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 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/mm² 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.

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 μm²/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 μm²/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 ROI 4 reflecting the injury severity from 1.0 mm to 1.5 mm. ROI 1 and ROI 3 do not show functional relevance to the signal conduction.

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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