Directional Diffusivities in Human Spinal Cord Correlate with Functional Outcome

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Introduction
The heterogeneity of lesion histopathology among individuals with multiple sclerosis (MS) is hypothesized to account for the differences in the disease course and prognosis.¹ Demyelination, axonal loss, and inflammation are key pathologic components. Axonal loss is believed to be a major contributor to long-term disability in MS.² Directional diffusivities derived from diffusion tensor imaging (DTI) measurements describe water movement parallel to \( \lambda_\parallel \) (axial diffusivity) and perpendicular to \( \lambda_\perp \) (radial diffusivity) axonal tracts. In this study, abnormalities in the specific cervical spinal cord tracts of stable MS and neuromyelitis optica (NMO) patients were quantified using \( \lambda_\parallel \) and \( \lambda_\perp \).

Material and methods

Subjects
Six stable MS patients with good recovery and two stable NMO patients with poor recovery were enrolled. Seventeen healthy volunteers were enrolled as normal control.

DTI
MR data were acquired using a neck receiver coil on a 3T scanner. An inner volume imaging technique was implemented,³ on a single shot spin-echo echo planar imaging (SE-EPI) diffusion sequence with fat-suppression. Diffusion weighted (DW) images were acquired transaxially (FOV 72 mm × 28.8 mm, matrix 80 × 32, TR/TE ~5000/99 ms, and slice thickness 5mm). A total of 18-20 imaging slices were broken into 3 groups (C1C2, C3C4 and C5C6) to account for the natural curvature of the spine. Data acquisition was peripherally gated. Twenty-five DW images with\( b \) values between 400-800 s/mm² and randomly distributed diffusion encoding directions were acquired in addition to two b0 images. Four repetitions, two of which with opposite gradient polarity, were averaged to increase signal-to-noise ratio (SNR). In addition, sagittal T2-weighted and axial steady state free precession (SSFP) images were acquired. The total scan time was about 1 hr.

Analysis
Regions of interest (ROI) in posterior column, left, and right cortical spinal tracts were placed on the b0 image based on anatomy of the cord. T2 hyperintense lesions and normal appearing white matter (NAWM) were defined from the anatomical images.

Results
Control
No significant differences were observed between cord segments, neither were left vs. right differences in posterior column or cortical spinal tracts. The values of \( \lambda_\parallel \) and \( \lambda_\perp \) in these normal white matter spinal cord tracts were 1.86 ± 0.13 \( \mu m^2/ms \) and 0.24 ± 0.05 \( \mu m^2/ms \), respectively.

MS patients good recovery (Fig. 1)
No significant differences (\( p > 0.05 \)) in \( \lambda_\parallel \) were observed in the posterior column (Fig. 1A vs. 1B) or cortical spinal tracts (not shown). Significant, though moderate, increases of (\( p < 0.05 \)) \( \lambda_\parallel \) were observed in C1-C4, but not in C5-C6.

NMO patients poor recovery (Fig. 2)
In subject 1 (Fig. 2, top), increased \( \lambda_\parallel \) and normal \( \lambda_\parallel \) in the posterior column, and normal \( \lambda_\parallel \) and \( \lambda_\perp \) in the cortical spinal tract were associated with sensory deficits, relatively preserved motor function, and mild functional impairment. In subject 2 (Fig. 2, bottom), increased \( \lambda_\perp \) (suggesting demyelination) in the posterior column, and increased \( \lambda_\perp \) and deceased \( \lambda_\parallel \) (axonal injury) in the cortical spinal tracts were associated with severe neurological deficits in both sensory and motor function systems.

Discussion
The normal \( \lambda_\parallel \) in MS patients with good recovery is reassuring of little permanent axonal damage in these patients. The moderate \( \lambda_\perp \) increase in C1-C4 suggests less intact myelin sheaths. The lack of an observed difference in C5-C6 is probably due to the increased measurement variability caused by respiratory motion at the lower part of the cervical region.

In summary, the good correlations between directional diffusivities and functional outcome presented herein, though preliminary, suggest that directional diffusivities are promising biomarkers as a surrogate endpoint for developing disease modifying therapies in MS patients.

References

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Figure 1. Group comparison of \( \lambda_\parallel \) and \( \lambda_\perp \) (y axis, \( \mu m^2/ms \)) in posterior column for each cord level (x axis) between normal control (A) and stable MS patients with good recovery (B). * indicates significant differences (\( p < 0.05 \)). Representative \( \lambda_\parallel \) (C, D; grey scale 0.5 – 2.5 \( \mu m^2/ms \)) and \( \lambda_\perp \) (E, F; grey scale 0 – 1.5 \( \mu m^2/ms \)) map for each group shows ROI definition for posterior column (black circle) and cortical spinal tracts (white circle).

Figure 2. \( \lambda_\parallel \) and \( \lambda_\perp \) (\( \mu m^2/ms \)) in the posterior column (PC) and cortical spinal tract (CST) of two stable NMO patients (each row) with poor recovery correlate with functional tests, respectively. VPT = vibration perception test, MMNT = manual muscle test, 9HPT = 9-hole peg test, 25FTW = 25-foot timed walk, and EDSS = expanded disability status scale. Representative \( \lambda_\parallel \) (B, D; grey scale 0.5 – 2.5 \( \mu m^2/ms \)) and \( \lambda_\perp \) (C, E; grey scale 0 – 1.5 \( \mu m^2/ms \)) map for each patient shows ROI definition for posterior column (black circles, left = dotted, right = solid) and cortical spinal tracts (white circle, left = dotted, right = solid).

References