple Sclerosis

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Introduction: Corticospinal tract (CST) is the longest descending pathway that originates from upper motor neurons and crosses over to the contralateral side in the medulla and regulates the fine motor activities, mainly of the contralateral limbs.^{1,2} Pathological studies³ using postmortem specimens from multiple sclerosis (MS) patients have reported widespread degeneration of axons and variable degree of astrocytosis along the trajectory of CST. A number of studies⁴⁻⁶ have reported significant alterations in diffusion tensor imaging (DTI) derived indices from normal appearing white matter (NAWM) and lesions in MS patients. However, assessment of specific white matter tract (e.g. CST) with imaging may improve the correlations with clinical disability measures such as expanded disability status scale (EDSS). In the present study, fiber tracking method was used to quantify the water diffusion changes along the course of whole CST in MS patients.

Materials and Methods: A cohort of 33 patients with clinical definite relapsing-remitting MS (with sporadic episodes of attacks) and 17 healthy subjects were included in this study. DTI was performed on a 3 Tesla MR system with a 12-channel phased-array head coil. MR imaging protocol included acquisition of structural images with standard parameters. DTI data were acquired using 30 non-collinear/non-coplanar directions with a single-shot spin-echo, echo-planar sequence using GRAPPA with acceleration factor of 2. Sequence parameters were as follows: TR/TE = 5400/88ms, NEX = 2, FOV = 23 x 23 cm², in-plane resolution = 1.8 x 1.8 x 3 mm³, matrix size=128x 128, number of slices=42 covering the whole brain, b = 1000 s/mm². The data were processed offline using DTI studio, version 3.0. The diffusion-weighted images were co-registered to the non-diffusion weighted (b = 0 s/mm²) images to minimize eddy-current and/or subject motion induced artifacts using affine transformation with automated image registration algorithm. The corrected raw images were combined to construct axial diffusivity (AD), radial diffusivity (RD), mean diffusivity (MD), and fractional anisotropy (FA) maps. Fiber tractography was performed on the basis of the fiber assignments derived by continuous tracking (FACT) method.⁷ Propagation in each fiber tract was terminated if a voxel with an FA value of ≤ 0.2 was reached or if the turning angles of 2 consecutive vectors were $\geq 41^\circ$. To reconstruct CST, 2 ROIs were segmented on transverse b0 images. The first ROI was drawn on cerebral peduncle using "OR" operation, whereas the second ROI was at the ipsilateral precentral gyrus using "AND" operation. Fibers projecting into the contralateral hemisphere were removed by "NOT" operation. To investigate the architectural integrity of CST, DTI parameters (AD, RD, MD and FA) were computed through the whole CST from controls and patients. Kolmogorov-Smirnov tests were used to determine the nature of data distributions. As the data did not depart from Gaussian distribution, two-tailed "t" tests assuming unequal variance were performed to look for differences in DTI parameters between the two groups. Logistic regression and receiver operating characteristic (ROC) analyses were also performed to ascertain the best model to discriminate MS subjects from controls. Spearman's correlation analyses between clinical scores (EDSS) and DTI parameters from patients were also performed.

Results: Figure 1a demonstrates CST overlaid on a color coded map from a representative MS patient. Figure 1b-d demonstrates segmented CST overlaid on b0 map through different regions of the brain. Significant reduction in FA (mean \pm SD; 0.598 ± 0.025 vs 0.579 ± 0.022 ; $p=0.020$) and significant elevation in MD ($0.747 \pm 0.031 \times 10^{-3}$ mm²/s vs $0.786 \pm 0.076 \times 10^{-3}$ mm²/s; $p=0.015$) was observed in patients compared to those values in controls. Trends towards increase in RD ($p=0.049$) and AD ($p=0.065$) were also observed in patients compared to controls. Variations in DTI parameters between controls and patients are shown in box-whisker plots (Fig. 2). Logistic regression and ROC analyses predicted a combination of MD and FA as the best model to distinguish patients from controls with a sensitivity of 88.2% and a specificity of 63.6%. A significant inverse correlation ($r=0.541$, $p=0.001$) between FA and EDSS and a moderate direct correlation ($r=0.347$, $p=0.051$) between RD and EDSS were observed from patients (Fig. 3).

Discussion and Conclusion: Our multiparametric analysis within the trajectory of CST revealed significant alterations in the DTI metrics in MS patients compared to those in controls. We believe that synergetic interaction between the MD and FA in regression analysis provided the best discriminatory model. Our findings support the hypothesis that there is a considerable degeneration of CST in MS patients characterized by predominant demyelination, axonal degeneration, and incoherent orientation of the fibers.³ Since EDSS is a clinical index heavily weighted on motor-sensory disability, a significant correlations between DTI parameters and EDSS from patients in the current study suggests that assessment of CST integrity has the potential to monitor disability and progression of the MS disease. Future studies are required to examine the correlation between regional specific abnormalities along the CST and functional disabilities in MS patients.

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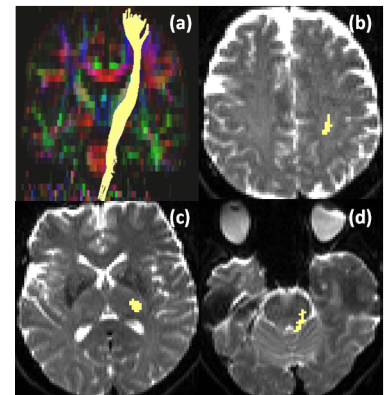


Fig 1. Representative reconstructed CST (yellow fibers) overlaid on color map is shown (a). Segmented CST overlaid on b0 images is shown at the levels of corona radiata (b), periventricular region (c) and brain stem (d) is shown.

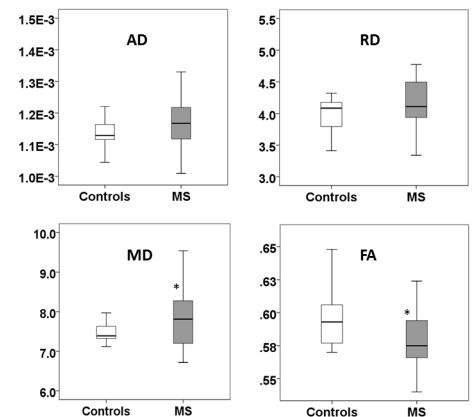


Fig 2. Box-and-whisker plots demonstrating the range of distribution of DTI parameters between controls and MS patients. Boxes represent the median, the 25th percentile, and the 75th percentile values. * represents significant difference.

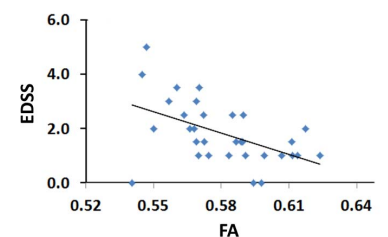


Fig 3. Spearman's correlation plot showing a moderate inverse relationship ($r=-0.541$, $P=0.001$) between FA and EDSS from patients.