Acute diffusion MRI measurements predict chronic axonal function assessed using electrophysiology

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Introduction

Traumatic spinal cord injury (SCI) causes devastating neurological dysfunction in patients. Currently, acute SCI diagnosis relies on a combination of conventional imaging methodologies such as x-ray, CT, and MR. However, there is no existing diagnostic method is capable of acute assessment of the injured cord depriving a critical time window for effective intervention. Herein, we describe the use of *in vivo* diffusion tensor imaging (DTI) to assess axonal integrity in rat SCI model immediately after injury. Our results demonstrate for the first time that the acute in vivo DTI derived axial diffusivity (λ‖) reflects axonal integrity accurately predicting long-term axonal function assessed by electrophysiology.

Methods

Twelve 175g female Sprague Dawley rats received one of three different severities (1.0, 1.25, and 1.5 mm) of contusion injuries. *In vivo* DTI examinations were performed immediately after injury on a 4.7 T scanner with b = 1000 s/mm^2 and Icosa-6 scheme using volume (10-cm inner diameter, RF excitation) and surface coil (25 mm x 20mm, signal receiver). All images were obtained within one hour. Four weeks after injury, magnetic motor evoked potential (MMEP, descending) and magnetically evoked inter-enlargement response (MIER, ascending) measurements were performed in vivo.

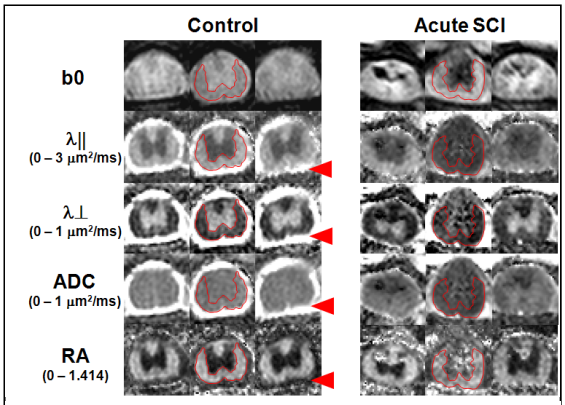

Figure 1. Acute in vivo DTI maps of control and injured mouse cords at the epicenter. The isotropic CSF indicated with arrow head is brighter than tissue in diffusivity maps. The best tissue contrast is shown in relative anisotropy (RA) maps for both control and SCI. The manually drawn ROI encompassing total VLWM is shown with red line.

Results and Discussion

Acute in vivo DTI derived parameter maps, RA and radial diffusivity (λ⊥), exhibit clear gray/white matter contrast enabling manual segmentation of total ventrolateral white matter (VLWM) in both control and SCI cords (Figs. 1 and 2a). The mean λ‖ of control rat spinal cord ventrolateral VLWM was 1.9 μm^2/ms. The experimental scheme of MMEP (Fig. 2b) and MIER (Fig. 2c) are shown with conduction latency (Fig. 2d) where □, △, and x represents normal, delayed and no response respectively. The region of interest (ROI) traditionally thought corresponding to the tracts for MMEP (ROI 1 and 2) and MIER (ROI 3 and 4) epicenter were identified (Fig. 2). In MMEP, normal response was only seen when λ‖ in ROI 2 was higher than 1.7 μm^2/ms (Fig. 2f) localizing the medial tract responsible for the descending signal conduction (Fig. 2g). In contrast, MIER response was only seen with normal λ‖ in ROI 4 (Fig. 2i), localizing outer lateral tract (ROI 4) for the ascending signal transduction (Fig. 2j). In addition, the latency of MIER signal correlated with the extent of reduced λ‖ in ROI4 reflecting the injury severity from 1.0 mm to 1.5 mm. ROI1 and ROI3 do not show functional relevance to the signal conduction.

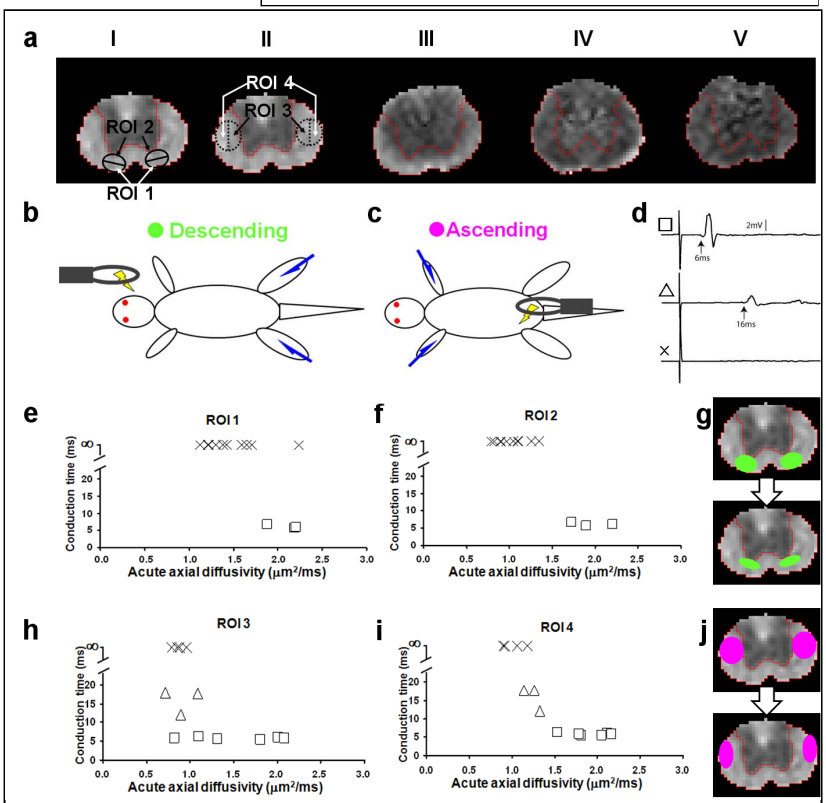

Figure 2. (a) In vivo acute axial diffusivity (λ‖) maps of control (I and II) and SCI (1.0 mm (III), 1.25 mm (IV), and 1.5 mm (V) cords. (b – d) Electrophysiology measurements . (e – g) MMEP at 4wks after SCI. (h – k) MIER at 4wks after SCI. Panel a-I and a-II shows ROIs for descending (ROI 1 and 2) and ascending (ROI 3 and 4) tracts respectively. Each ROI is divided into inner (ROI 2 and 3) and outer regions (ROI 1 and 4). Normal MMEP responses is observed only if λ‖ in ROI 2 is normal (e) where a normal MIER is observed when the λ‖ in ROI 4 is normal (i).

Conclusion

The current results suggest that in vivo DTI derived axial diffusivity may be a potential acute biomarker of axonal integrity capable of predicting long-term outcome after SCI. It may be used as a surrogate endpoint to predict functional outcome and therapeutic efficacy. Thus, translating these findings to the clinical situation will allow effective stratification of SCI patient managements.

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