MRI correlates of white matter structure in intact myelin vs. myelin debris –*ex vivo* study in injured rat spinal cord

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Introduction

A wide array of processes occurs after spinal cord injury, including white matter demyelination and proximal and distal Wallerian degeneration. The demyelination and interruption of the axonal tract ultimately leads to the functional loss seen in spinal cord injuries. Therefore it is important to have a non-invasive technique that is able to track myelin in spinal cords. There are several MR techniques aimed at this, including quantitative T2, diffusion tensor imaging (DTI), and quantitative magnetization transfer. Because myelin cannot be imaged directly with MR, these techniques focus on indirect measurement of myelin through probing the properties of the surrounding water. While quantitative T2 and DTI are able to generate indirect measures of myelin and axonal density, there is currently no technique capable of distinguishing between intact/functioning myelin and myelin debris. This study focuses on comparing several MR parameters between intact myelin and myelin debris in a rat spinal cord injury model.

Methods

DTI, quantitative T2, and T1 mapping experiments were used to characterize eight excised rat spinal cord samples at 3 weeks following dorsal column transection (DC Tx) injury [1]. DTI data was acquired using a multi-slice spin-echo (SE) based sequence; quantitative T2 data was acquired using a single slice multi-echo CPMG sequence [2]; and T1 data was acquired using a series of SE inversion recovery scans. Slices were acquired at 5 mm cranial to injury with resolution of 100 μm × 100 μm × 1000 μm. DTI data were processed to generate maps of apparent diffusion coefficient (ADC), transverse diffusivity (D_{trans}), longitudinal diffusivity (D_{long}), and fractional anisotropy (FA). CPMG data were processed using a non-negative least square analysis technique [3] to generate myelin water fraction (MWF), myelin water (MW) and geometric mean T2 (GM T2) maps. Region of interest (ROI) analysis was used to obtain average value of ADC, D_{trans}, D_{long}, FA, MWF, MW, and GM T2 from the injured *fasciculus gracilis* and adjacent uninjured region of white matter. Statistical significance of difference between group mean was assessed using two tailed *t*-test. MRI results were qualitatively compared to the high resolution optical microscopy and electron microscopy of plastic sections of the injured cords.

Results and Discussion

A summary of the results from the ROI analyses is shown in Table 1. DC Tx injury results in damage to *fasciculus gracilis* (ascending sensory tract) cranial to injury [4]. The axonal damage is demonstrated by the significant decrease in D_{long} and FA. Myelin damage is more difficult to assess due to presence of myelin debris as a result of Wallerian degeneration. Both MWF and MW increased as a result of injury, although differences were not statistically significant. Such increase is consistent with the histology of plastic sections (see Fig. 1) showing increased spaces between myelin bi-layers in myelin debris. This is also consistent with a previous report by Webb [5] suggesting that the amount of myelin water is a measure of both intact myelin and myelin debris. It is somewhat surprising that the average T2 showed small decrease as a result of injury, as one would expect increase in T2 of myelin water due to increased volume of the myelin water compartment. This decrease in average T2 may reflect potentially significant decrease in T2 of intra-/extra-cellular water judging from the morphological change observed in electron microscopy images (see Fig. 1b), which would mitigate a potential increase in T2 of myelin water. Increased D_{trans} likely reflects morphological changes in WM following axonal degeneration as a result of injury. As the axons disintegrate, myelin debris become onion-shaped structures, no longer aligned in one distinct direction. As a result the diffusion process becomes more isotropic, which is reflected by decrease in FA and D_{long}, and increase in D_{trans}.

Table 1: Average value, standard deviation, and *p*-value of various MR parameters. Bolded parameters and *p*-values show statistically significant difference ($p < 0.05$) between injured and controlled region. T_2 is geometric mean T_2.

	Average		Standard Deviation		*p*-value
	Injured	***Controlled***	***Injured***	***Controlled***	
MW	15933	12822	2707	5264	0.3337
MWF	0.515	0.385	0.0656	0.1377	0.1392
T1 (s)	0.705	0.695	0.2207	0.2219	0.9511
T2 (ms)	20.855	22.762	1.749	2.195	0.2229
D_{trans}	0.2804	0.1251	0.1160	0.05974	**0.0154**
D_{long}	0.5413	0.7753	0.1043	0.09899	**0.0026**
ADC	0.3674	0.3417	0.1112	0.07136	0.6439
FA	0.45	0.83	0.13	0.060	**0.0001**

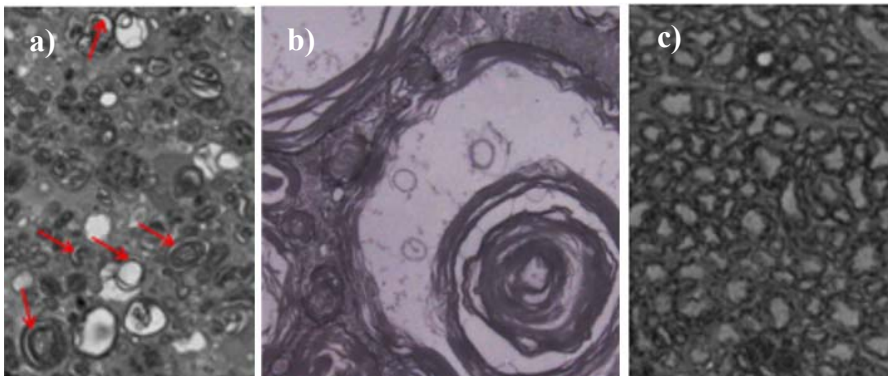

Figure 1: Histological cross-sections of injured (a) and uninjured white matter (c), and electron microscopy image of myelin debris. The myelin membranes in the uninjured white matter show tight packing around the axons. Arrows in (a) point to myelin debris, characterized by increased spacing between lipid bi-layers, which is shown more clearly in the electron microscopy image (b).

References

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