Logitudinal in vivo DTI assessment of contusion injury and secondary degeneration in mouse spinal cord.

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Introduction

Traumatic spinal cord injury can lead to severe disabilities. Rodent models of spinal cord injury are used in the development of new therapeutic interventions. MRI has been used to evaluate the efficacy of such treatments. Diffusion tensor imaging (DTI) is a widely employed method to characterize tissue morphology and pathology. Its use in assessing mouse spinal cord injury was reported previously in a cross-sectional study of perfusion fixed cord (1). In the present study, longitudinal DTI measurements were performed *in vivo* on the spinal cord from contusion injured mice at 1, 3, 7, and 14 days post injury (DPI). DTI parameters, including relative anisotropy (RA), axial ($\lambda_{\parallel}$) and radial ($\lambda_{\perp}$) diffusivities, were derived for assessment of the extent of damage. The ventrolateral white matter at vertebral segments between T11 – 13 was examined. The currently findings confirm (with reduced inter-animal variability) the previously reported cross-sectional study of perfusion fixed cord.

Methods

Ten 16-week-old female C57BL/6 mice were randomly divided into control and contusion groups. The latter underwent a severe contusion injury (1.7 mm diameter impactor tip, 0.9 mm displacement, 4 ms time from zero to 0.9mm) at vertebral segment T12 with an electromagnetic force driven impactor (2). The control group underwent laminectomy without contusion. Postoperative care procedures including manual bladder expression were performed as previously reported (2). *In vivo* DTI data were acquired before (naïve) and after injury (serially at 1, 3, 7 and 14 DPI). An inductively coupled surface coil (15 mm $\times$8 mm) was used as the receiver, covering the thorasic cord T11 through T13, with a 9 cm i.d. Helmholtz coil as the RF transmitter. A Stejskal-Tanner spin-echo diffusion-weighted sequence was modified to acquire images under respiratory gating (3). All images were acquired with acquisition parameters of TR 1.5 sec (gated acquisition), TE 43 msec, Δ25 msec, δ10 msec, slice thickness 0.75 mm, field-of-view 1 $\times$1 cm^2, data matrix 128 $\times$128 (zero filled to 256 $\times$256), total data acquisition time ~ 2.5 hrs. (Gx,Gy,Gz) = (1,1,0), (1,0,1), (0,1,1), (-1,1,0), (0,-1,1), and (1,0,-1), and b = 0 and .785 μm^2/ms. Image resolution was 78 $\times$78 $\times$750 μm^3.

Results and Discussion

RA maps of contusion injured mouse spinal cord covering T11 – 13 (Fig. 1) demonstrate excellent contrast between gray and white matter. Evolution of injury at the epicenter (Fig. 1B) and remote slices (2.25 mm from the epicenter; Fig. 1A and C) is qualitatively visible. Interestingly, although the two remote slices (Fig. 1A and C) were at equal distance from the epicenter, a more severe loss of brightness in white matter is seen in the caudal slice (Fig. 1C). Region of interest (ROI) analysis of the residual white matter, thresholding based on the mean RA value of normal gray matter (~0.3), was employed to estimate the severity of the injury. The same ROI defined using the RA map was applied to $\lambda_{\parallel}$ and $\lambda_{\perp}$ maps for quantification.

The apparent diffusion coefficient (trace in this study) showed a significant decrease at 1 DPI but increased over time returning to normal value at 14 DPI (Fig. 2A). White matter damage is clearly demarked by the time course of RA (Fig. 2 B) with the lowest value seen at the epicenter (marked as 0 on plot) 1 DPI. A downward trend is seen caudal to the epicenter at 3 and 14 DPI suggesting progression of secondary injury. Secondary injury progression is not symmetric in caudal and rostral directions, with more severe injury evident caudally.

Axial diffusivity showed the most significant decrease at the epicenter 1 DPI (Fig. 2C). An upward trend is seen over time across most slices examined. This upward evolution of $\lambda_{\parallel}$ does not necessarily suggest a recovery. There is no significant increase in $\lambda_{\perp}$ (Fig. 2D) at 1 DPI suggestive of intact myelin sheath. However, a steady increase in $\lambda_{\perp}$ over time across all slices examined suggests demyelination following axonal injury.

In the present study, longitudinal examination of contusion injured mouse spinal cord was performed *in vivo* up to 14 DPI. The results confirm (with a reduction in inter-animal variation) a previously preliminary cross-sectional study of perfusion fixed cord conducted over a shorter duration of post injury examination. In summary: longitudinal DTI measurements performed *in vivo* examining contusion injured mouse spinal cords achieve sufficient quality for a detailed analysis of white matter injury.

References

1. Kim *et al*., *ISMRM*, 806, (2005).
2. Ma *et al*., *Exp Neurol* 169:239-254 (2001).
3. Kim *et al., Neurobiol. Dis.* : in press (2005).

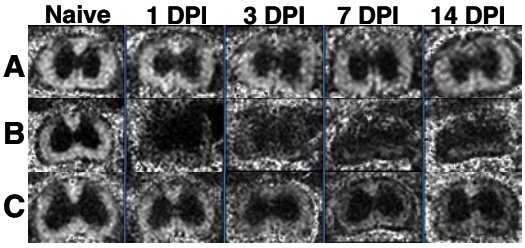

Figure 1. Representative RA maps covering three slices at 2.25 mm rostral (A) and 2.25 mm caudal (C) to the epicenter (B). Lower RA intensity suggests more severe white matter injury.

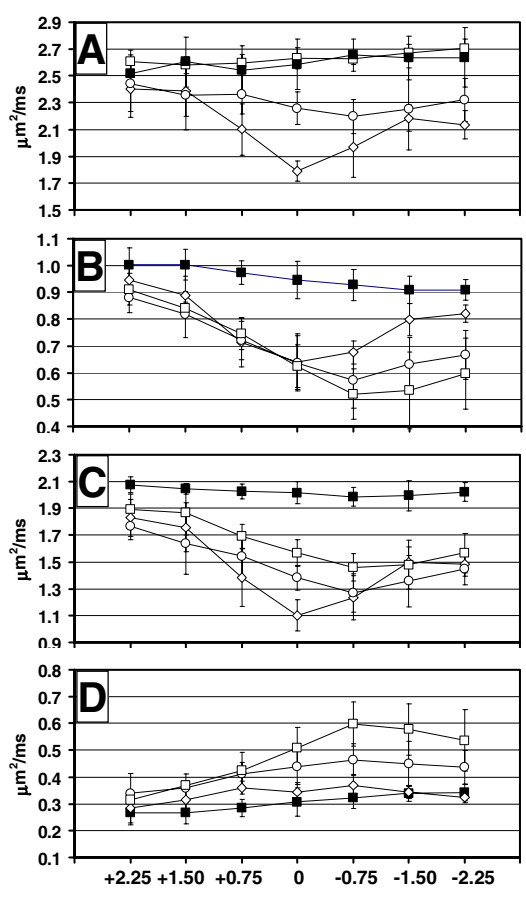

Figure 2. Time courses for trace (A), RA (B) , $\lambda_{\parallel}$ (C), and $\lambda_{\perp}$ (D) from residual ventrolateral white matter at different time poinst: ■ - control, ◇ - 1 DPI, ○ - 3 DPI, □ - 14 DPI. 7 DPI data were omitted for clarity of presentation. (7 DPI data coincide with 14 DPI data.) X-axis scale given in mm, distance from the epicenter. The positive numbers along the x-axis indicate positions rostral to the epicenter. Data are mean ± standard deviation with n =5.