Sensitivity of the MRI water proton resonance to myelin

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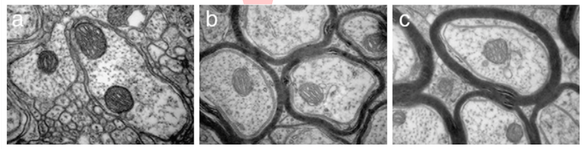
INTRODUCTION

Dysmyelinating diseases are characterized by abnormal myelin formation and function. Such microstructural abnormalities in myelin have been demonstrated to produce measurable effects on the magnetic susceptibility weighted MR signal.

This work examines these effects from postmortem fixed control and shiverer mouse brains on voxel-wise, high-resolution water spectra acquired using a multi-gradient echo (MGE) pulse sequence. Results demonstrate that components of the spectra are differentially affected by myelin concentration. This suggests that water proton spectra may be sensitive to the tissue microenvironment, specifically myelin, and could serve as a potential source of model-free MRI-based biomarkers of dysmyelinating disease.

Shiverer mice were used as a model of dysmyelination. As seen in the EM images below, (a) homozygous shiverer mice produce sparse, disorganized myelin compared with (b) their heterozygous counterpart and (c) wild type control mice.



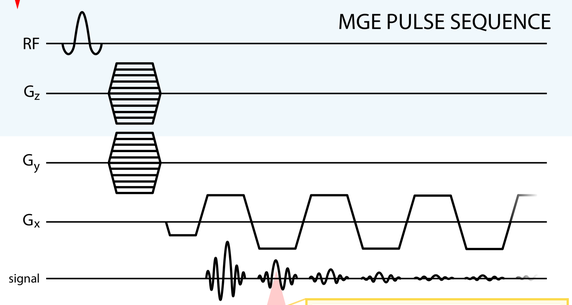
D. Pitt, et al. Brain Research, Oct 2009

METHODS

Perfusion fixed control (n=5) and shiverer (n=4) mouse brains were imaged at 9.4T (Bruker). Samples were placed in Fluorinert (FC-3283, 3M) for susceptibility matching and 3rd order shimming was iteratively performed using mapshim.

MGE IMAGING PROTOCOL
Spatial/Spectral resolution: 100μm isotropic/1.9Hz
TR/TE/Echo spacing: 1000ms/2.74ms/2.74ms
Number of echoes: 192
FID sampling duration: 526.1ms
Receiver bandwidth: 75kHz
Flip angle: 68°
Averages: 8
Duration: 3 hours per average (24 hours total)

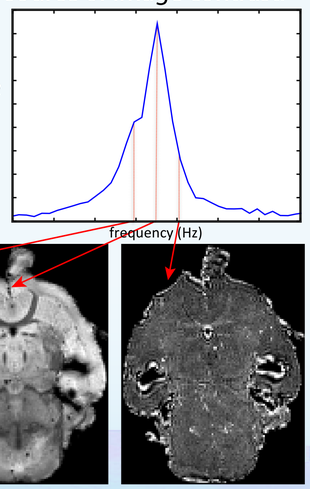
SPECTROSCOPIC IMAGING



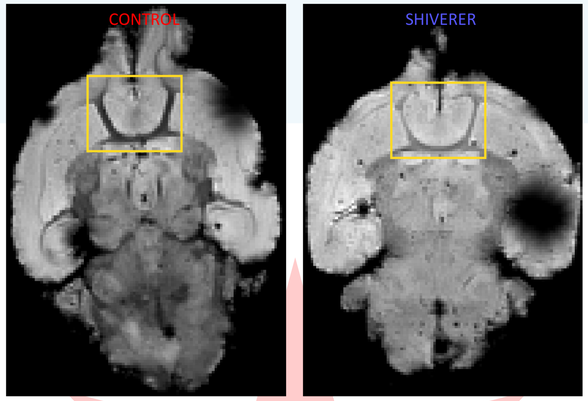
(a) Using the MGE sequence, the free induction decay (FID) for each high spatial resolution voxel is sampled to the noise floor. (b) Performing a Fourier transform along the time dimension produces a water spectrum, the details of which can be investigated for microstructurally dependent frequency components.

FOURIER COMPONENT IMAGES (FCIs)

Different frequency components of the voxel-wise spectra can be used as a source of image contrast. Any microstructurally dependent asymmetric feature of the resonance about the peak will be seen as varying image contrast between different FCIs.



WATER PEAK HEIGHT CONTRAST



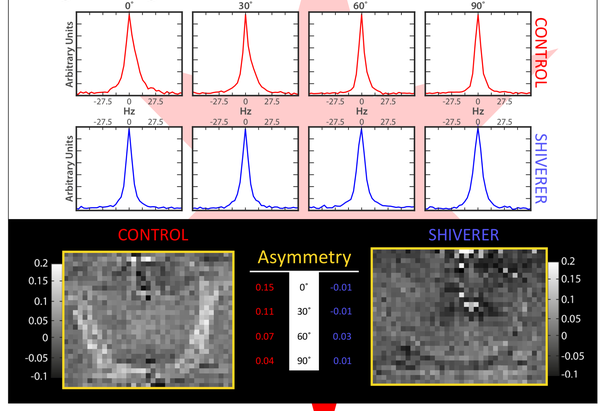
Grey/white matter contrast in water peak height images are clearly seen above. Grey/white CNR across pooled samples was statistically significantly larger in control compared with the shiverer (55.8 +/- 10.0 and 26.7 +/- 8.0, respectively - $p < 0.0003$ by two tailed Student's t-test). Since myelin is the dominant source of microstructural magnetic susceptibility difference between the samples, this suggests that this contrast difference is myelin dependent.

SPECTRAL ASYMMETRY

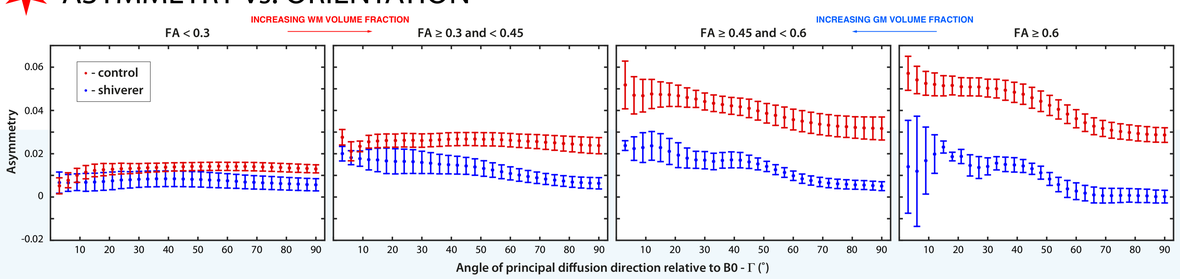
Voxel-wise asymmetric broadening of the resonance was quantified by computing the asymmetry about the main water peak (designated 0Hz):

$$ASYM(x,\ y,\ z) = \frac{\int_0^{58} f(x,y,z,\upsilon)d\upsilon \ - \ \int_{-58}^{0} f(x,y,z,\upsilon)d\upsilon}{\int_{-58}^{58} f(x,y,z,\upsilon)d\upsilon}$$

This produced both qualitative maps and quantitative results. Below are typical spectra and corresponding asymmetry maps and values from the anterior commissure (yellow boxes in water peak height images to the left).



ASYMMETRY vs. ORIENTATION



Pooled asymmetry for different ranges of grey/white matter volume fractions is plotted vs. the orientation of the underlying fiber population (as measured with DTI). As the white matter volume fraction increases, there is an increase in asymmetry in control compared with shiverer. There is also an orientational dependence that becomes prominent with increasing white matter volume fraction of both models. This suggests that myelin is driving the magnitude of the asymmetry in the resonance, but the variation with orientation is, at least in part, dependent on something else.

CONCLUSIONS

- The presence of myelin has a measureable effect on the resonance line shape of white matter
- This suggests that the water spectrum could be used as a model-free MRI biomarker of neurodegenerative diseases that specifically affect myelin