Magnetization transfer spectroscopy of metabolites and macromolecules in human brain in vivo

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Introduction

The *in vivo* water signal has long been known to be reduced following presaturation of the broad signals several kHz away from it, though magnetization transfer (MT)[1]. Reductions have also been shown in human brain for creatine (Cr), lactate, and ethanol[2], but it has been thought that the other metabolites were not significantly affected. One study in animals has however shown significant although small effects of off-resonance MT pulses on most metabolites[3]. The objective of the current study was to implement MT spectroscopy on a clinical 1.5T scanner and characterize its effect on brain metabolites and macromolecules in normal controls.

Methods

The MT sequence was based on standard PRESS (TE/TR = 30/3000ms). Presaturation was achieved using 3 hard pulses, each of duration 132 ms and amplitude 0.745 uT (calculated equivalent on-resonance flip angle = 15070°). For a subject of average weight (75 kg), the Average, Average Head, and Peak SAR calculated for the sequence were 0.06, 1.44, and 3.89 W/kg respectively; for all subjects the SAR was within the National Radiation Protection Board guidelines. PROBE spectra (with and without CHESS water suppression using Gaussian pulses) were collected under 3 conditions: MT off; MT on, offset 2.5 kHz; and MT on, offset 30 kHz. In addition to the PROBE spectra, data were acquired at each MT offset with an inversion pulse (TI 650 ms) to null small metabolites. These spectra were assessed for an MT effect on macromolecule signals, and were subtracted from the metabolite spectra to improve the baseline for LCModel analysis[4]. Spectra were acquired in 28cc voxels in human right frontal lobe (n=5), and in 3 phantoms: GE MRS Head, distilled water, and 20% gelatin. Total spectroscopy acquisition time was c. 15 min.

Results and Discussion

On-resonance saturation (0 Hz offset) reduced water signal by about 90% both in distilled water and in gelatin, and by 84% *in vivo* (Fig. 1). The 30 kHz offset pulses were found to have a 1% effect on the gel compared to a spectrum with no MT pulses, and the 2.5 kHz pulses had a 4% direct effect on pure water. The direct effect on metabolites should be less than this, as the frequency separation is greater for metabolites than for water (range 2.6 – 2.72 kHz). The frequency response of the *in vivo* water peak to MT offset was very similar to that for the gel. At 30 kHz offset, there was only about a 2% effect, whereas at 2500 Hz offset, the water resonance was reduced by almost 50% (Table 1). It was confirmed that there was <4% direct saturation of the metabolite peaks at 2.5 kHz offset by comparing spectra obtained at the 2 offsets on the GE MRS Head phantom, which should show no MT. Both superimposed almost perfectly with the spectrum acquired with no MT pulses (Fig. 2). *In vivo*, the metabolite-nulled spectra obtained at the 2 offsets also superimposed almost perfectly, indicating that the MT pulses have very little effect on the macromolecule signals (Fig. 3). Subtracting these spectra from the raw data gives metabolite spectra nearly free from macromolecule signal. Overlays of these at the 2 frequency offsets show a small but consistent reduction in signal in the 2.5 kHz offset condition.

In agreement with previous studies[2,3], the largest percentage effect of the MT pulses (13%) was seen on Cr (Table 1). However, there was also a significant effect seen on NAA+NAAG (8%), which was not previously found in humans[2], and a nonsignificant trend of an effect on choline (7%).. We also found a significant effect on myo-inositol (Ins) (6%) and a larger although non-significant effect on glutamate plus glutamine (Glx) (10±20%). These results concur with the animal studies of de Graaf [3], suggesting that this method will be similarly powerful in humans for investigating the MT effect *in vivo* for all metabolites visible in short-echo time spectra.

References

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[4] McLean MA, Simister RJ, Barker GJ, Duncan JS (2004). Faraday Discuss. 126 (in press).

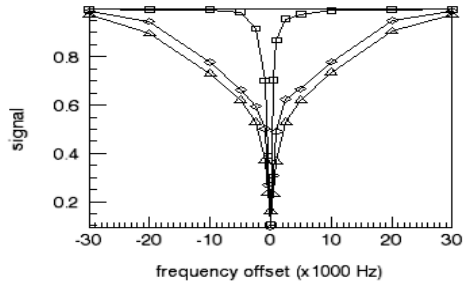

Figure 1: Water signal vs frequency offset of the MT pulses in: pure water (□); 20% gelatin (◊); frontal lobe *in vivo* (Δ).

Table 1: Mean *in vivo* frontal lobe concentrations (mM ± 1SD) with MT pulses at offsets of 30 kHz (C_{30}) and 2.5 kHz ($C_{2.5}$); P values for paired t-tests C_{30} vs. $C_{2.5}$; and mean percentage MT (%MT: $100*(C_{30}-C_{2.5})/C_{30}$).

metabolite	C_{30}	$C_{2.5}$	P	%MT
NAA+NAAG	7.5 ± 0.3	6.8 ± 0.2	<.01	8 ± 3
Creatine	4.7 ± 0.1	4.1 ± 0.2	<.01	13 ± 5
Myo-inositol	3.1 ± 0.3	3.0 ± 0.4	<.05	6 ± 4
Choline	1.10 ± .11	1.02 ± .06	0.13	7 ± 8
Glu+Gln	6.7 ± 1.1	5.9 ± 1.1	0.27	10 ± 20
water	ND	ND	ND	47 ± 1

(ND = not determined).

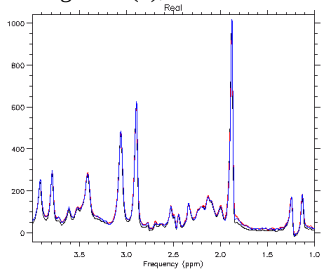

Figure 2: Overlay of spectra acquired in GE MRS Head phantom with MT pulses: at 30 kHz offset (red); at 2.5 kHz offset (blue); no MT pulses (black).

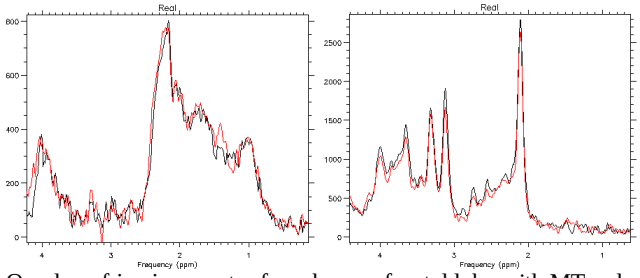

Figure 3: Overlay of *in vivo* spectra from human frontal lobe with MT pulses at 2.5 kHz (red) and 30 kHz (black) offsets. Left: metabolite-nulled spectra (TI 650 ms); right: macromolecule-corrected spectra (raw minus nulled).