Resolving Cellular Specific Microarchitectures Using Double Pulsed Field Gradient Weighted, Relaxation-Enhanced Magnetic Resonance Spectroscopy

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Introduction

Cellular-specific microarchitectures can be altered by neurodegeneration and neuroplasticity [1]. Water-based MR approaches for characterizing such changes are handicapped by the ubiquitous presence of water in every cell type and every micron-scale substructure in the brain. By contrast, ^{1}H MRS that targets selectively compartmentalized metabolites could offer a glimpse into specific compartments in vivo and noninvasively [2]. Here, a Relaxation-Enhanced MRS (RE-MRS) [3], which is capable of depicting specific cellular microarchitectures *in vivo* through the application of a double Pulsed Field Gradient (dPFG) filter, is employed to target N-Acetylaspartate (NAA) and myo-Inositol (mI) resonances specifically compartmentalized in neurons [4] and astrocytes [5], respectively.

Experimental

All experiments were performed at the National High Magnetic Field Laboratory using the 21.1-T, 900-MHz ultra-widebore magnet. Juvenile Sprague-Dawley rats (N=6) weighing 220-300 g were examined. The RE-MRS sequence (Fig 1) involved 8-ms excitation pulses focusing on two bands incorporating the NAA singlet resonance at 2.02 ppm and mI multiplet resonances at 3.51 and 3.61 ppm. The dPFG module incorporates a CPMG block consisting of six refocusing pulses to eliminate susceptibility-induced cross-terms. dPFG parameters were: $\delta_1=\delta_2=4.5$ ms, $\Delta_1=\Delta_2=64$ ms, $t_m=25$ ms $|G_1|=|G_2|=24$ G/cm, TR/TE=2500/167 ms, NA=160. Angular dPFG experiments were performed by changing the G_1-G_2 angle (0:45°:360°) in the X-Y plane.

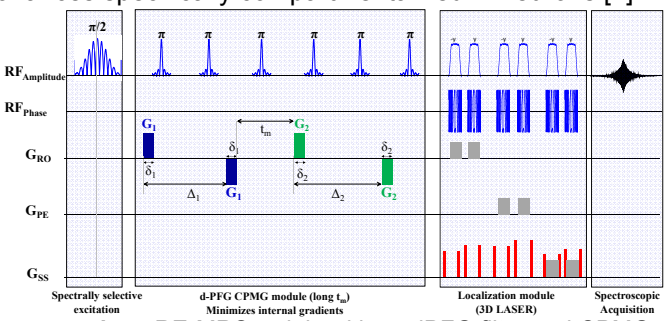

Fig 1. RE-MRS weighted by a dPFG filter and CPMG pulses.

Results and Discussion

One goal was to investigate whether mI and NAA could be resolved in the same spectrum, especially with the relatively low intensity of mI and its proximity to water. Clearly, mI and NAA are selectively excited, with no water signal residuals (Fig. 2). Representative spectra (Fig. 3) demonstrate the characteristic dPFG oscillation, whose origin can only be attributed to restricted diffusion within an ensemble of randomly oriented compartments. When neuronal vs. astrocytic oscillations are examined, good reproducibility and unequivocal restriction of diffusion are evident. Quantifications of these signal modulations reveal similar microstructures for both, likely arising from the "filter" imposed by the experiment, and correspond to neuritis and astrocytic processes.

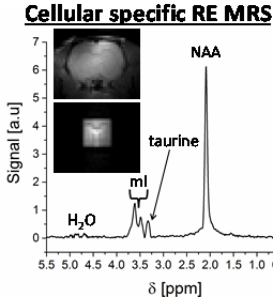

Fig 2. NAA and mI localized spectrum.

Conclusions

We present the first demonstration of unequivocal restricted diffusion signatures of cellular-specific metabolites, and show that a subset of microstructures can be probed.

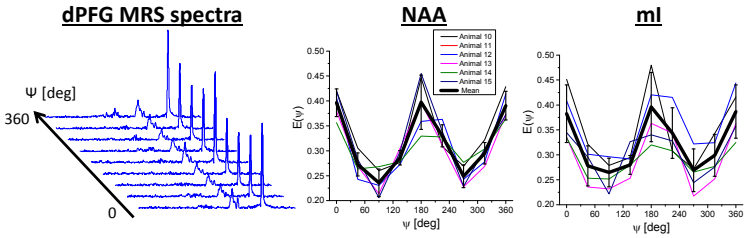

Fig 3. dPFG MRS spectra showing cos(2ψ)-like modulations for both NAA and mI indicative of restricted diffusion in randomly oriented

Acknowledgements

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References

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