Quantitative assessment of the cervical spinal cord damage in neuromyelitis optica using diffusion tensor imaging at 3T

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Introduction: Neuromyelitis optica (NMO, also known as Devic's disease) is an inflammatory and demyelinating disease of central nervous system that preferentially affects the optic nerve and spinal cord [1]. There has been the long debate of whether NMO is a variant of multiple sclerosis (MS), however clinical, immunological and pathological characteristics of NMO involving aggressive and severe attacks of optic neuritis and myelitis unlike MS, distinguish NMO from MS [1, 2]. Thus, diagnosis in the early stage of NMO is crucial in order to provide the proper treatment especially when frequent relapses and disabilities commonly occur. Currently, the assessment of spinal cord involvement in NMO has been mainly limited to neurophysiologic, serological testing and negative lesions in conventional T2-weighted (T2w) magnetic resonance imaging (MRI). Recently, MRI studies using diffusion tensor imaging (DTI) demonstrated that DTI indices can assess normal appearing brain tissues damage in NMO [3, 4]. However, tissue damage in cervical spinal cord has not been widely investigated due to technical limitations, although understanding pathological mechanism in the cervical spinal cord is crucial in research of NMO. In the present study, therefore, we performed DTI in cervical spinal cord of patients diagnosed with NMO to test whether DTI-derived metrics are sensitive to early changes in tissue microstructure in NMO.

Methods: Seven NMO patients (1 male, 6 females; mean age = 54 ± standard deviation (SD) = 12 years; mean Expanded Standard Disability Status Scale (EDSS) = 3.7; range = 1 - 7) and five healthy volunteers (1 male, 4 females; mean age, 30 ± 3years) were studied after signed, informed consent. All studies were approved by the local institutional review board. All scans were performed on a Philips 3T MRI Achieva scanner (Philips Healthcare, Best, The Netherlands) with a body coil excitation and a 16-channel neurovascular coil for reception. Two imaging volumes covered upper and lower portions of cervical spinal cord, C1 to C3 and C4 to C6, respectively in order to minimize motion artifacts. Four averaged minimally weighted (b_0) and 15 diffusion-weighted volumes (b-value = 500 s/mm^2) were acquired using single-shot EPI sequence. The imaging parameters were: TR/TE= 3000/58ms, nominal resolution = 1x1.256 mm^2, 20/10 slices (upper/lower), slice thickness= 2.5/5 mm (upper/lower), 2 averages and total scan time = 10/3 min. (upper/lower). The diffusion tensor was estimated as described in Mori et al. [5] and the fractional anisotropy (FA), parallel/longitudinal diffusivity ($\lambda_{||}$), perpendicular/transverse diffusivity ($\lambda_{\perp}$), and mean diffusivity (MD) were derived using DtiStudio [6]. The regions-of-interest (ROIs, Area= 2.344 mm^2) of lateral and dorsal columns were manually drawn using ImageJ (National Institutes of Health, Bethesda, MD, USA). Fig. 1 shows the representative location of ROIs in a control subject selected on the FA map where the distinction between gray and white matter (WM) can be observed. Using same ROIs, the average DTI-derived metrics including FA, $\lambda_{||}$, $\lambda_{\perp}$ and MD were computed for both control subjects and NMO patients at each spinal cord level. Sagittal T2w images covering same area of the spinal cord were obtained using multishot-TSE sequence as a reference (TR/TE= 2500/100 ms, nominal resolution = 0.84x1.06 mm^2, 15 slices, slice thickness= 3 mm and total scan time = 3 min.).

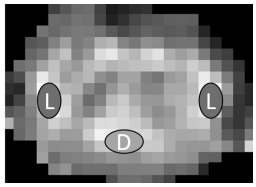

Fig. 1. Location of ROIs on the FA map of a control (L, lateral; D, dorsal).

Results and Discussion: Fig. 2 shows the mean ± SD of each DTI-derived metric in the lateral and dorsal columns for both control subjects and NMO patients. These values were obtained by averaging the each ROI-based metric from C1 to C6 in both control subjects and NMO patients. Both left and right ROIs were averaged for the lateral column. In dorsal and lateral columns of cervical spinal cord in NMO patients, the mean FA values are significantly decreased ($p < 0.001$) while the mean values of $\lambda_{\perp}$ and MD are significantly increased ($p < 0.001$ and $p < 0.01$, respectively). However, the mean $\lambda_{||}$ is unchanged in neither column ($p = 0.94$ and $p = 0.69$, for dorsal and lateral, respectively). Our results on reduced mean FA and increased MD agree well with pathologic expectations and histology reports in the literature suggesting the loss of myelin and inflammations in cervical spinal cord of NMO patients [1]. Interestingly, increased $\lambda_{\perp}$ with no significant change in $\lambda_{||}$ was also observed, which may indicate early sign of noncystic WM injury with reduced myelination before severe damage in structural integrity and necrosis as proposed in a validation study by Wang et al. [7]. In contrast, no macroscopic lesions were identified using conventional T2w images in any cervical spinal cord in NMO patients except one subject. This may suggest that quantitative DTI-derived metrics are more sensitive to reflect the early stage of NMO in comparison with conventional T2w imaging.

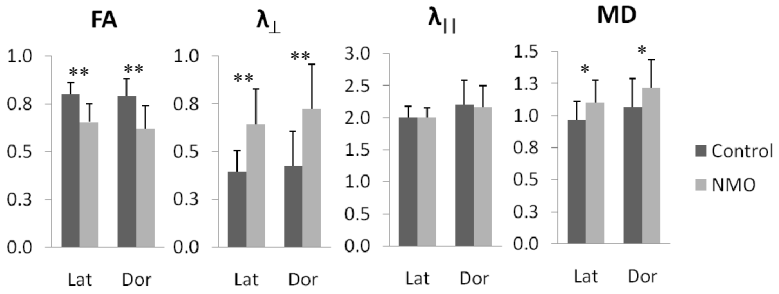

Fig. 2. Mean DTI-derived metrics of dorsal and lateral columns from C1-C6 in controls and NMO patients. The error bar represents the SD. Significant differences between groups are indicated by * $p < 0.01$ and ** $p < 0.001$ (Lat, lateral; Dor, dorsal).

Conclusion: Our results demonstrate that DTI-derived metrics can sensitively assess the cervical spinal cord damage in NMO using quantitative capability of DTI. In addition to existing clinical methods, DTI may potentially be a useful biomarker in treatment selection and monitoring degenerative changes in patients with NMO.

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