Concentrations and magnetization transfer ratios of metabolites in grey and white matter

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Introduction

We have previously shown higher concentrations of most metabolites in grey matter than white using short-TE MRSI (1). This was most marked for glutamate+glutamine (Glx); however, the quantification of Glx was hampered by the contribution of macromolecule (MM) resonances at the same frequencies, which can be removed by using metabolite-nulling (2).

Most metabolite signals show a small attenuation following the application of magnetization transfer (MT) presaturation pulses (3,4). This study investigates for the first time using MRSI whether the percentage MT effect on metabolites differs in white and grey matter, and also re-investigates the concentration differences in white and grey matter when correction for macromolecules is incorporated.

Methods

Seven normal volunteers were studied using a 1.5T GE SIGNA scanner and the standard birdcage head coil. Three PRESS-localized MRSI datasets were acquired (TE/TR = 30/3000 ms, 16x16 matrix, 24 cm FOV, 1.5 cm thick, nominal VOI 3.375 cc): one with an inversion pulse of TI 650ms to null small metabolite signal; one with 3 MT pulses applied at an offset of 2500 Hz from the water resonance (4); and one with neither MT nor inversion pulses. A single average was acquired for each dataset, for a total spectroscopy scan time of *c.* 45 minutes.

Spectra were analyzed using LCModel, with and without subtraction of the metabolite-nulled datasets. Metabolite concentrations reported by LCModel were corrected for voxel CSF content estimated using SPM2 (Wellcome Dept. of Imaging Neuroscience, UCL, London) and plotted against the fractional content of grey matter in the voxel (1). The concentrations and also SNRs and standard deviations (SDs) reported by LCModel were compared between raw and MM-subtracted data, and between MT pulses off and on.

The MT ratio (MTR) was calculated as the difference in apparent concentration with MT pulses on and off, divided by that with no MT pulses.

Results

Unlike in single voxel spectroscopy (5), subtraction of the macromolecule baseline was found to have a negative effect on quantification. The SD reported by LCModel, a reflection of the Cramer-Rao lower bounds, was higher for all metabolites after MM-subtraction. As in (5), the SNR was reduced by MM-subtraction by a factor of root 2, but the lower starting point (mean raw SNR=17 vs. 36) increased the importance of this effect.

A map of the MM signal, created by integrating the area from 0-3ppm in the metabolite-nulled spectrum, suggested slightly higher MM content along the midline, an area of greater grey matter than white (Fig. 1). This disagrees with an earlier study which found equal content of MM in grey and white matter (2). Correlations of metabolite concentrations with grey matter fraction (Table 1) were slightly weaker following MM-subtraction, as reflected in reduced R^2, perhaps partly due to the increased variance in the data for most metabolites, e.g. Cr (Fig. 1). However, Glx was altered more substantially and plausibly by MM-subtraction: the estimated concentrations in grey matter (i.e., when x=1.0 in Table 1) were reduced from 14.8 to 11.8 mM.

All metabolites showed significantly lower apparent concentrations with MT pulses on than off in paired t-tests ($P<0.005$ for all), but no significant relation between MTR and grey matter fraction was found ($R^2<0.1$ for all).

Conclusion

Metabolite nulling did not improve the precision of quantification of metabolites in MRSI of the brain *in vivo*, although it may have improved the accuracy for Glx, which is presumed to be overestimated when macromolecule signal is present. The concentrations of Glx and Cr were strongly correlated with grey matter content even after MM-subtraction.

An MT effect was observed on all metabolites, similar to that found in a single voxel study with similar methodology (4). The MTR did not correlate with grey matter content of voxels, suggesting that unlike the MT effect on water, it is not mediated through myelin.

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Table 1: Metabolite concentrations as a function of grey matter fraction (x); and mean MTR, with (MM-sub) and without (raw) subtraction of a metabolite-nulled baseline.

metabolite	Raw (mM)	R^2	MM-sub (mM)	R^2	Raw MTR (%)	MM-sub MTR (%)
total NA	7.6 + 2.1x	.21	7.5 + 1.7x	.16	5 ± 6	6 ± 6
Creatine	3.6 + 3.7x	.64	3.9 + 3.2x	.55	11 ± 10	10 ± 9
Choline	1.16 + 0.02x	<.01	1.17 – 0.06x	<.01	3 ± 14	3 ± 14
Inositol	2.9 + 2.2x	.27	3.2 + 2.3x	.19	7 ± 20	4 ± 20
Glx	5.8 + 9.0x	.54	4.4 + 7.4x	.49	6 ± 15	10 ± 18

References

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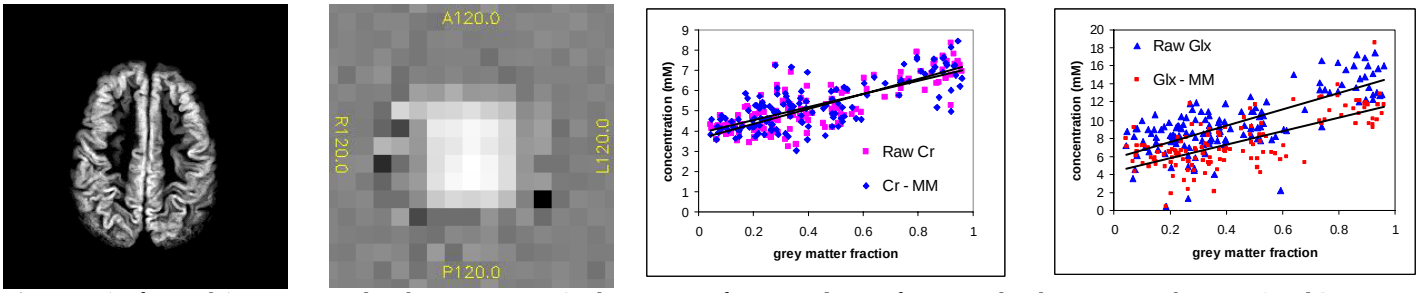

Figure 1: (Left to right) grey matter distribution over MRSI slice; image of integrated area of macromolecule resonances between 0 and 3 ppm; dependence of concentration on grey matter fraction of voxel for creatine, with (- MM) and without (raw) macromolecule subtraction; and for Glx.