Microanatomical correlates of Multi-exponential T_2 and Quantitative MT in Pathological Rat Spinal White Matter

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Introduction

The myelin water fraction (MWF) measured by multi-exponential T_2 (MET_2) and the pool size ratio (PSR) measured by quantitative magnetization transfer (qMT) have both been proposed as quantitative techniques to measure the amount of myelin within white matter; however, these measure do not co-vary across white matter tracts [1, 2]. Recent ex-vivo & in-vivo MRI and histology-based simulation of water diffusion and relaxation has indicated that MET_2 is sensitive to micro-structure of normal spinal white matter, particularly axon diameter and myelin thickness [2,3]. This work presents preliminary studies in rat spinal cord with hexacholorphene (HCP)-induced pathology [4], which will be used for further investigation of the micro-structural basis of MET_2 and qMT measurements.

Methods

A total of 12 female Sprague Dawley rats (212-246g) were studied, with varied degrees of myelin edema induced by addition of HCP to the diet at 0 (control, 4 rats), 300ppm (4 rats) and 600 ppm (4 rats) for four days. Rats were anesthetized and imaged on a 9.4T Varian scanner with a 38 mm Doty quad coil used for transmission and reception, 128x128 sampling (reconstructed to 256x256) over a 25.6x25.6 mm FOV. MET_2 was measured using an inversion-recovery prepared multiple spin echo imaging sequence with 40 echoes (9ms echo spacing, 7.4ms to 286.4ms plus 8 echoes spaced at 50ms), TR = 6 s, and TI = 2 s (to null signal contamination from CSF). qMT measurements were made using an inversion-recovery prepared fast-spin echo sequence, with 8 echoes, TE_{eff} =10ms, 1.5s pre-delay, a 1.5ms duration hard inversion and 25 inversion times (21 inversion times log-spaced between 3.5ms to 150ms plus 0.3, 1.0, 2.0 and 10.0s). ROIs were manually drawn in 4 different spinal cord tracts—the dorsal corticospinal tract (dCST), funiculus gracilis (FG), rubrospinal tract (RST), and the vestibulospinal tract (VST). From each tract, T_2 spectra were estimated by fitting the multiple spin echo magnitudes to a distribution of exponential decays, constrained by non-negativity and curvature, and the MWF was extracted as the fractional area of the short-T_2 spectral component. Likewise, from each tract the PSR was extracted from a biexponential fit of the signal relaxation with inversion time [5].

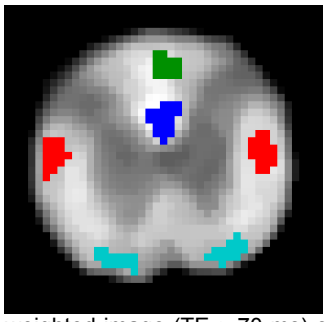

Figure 1: T_2-weighted image (TE ≈ 70 ms) of a rat spinal cord, with ROIs for the four spinal cord tracts analyzed: blue = dCST, green = FG, red = RST, teal = VST

Results and Discussion

Figure 1 shows an example median filtered T_2 weighted image (TE≈70ms) of a rat fed with 600ppm HCP, with four ROIs depicting the four spinal cord tracts analyzed. The mean PSR and MWF, shown in **Table 1**, decreased after HCP intoxication. **Figure 2** shows the T_2 spectrum averaged across the four animals within each group. The HCP intoxicated rats showed an additional long-T2 component. Future work will employ numerical simulations based upon histological sections of the rat spinal cord to correlate individual tissue parameters and HCP induced changes in tissue microstructure with the observed changes in MET_2 and qMT measurements.

Conclusion

This work supports the utility of HCP to alter myelin within the rat spinal cord for investigation of micro-anatomical correlates of MET_2 and qMT.

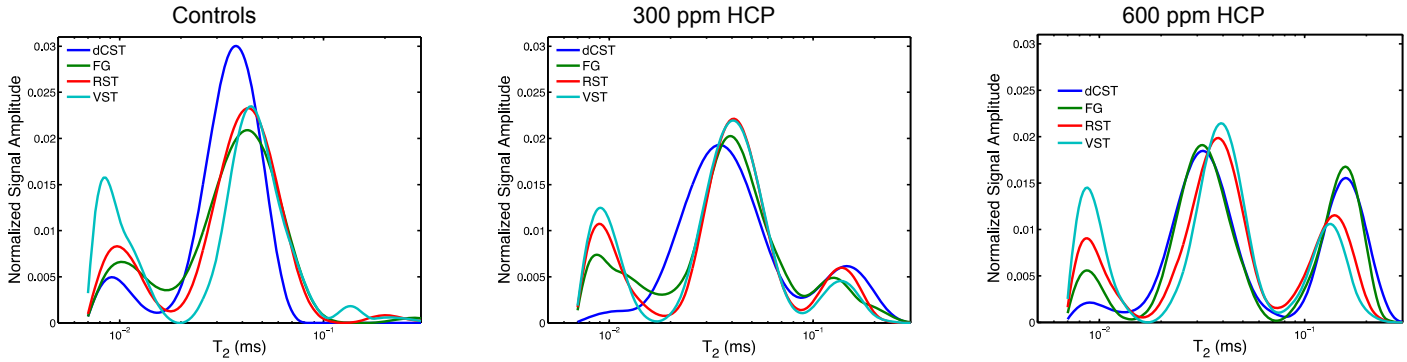

Figure 2: Average T_2 spectrum across the animal population within four spinal cord tracts.

N=4	Controls		600 ppm HCP	
	PSR	MWF	PSR	MWF
dCST	0.142 (0.012)	0.097 (0.051)	0.096 (0.017)*	0.046 (0.055)
FG	0.155 (0.013)	0.173 (0.087)	0.097 (0.004)*	0.087 (0.076)
RST	0.106 (0.006)	0.187 (0.040)	0.086 (0.007)*	0.159 (0.062)
VST	0.128 (0.012)	0.306 (0.022)	0.112 (0.006)	0.236 (0.024)*

Table 1: Mean (SD) PSR and MWF from four spinal cord tracts of rats fed with HCP. *Statistically significant (P<0.01) via two-tailed t-test.

References

1) Sled et al. MRM 2004; 51:299-303
2) Dula et al. MRM 2010; 63:902-909
3) Harkins et al. Proc. ISMRM 2010;
4) Persson et al. Acta Neuropath 1978; 42:115-120
5) Gochberg et al. MRM 2007; 57:437-441

Acknowledgements

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