Diffusion tensor imaging in spinal cord injury

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Abstract

Background and Purpose: To assess the feasibility of spinal tractography in patients of spinal cord injury vs a control group and to compare fractional anisotropy (FA) values between the groups. **Materials and Methods:** Diffusion tensor imaging (DTI) was performed in the spinal cord of 29 patients (18 patients and 11 controls). DTI was done in the cervical region if the cord injury was at the dorsal or lumbar region and in the conus region if cord injury was in the cervical or dorsal region. FA was calculated for the patients and the controls and the values were compared. **Results:** The mean FA value was 0.550±0.09 in the control group and 0.367±0.14 in the patients; this difference was statistically significant (*P*=0.001). **Conclusion:** Spinal tractography is a feasible technique to assess the extent of spinal cord injury by FA, which is reduced in patients of spinal cord injury, suggesting possible Wallerian degeneration. In future, this technique may become a useful tool for assessing cord injury patients after stem cell therapy, with improvement in FA values indicating axonal regeneration.

Key words: Fractional anisotropy; MRI; spinal cord injury; tensor imaging

Introduction

Spinal cord injuries result in damage to the myelinated fibers of the spinal cord and/or nerve roots, causing myelopathy.[1] There are various causes of spinal cord injuries, e.g., trauma, tumor, and demyelination. These injuries can cause damage to the central gray matter, involving interneurons and motor neurons. Pathologically, such spinal cord insult can cause Wallerian degeneration either above or below the level of injury. MRI can detect these changes as increased signal intensity on T2W(T2 weighted) images.[2] However diffusion tensor imaging (DTI) has the potential to detect abnormalities in the spinal cord, even in cases where routine MRI (Magnetic resonance imaging) may be normal.[3] We evaluated the feasibility of DTI for quantification of the extent of Wallerian degeneration in spinal cord injuries in both the cervical and the dorsal cords.

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Materials and Methods

Subjects

The study was performed after taking ethics committee approval. DTI was done in 29 subjects: 18 patients of spinal cord injury and 11 age-matched controls. There were 12 males and 6 females in the patient group; the ages ranged from 19 years to 59 years, with a median age of 33.5 years. Tensor imaging was also done in 11 age-matched controls, of which ten were males and one female. The same protocol was followed in both groups. The age of the subjects in the control group ranged from 20 years to 53 years, with a median age of 33 years. All patients had spinal cord injury following road traffic accident, except one patient who had spinal cord injury due to assault (patient no. 7). Time since injury and imaging varied from 3 months to 84 months.

MR imaging

MRI was done in a 1.5-T machine (Wipro GE, Milwaukee, WI, USA). T2W images in the sagittal and axial planes were obtained at the region of interest (ROI). If cord myelomalacia or signal changes (post-traumatic) were seen in the cervical region, then tensor imaging was done in the dorsal cord or in the conus region, and if cord changes were in the dorsal or conus region then tensor imaging was done in the cervical region. DTI was performed in the axial plane, perpendicular

to the long axis of the cord, using an 8-channel cervical thoracic lumbar CTL (Cervical thoracic lumbar) array spine coil with the following parameters: 25 directions EPI tensor imaging (TR (Repetition time): 8500; TE (time to echo): 97.6; b value: 1000; frequency: 128; phase: 128; NEX (number of excitations): 1; FOV (field of view): 26 × 20.8; slice thickness: 5 mm with zero interslice gap; and bandwidth: 250 kHz).

Image processing

Image processing was done using the Functool™ software provided by GE, and quantitative analysis was performed to calculate the fractional anisotropy (FA) using standard methods. Three ROIs were placed randomly across the cord and their mean was calculated.

Statistical analysis

The paired student's '*t*' test was applied to compare FA values between patients and controls, and a *P* value of less than 0.05 was considered statistically significant.

Results

FA values were calculated in three ROIs in either the cervical region or at the conus region. Details of FA values, including clinical data, are given in Tables 1–3. Figure 1 (B–D) shows the placement of ROIs on the axial image with colored maps of ADC and FA, and Figure 1E shows the fiber tractography image. The FA value was found to be 0.550±0.09 in the control group and 0.367±0.14 in patients; this difference in FA values was statistically significant (*P*=0.001). Conventional T2W imaging did not show any signal changes in the cord above or below the lesion and at the same levels the FA values were obtained. Figure 1A shows reconstructed T2W image of a patient with cervical cord injury, with signal loss due to postoperative screws in the pedicles and normal appearing dorsolumbar cord where FA values were calculated.

Discussion

DTI is being widely used in the brain for various applications. DTI in diffuse axonal injury has been extensively studied.[4,5] Recently, the feasibility of tensor imaging in the spinal cord has been tested both in the cervical and the lower cords.[3,6] The clinical application of tensor imaging in spinal cord lesions due to trauma, tumors, and inflammation has shown the usefulness of this technique. DTI has even been able to demonstrate displaced white matter tracts or their involvement by lesions in the cord, thus helping treatment planning and follow-up of cases.[7]

The greatest advantage of tensor imaging is that it can show changes in white matter tracts even in cases where

Table 1: Time since injury for imaging with fractional anisotropy (FA) values in patients

Patient no	Age	Sex	Time since injury (months)	Level of injury	FA values
1	24	M	6	D12 fracture; myelomalacia at D6-D8	0.279±0.028 0.316±0.133 0.400±0.030
2	29	F	36	C-6 fracture, with myelomalacia from pons to C5	0.212±0.134 0.288±0.205 0.309±0.153
3	19	F	12	D4-D5 fracture	0.365±0.188 0.445±0.121 0.696±0.114
4	59	F	84	Injury at conus medullaris, with fracture at D3-D5	0.336±0.101 0.239±0.101 0.234±0.104
5	31	M	48	Injury at conus medullaris, with fracture at L1	0.689±0.155 0.736±0.199 0.681±0.208
6	46	M	36	Fracture at D12, with cord injury at D2-D12	0.321±0.0655 0.335±0.0463 0.424±0.117
7	49	M	48	Cord injury at D6; stab injury	0.182±0.0104 0.132±0.0145 0.278±0.0288
8	26	M	6	Fracture at D3	0.325±0.0713 0.290±0.0701 0.249±0.0645
9	46	M	6	Fracture C3-4 and L1; cord injury at C4,6,7	0.349±0.0849 0.217±0.0515 0.308±0.0714
10	36	M	3	Cord injury at C6-7	0.396±0.0767 0.380±0.0702 0.346±0.103
11	22	M	18	Cord injury at C5-6	0.248±0.0488 0.479±0.0896 0.432±0.0925
12	31	M	48	Cord injury at C6-7	0.275±0.0471 0.315±0.0593 0.393±0.0687
13	31	M	9	D4 fracture	0.421±0.0740 0.384±0.0371 0.346±0.0688
14	46	M	24	Fracture D12, with cord injury	0.0534±0.0359 0.0721±0.0153 0.0510±0.0227
15	50	F	6	Atlantoaxial dislocation	0.544±0.221 0.540±0.250 0.378±0.178
16	46	F	10	Dorsal cord injury	0.350±0.141 0.374±0.0692 0.364±0.0975
17	26	F	20	Cord injury at C4-7; grade 3 listhesis of C5 over C6	0.546±0.174 0.453±0.113 0.546±0.101
18	47	M	32	Injury at conus medullaris	0.529±0.123 0.467±0.0406 0.519±0.0859

Table 2: Fractional anisotropy values in the control group

Sl no	Age	Sex	FA values
1	20	M	0.344±0.108 0.667±0.132 0.677±0.216
2	42	M	0.427±0.144 0.425±0.042 0.656±0.024
3	39	M	0.537±0.061 0.338±0.119 0.305±0.041
4	31	M	0.647±0.161 0.632±0.101 0.627±0.118
5	33	F	0.570±0.046 0.689±0.233 0.650±0.110
6	53	M	0.626±0.177 0.677±0.108 0.651±0.070
7	38	M	0.620±0.224 0.640±0.263 0.685±0.234
8	28	M	0.514±0.043 0.455±0.036 0.413±0.056
9	32	M	0.506±0.111 0.428±0.053 0.479±0.054
10	33	M	0.516±0.556 0.429±0.089 0.566±0.052
11	36	M	0.674±0.058 0.504±0.063 0.589±0.127

Table 3: Clinical details of patients

Patient no.	Clinical findings
1	UL 5/5 and LL 0/5; preserved pain in both LL; DTR brisk; extensor plantars
2	UL 3/5; LL 0/5; hypotonia
3	UL normal; LL 0/5
4	Paraplegic; LL 0/5; loss of sensation below D4
5	UL 5/5; LL 4/5
6	UL normal; LL 0/5; hypoesthesia at D12
7	UL 5/5; both hips 1/5; knee and ankle 0/5; DTR 1+; no sensation below D8 on right side and 50% loss below D10 on left
8	UL normal; 2/5 at hips; 1/5 at knee for flexion and 2/5 for extension; ankle 0/5
9	UL at shoulder and elbow 5/5 and at wrist 4/5; hips 1/5 and below hips 0/5; spasticity with wasting of both LL; impaired sensation from C5 to D4 and anesthesia below D5; extensor plantars; DTR brisk at all joints except knee and ankle
10	UL 3/5; LL 0/5; complete sensory loss below D12
11	UL 3/5; LL 0/5
12	UL proximally 4/5 and distally 0/5; LL 0/5 bilaterally; hypoesthesia from C7 downwards bilaterally; DTR brisk at biceps
13	UL 5/5; LL 0/5; sensory anesthesia below D6
14	Burning sensation in both UL, with stiffness in both LL; dysesthesia right LL
15	Numbness in both UL; left UL 4/5, with weak handgrip; right hypoesthesia below D7 and left below C2; LL normal
16	Left LL 3/5; right LL 0/5; numbness of thighs; hypoesthesia both LL
17	All limbs flaccid; at both shoulder 3/5 and distally 0/5; both LL 0/5; anesthesia below C6; absent UL DTR and exaggerated at knee and ankles
18	UL normal; grade 0/5 both LL

UL: Upper limb, LL: Lower limb, DTR: Deep tendon reflex

routine imaging is normal. In diffuse axonal injury, where routine CT (Computed tomography) scan and MRI were normal, there was reduction in diffusion anisotropy after 24 h, suggesting axonal injury.[4] Similarly, in demyelinating disease such as multiple sclerosis, reduced FA in the cervical cord has been demonstrated in patients as compared to controls, although routine MRI imaging was normal.[3] Also, it has been well documented that signal changes seen on routine MRI may not correlate with neurological deficits and clinical findings, whereas DTI has been shown to correlate with motor deficits.[8] In experimental studies, changes in axial diffusivity on DTI in the spinal cord injury as early as 3 h after trauma were seen to be a predictor of long-term motor recovery as DTI can detect early subclinical physiological changes in the cord.[9]

We have studied changes in DTI metrics in the cervical and lower cord in the spinal cord injury patients. We found significantly reduced FA in the cord either above or below the site of injury, although routine imaging did not show any signal changes. We found reduced FA values in the lower cord if there was injury in the cervical region and reduced FA in the cervical region if there was injury to the lower cord. This finding suggests that there is associated ascending and descending Wallerian degeneration, which can be detected by tensor imaging. Similar findings were detected by Mohammed *et al*, on DTI imaging in children with spinal cord injury.[10]

Wallerian degeneration above or below the injury level has also been demonstrated on pathological examination.[2] Buss *et al*, has shown that there is sequential loss of myelin proteins during Wallerian degeneration after spinal cord injury that can be seen years after injury.[11] Similarly, tensor imaging in a rat model with spinal cord contusion has shown evolving changes in the ADC with recovery in ADC values with time suggesting that recovery from spinal cord injury is a dynamic process that goes on for years.[12]

Recently, stem cell therapy for spinal cord injury patients is being tried with the hope of achieving axonal regeneration and recovery.[13,14] Studies show that persistence of axon growth-inhibitory proteins such as NOGO-A in degenerating fiber tracts may keep the environment

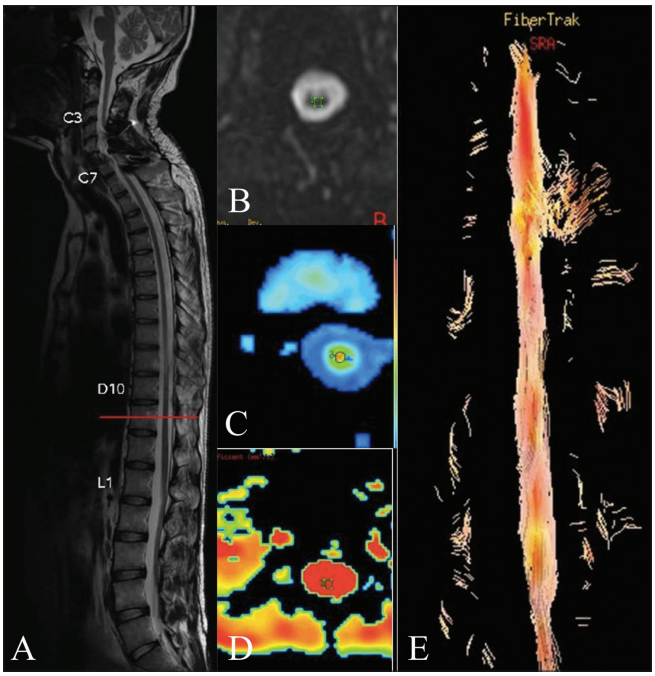

Figure 1 (A-E): This patient sustained a road traffic accident with cervical cord injury. He had 0/5 power in both lower limbs and 4/5 power in both upper limbs. T2W sagittal MRI (A) shows cervical cord injury with a normal appearing lower cord. The line drawn at D11 shows the level of axial images. Figure B shows placement of the ROI with a colored map of the FA (C) and a colored ADC map (D). Figure E shows a colored fiber tractography image. The FA values at three ROIs were 0.275±0.0471, 0.315±0.0593, and 0.393±0.0687 which are significantly lower than the control group, suggesting possibly descending Wallerian degeneration in the lower cord.

favorable for axonal regeneration long after injury.[11] Thus in the future, the use of stem cells in patients with spinal cord injury may perhaps prove to be a promising therapy. Thus, tensor imaging has the potential to noninvasively identify axonal regeneration after stem cell therapy.

In conclusion, DTI in the spinal cord is a feasible technique. As seen in our study, it can detect Wallerian degeneration, which is not detected on routine imaging. Also, as documented in other studies, it correlates well with motor deficits and is a predictor of long-term motor recovery.

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