Retrograde Wallerian Degeneration of Cranial Corticospinal Tracts in Cervical Spinal Cord Injury Patients using Diffusion Tensor Imaging

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Introduction: Spinal cord injury (SCI) results in acute as well as progressive secondary destruction of local and distant nervous tissue through a number of degenerative mechanisms referred to as Wallerian degeneration (WD) with initiation of endogenous neuroprotective and regenerative responses[1]. The lesion in end stage is more or less static except for the continuously advancing WD of spinal tracts above and below the lesion and the effects of plasticity on the neuronal synaptic network[2]. Diffusion tensor imaging (DTI), a noninvasive modality, is capable of examining the organization and integrity of compact white matter fiber tracts such as corticospinal tract (CST). The degree of diffusion anisotropy depends upon the degree of hindrance to water diffusion by neurotubules, axonal membranes and myelin sheaths[3]. When white matter tracts degenerate, as occurs in WD, a decrease in anisotropy is observed[4]. The aim of our study was to assess the extent of retrograde WD in brain CST changes in patients with cervical SCI using DTI.

Material and Methods: ***Subjects:*** Thirteen SCI patients (twelve males, one female; 40.61±12.05 years (mean±SD); range: 22 to 55 years) with documented traumatic cervical SCI between 2nd to 6th cervical vertebrae with minimum duration of injury of 3 months were included in this study. All patients were right-handed, quadriplegic, presented with bowel and bladder incontinence and with neurological deficit more marked on right side. Patients with documented neurological deficit prior to trauma were excluded from the study. Informed consent was taken from each patient who underwent detailed clinical examination with emphasis on neurological examination including motor, sensory and mini mental state examination. Thirteen healthy age and sex matched controls with a mean age 41.81±13.22 years (twelve males, one female) were investigated using the same magnetic resonance imaging (MRI) protocol.

Image Acquisition and Data Processing: Conventional MRI and DTI of the head were acquired on a 1.5 Tesla MRI scanner using standard quadrature birdcage head coil. DTI data were acquired using a single-shot echo planar dual spin echo sequence with ramp sampling. The acquisition parameters were: TR=8sec/TE=100ms/number of slices=36-40/slice thickness=3mm/interslice gap=0/FOV=240mm/image matrix=256×256 (following zero-filling)/NEX=8/diffusion weighting b-factor=1000 s mm^{-2}. The DTI data was processed and evaluated using JAVA based in-house developed program[5]. Elliptical ROI's varying from 2×2 to 6×6 pixels were placed at the level of medulla, pons, midbrain, posterior limb of internal capsule (PLIC) and corona radiata for determining the fractional anisotropy (FA) and mean diffusivity (MD).

Results: In patients, a significant reduction in FA values was observed at the level of medulla, pons, midbrain, and PLIC on both left and right side compared to controls, indicating rostral extent of degeneration as high as PLIC. However, significant elevation of MD values was observed on both left and right side compared to controls. However, corona radiata showed high FA and low MD values bilaterally, changes more marked in those with duration of injury greater than 12 months.

Discussion: To the best of our knowledge, this is the first brain DTI study that investigated the time course of focal changes in the CST in traumatic cervical SCI patients. Based on the observations in the present study, it appears that patients have widespread microstructural changes in the CST. These observations of significantly decreased FA values in white matter tracts in patients are presumably related to WD and suggest a net loss and disorganization of the structural barriers to molecular diffusion of water, and may be explained by documented pathological characteristics like demyelination, axonal loss and astrogliosis[6]. The increase in MD is consistent with the presence of gliosis and the possible increase in extracellular matrix found histologically in WD[7]. However, the findings of increased FA and low MD values are consistent with neuronal plasticity, which could be attributed to the reorganization of axonal microstructure as evidenced in animal studies[8].

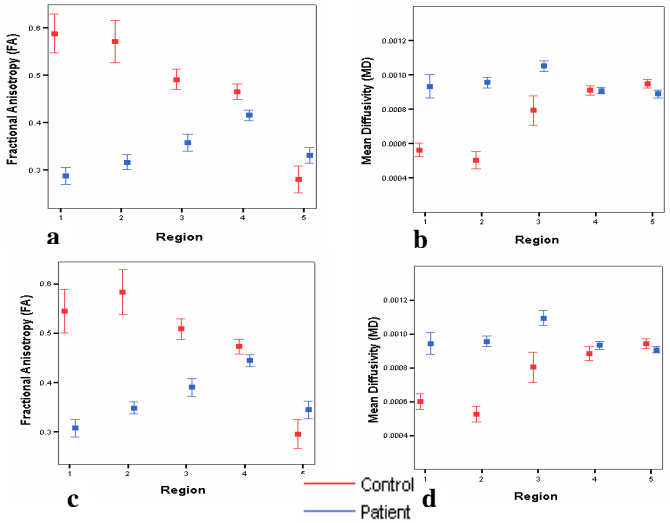

Figure 1. Plots of FA (a, c) and MD (b, d) values (mean±SD) in controls and SCI patients on left and right side respectively at various levels of CST region (1 = medulla, 2 = pons, 3 = midbrain, 4 = PLIC, 5 = corona radiata). Error bars show 95.0% confidence interval of mean

Table 1

Regions	*[a]Controls*		*[b]Patients*		*p values*	
	FA	*MD ($\times 10^{-3}$ mm^2/s)*	*FA*	*MD ($\times 10^{-3}$ mm^2/s)*	*pFA*	*pMD*
Medulla	0.58±0.08	0.56±0.08	0.28±0.05	0.93 ± 0.21	p=0.00	p=0.00
Pons	0.57±0.08	0.50±0.09	0.31±0.05	0.95 ± 0.09	p=0.00	p=0.00
Midbrain	0.49±0.04	0.79±0.16	0.35±0.06	1.05 ± 0.10	p=0.00	p=0.00
Internal Capsule	0.46±0.03	0.90±0.05	0.41±0.05	0.90 ± 0.09	p=0.00	p=0.89
Corona Radiata	0.28±0.04	0.94± 0.04	0.33±0.06	0.88 ± 0.08	p=0.00	p=0.00

Table 2

Regions	*[a]Controls*		*[b]Patients*		*p values*	
	FA	*MD ($\times 10^{-3}$ mm^2/s)*	*FA*	*MD ($\times 10^{-3}$ mm^2/s)*	*pFA*	*pMD*
Medulla	0.54±0.08	0.60±0.09	0.30±0.05	0.09±0.19	p=0.00	p=0.00
Pons	0.58±0.08	0.52±0.08	0.34±0.04	0.95±0.10	p=0.00	p=0.00
Midbrain	0.50±0.04	0.80±0.17	0.39±0.06	1.09±0.14	p=0.00	p=0.00
Internal Capsule	0.47±0.03	0.88±0.07	0.44±0.06	0.93±0.12	p=0.00	p=0.04
Corona Radiata	0.29±0.05	0.94±0.05	0.34±0.07	0.90±0.08	p=0.00	p=0.03

Tables.
Summary of fractional anisotropy and mean diffusivity (mean±SD) values at various levels of CST in left and right side of SCI patients and their comparison with controls are shown in Table 1 and Table 2 respectively.

References: 1. Johnson AC, et al. Arch Neurol Psychiat 1950;64:105-121, 2. Kakulas BA. Spinal Cord 2004;42:549–563, 3. Beaulieu C, et al. Magn Reson Med 1994;31:394-400, 4. Zelaya F, et al. Magn Reson Imaging 1999;17:331-348, 5. Purwar A et al. Proc. Euro. Mag. Reson. Med. 2006, 6. Ohya T, et al. Neurology 1974; 24:211-218, 7. Pierpaoli C, et al. Neuroimage 2001;13:1174-1185, 8. Kaas JH, et al. Adv Neurol 2003;93:87-95.