Clinical Correlates of High Cervical Fractional Anisotropy in Acute Cervical Spinal Cord Injury

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Key words
- Diffusion tensor imaging
- Fractional anisotropy
- Spinal cord
- Spinal cord injury

Abbreviations and Acronyms
ASIA: American Spinal Injury Association
CST: Corticospinal tract
DTI: Diffusion tensor imaging
FA: Fractional anisotropy
SCI: Spinal cord injury

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■ OBJECTIVE: **Fractional anisotropy (FA) of the high cervical cord (C1-C2), rostral to the injury site, correlates with upper limb function in patients with chronic cervical spinal cord injury (SCI). In acute cervical SCI, this relationship has not been investigated. The objective of this study was to identify functional correlates of FA of the high cervical cord in a series of patients with acute cervical SCI.**

■ METHODS: **Traumatic cervical SCI patients who underwent presurgical cervical spine diffusion tensor imaging at our institution were reviewed for this study. FA of the whole cord as well as the lateral corticospinal tracts (CSTs) was calculated on axial images from C1-C2. Upper limb motor (C5-T1) and sensory (C2-T1) function scores were extracted from the admission American Spinal Injury Association (ASIA) examinations. Correlation analysis for FA with ASIA examinations was performed using a Pearson correlation.**

■ RESULTS: **Twelve subjects (9 men, 3 women; mean age 54.7 ± 4.0 years) underwent cervical spine diffusion tensor imaging at a mean duration of 3.6 ± 0.9 days postinjury. No patient had cord compression or intramedullary T2-weighted hyperintensities within the C1-C2 segments. FA correlated with upper limb motor score (whole cord: $r = 0.59$, $P = .04$; CST: 0.67, $P = .01$) and the ASIA grade (whole cord: $r = 0.61$, $P = .03$; CST: $r = 0.71$, $P = .009$). No correlation was found between FA and sensory scores.**

■ CONCLUSIONS: **FA of the whole cervical cord as well as the CST, rostral to the injury site, is associated with preserved upper limb motor function as well as superior ASIA grades after acute cervical SCI. FA of the high cervical cord is a potential biomarker of neural injury after acute cervical SCI.**

INTRODUCTION

Traumatic spinal cord injury (SCI) results in partial or complete loss of neuronal function below the neurological level of injury. In addition to anterograde injury, retrograde changes in structure and function are observed within neural pathways (12, 13, 22). The characterization of retrograde degeneration is important because it affects neural structures responsible for preserved neurological function and may play an important role in determining the success of rehabilitative strategies. Previous studies have described clinical correlates of these changes in chronic SCI; however, little is known about the clinical significance of retrograde injury in subjects with acute SCI.

Diffusion tensor imaging (DTI), which measures the diffusion of water molecules within tissues, offers a quantitative assessment of spinal cord microstructure in regions of the cord that appear normal on conventional magnetic resonance imaging (MRI). Retrograde microstructural degeneration in the high cervical cord (C1-C3) is detected by DTI in subjects with chronic SCI (4, 10, 11, 18). Fractional anisotropy (FA), remote from the injury site, correlates with neurological function, indicating that DTI is a potential biomarker for chronic SCI (11, 18). Although similar changes in FA are observed in acute SCI, few studies have investigated whether FA, rostral to the injury site, correlates with neurological function in the acute setting. The purpose of this study was to evaluate whether FA of the high cervical cord, rostral to the injury site, is associated with neurological function in subjects with acute cervical SCI.

METHODS

Subjects

We studied 15 subjects with acute cervical SCI who underwent presurgical DTI and T2-weighted MRI of the cervical spine at our institution between March 2007 and December 2012. Three subjects were excluded from this study: 2 subjects did not have American Spinal Injury Association (ASIA) scores at admission, and 1 subject had high cervical SCI. The final study sample included 12 subjects (9 men, 3 women; mean age 54.7 ± 4.0 years). A chart review was performed to acquire demographic data, neurological level of injury, and ASIA grades. We also recruited 12 neurologically intact subjects (8 men, 4 women; mean age

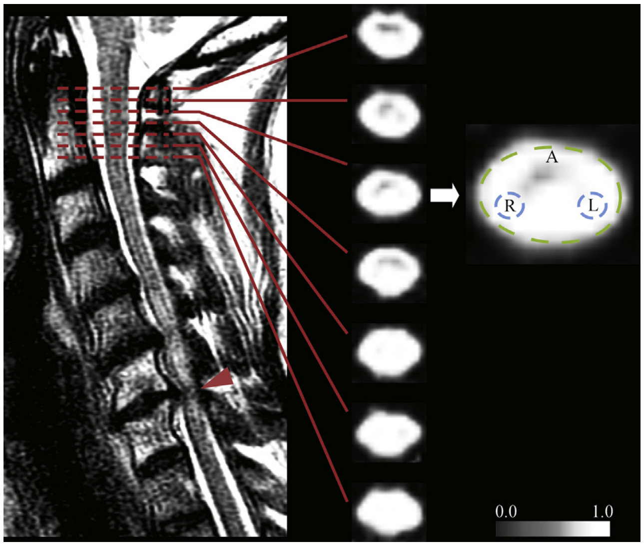

Figure 1. Sagittal cervical spine T2-weighted image of subject 8 showing 7 axial fractional anisotropy maps through the high cervical cord (red dotted line). *Solid arrowhead* shows the injury site at the C6-7 intervertebral disc level. A single fractional anisotropy map is magnified to show the whole cord regions of interest (*green*) and the regions of interest for the corticospinal tracts (*blue*). A, anterior; R, right; L, left.

52.2 ± 4.6 years) within the same age range to undergo cervical spine DTI. All subjects gave written informed consent, and all procedures were approved by the local institutional review board.

Upper Limb Function

Clinical data for motor and sensory function were extracted from the first complete ASIA examination performed on SCI subjects after injury. Upper limb motor function was calculated from the left and right ASIA motor scores for the C5-T1 levels, with a maximum possible score of 50. Upper limb ASIA sensory scores for light touch and pinprick (pain) were calculated for the C2-T1 levels, with a maximum possible score of 32.

DTI

All subjects underwent DTI scanning of the cervical spine (C1-T1) on a 1.5-T MR scanner (Signa Excite; GE Medical Systems, Milwaukee, Wisconsin) with a CTL spine coil. DTI scans of 7 SCI subjects and all healthy subjects were performed with the following protocol: 15 distinct directions, b-value of 600 s/mm^2, TR/TE of 5000/98.2 ms, matrix size of 128 × 128, and FOV of 19 cm^2. Five SCI subjects, who were recruited before May 2011, underwent DTI scanning on an older 1.5-T GE MR scanner along 25 equidistant directions at a b-value of 500 s/mm^2, TR/TE of 4500/80 ms, matrix size of 128 × 128, and FOV of 260 mm × 260 mm. Sagittal T2-weighted images of the cervical spine were also acquired for all subjects using a TR/TE of 4000/102 ms, matrix size of 384 × 224, and FOV of 20 cm^2.

To determine whether there were differences in data output between the old and new MR scanner, we performed cervical spine DTI scans on 4 healthy subjects on both scanners. Mean FA and signal-to-noise ratios of an axial image at the C4-C5 level was compared between scans from the old and new machines. No significant difference in either parameter (old vs. new scanner: mean FA 0.65 vs. 0.62, $P = .15$; mean signal-to-noise ratio 8.6 vs. 9.2, $P = .86$) was detected between the scans.

Image Processing

Diffusion images were analyzed using the MedINRIA software package (www.sop.inria.fr/asclepios/software/MedINRIA). Fractional anisotropy was calculated voxel by voxel from axial FA maps through C1-C2 (high cervical cord), using manually drawn regions of interest. Whole-cord regions of interest were drawn within the perimeter of the cord so as to avoid partial volume effects due to cerebrospinal fluid. Regions of interest also were drawn for the left and right corticospinal tracts (Figure 1) in a manner similar to previous studies (11, 16). Because FA was not significantly different between left and right corticospinal tracts for SCI subjects (Student t test, $P = .68$) and control subjects ($P = .39$), the mean FA of the left and right corticospinal tract (CST) was used for analysis.

Statistical Analysis

The Student t test was used to compare the mean FA of the whole cord and CST between SCI subjects and control subjects. Correlations between FA and upper limb function and ASIA grades were analyzed using the Pearson correlation. Statistical analysis was performed using SPSS 20.0 (Chicago, Illinois). ASIA grades were converted to numerical values to conduct the correlational analysis. Means were reported as ± standard error of the mean, and the level of significance was set at $P < .05$.

RESULTS

Clinical Data

Clinical and demographic data for individual SCI subjects are shown in Table 1. All subjects except 1 (subject 7) sustained blunt cervical spine injury. The neurological levels of injury ranged from C2-C7. All SCI subjects except 2 underwent an ASIA examination within 1 week of the DTI scan. All subjects upper limb motor impairment, and the mean upper limb motor score was 26.0 ± 4.2. Upper limb sensory scores were available for 11 SCI subjects, and of these, 6 subjects had intact light touch sensation and 4 subjects had intact pinprick sensation for the C2-T1 levels. The mean score for light touch was 27.2 ± 2.4, and the mean score for pinprick was 23.9 ± 2.7.

Imaging Data

The mean time interval between injury and DTI scan was 3.6 ± 0.9 days (range, 0 to 10 days). No SCI subject had cord compression or T2-weighted intramedullary hyperintensity above the C2-C3 disc space.