Unravelling Glutathione and other low concentration cerebral metabolites using 2D Correlated Spectroscopy on a 3T MRI scanner

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Introduction: In vivo detection of glutathione (GSH - a tri-peptide and powerful anti-oxidant) and neurotransmitters like GABA (inhibitory), Glx (Glutamate-excitatory and Glutamine-inhibitory) using non-invasive MRS techniques is an area of considerable interest and innovation due to its correlation with various pathologies (1). Detection of these metabolites using 1D MRS is often hampered, even at 3T due to overlap complicated by the small window of chemical shifts and multiplets caused by J-coupling. Localized 2D MR Spectroscopy enables resolving the overlapping metabolites *in vivo*. The major goal of this work was to assess the reliability of two groups of cerebral metabolites, first in the range of 0.5mm-2mM and the second with concentrations greater than 2mM using optimized post-processing of 2D L-COSY (2).

Methods: A GE 3T MRI/MRS scanner equipped with self-shielded gradients (40mT/m) and an extended visual coil was used for both excitation and signal reception. Two-dimensional L-COSY spectra were recorded in predominantly gray matter of the occipital-parietal region using a 3x3x3 cm^3 volume combined with the following parameters. TR=2s, minimal TE=30ms, 64 data points and linear predicted with 128 points along t_1 and 2048 complex points acquired along t_2. 2D MRS post-processing was performed using FELIX software. Squared sine-bell filters were applied along both dimensions before zero-filling to (2048x256) and subsequent double Fourier transformation. Two different sets of sine-bell filters were optimized for higher and lower concentrated metabolites. Six healthy human subjects (21-25 years) have been investigated so far.

Results and Discussion: Figure 1 shows theoretical 3T 1D MR spectra (0 - 5ppm) of GSH, glutamate (Glu), glutamine (Gln), aspartate (Asp), N-Acetyl-aspartate (NAA), GABA, and creatine (Cr) simulated by the GAMMA library (3). It is evident that GSH, GABA and glutamine/glutamate (Glx) overlap extensively with several metabolites. Figure 2 shows a 2D L-COSY spectrum recorded from the occipito-parietal region of a 22 year-old healthy volunteer. We can readily see that the cross peaks of several metabolites including GSH (4.5/2.9ppm), GABA (3.0/2.0 and 2.0/3.0 ppm), Glx (3.7/2.2 and 2.2/3.7), PCh (4.3/3.8 ppm), Threonine/Lactate (4.3/1.3 ppm), Asp (3.8/2.8 and 2.8/3.8) ppm can be unambiguously detected. The 2D peak volumes of these cross peaks, and the ratios with respect to Cr/PCr at 3ppm were calculated in six subjects. The ratios (mean±SD) and the coefficient of variance of the 2D cross peaks were (0.028039± 0.005, 18%), (0.01792±0.004, 22%), (0.0683±0.012, 17%), (1.096±.11,10%), (.0432±.012, 28%), (.0348±.010, 29%), (.0237±.005, 21%) for GSH, GABA, Glx, NAA, PC, ASP, and Threonine/Lactate respectively. Clear separation of the cross peaks from GSH and GABA due to the added second dimension reduces the coefficient of variance in the 2D experiment compared to the deconvolution process employed by the LC-Model.

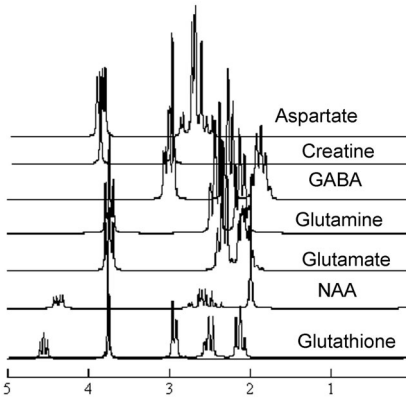

Figure 1

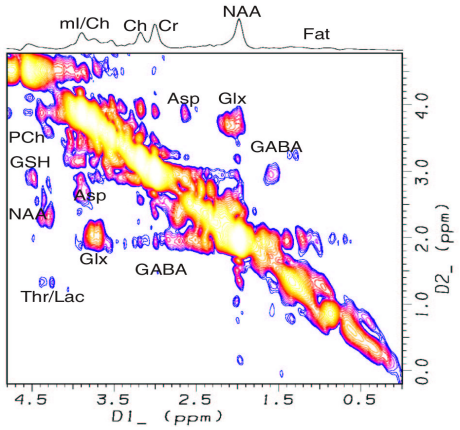

Figure 2

Conclusion: In contrast to depending on a post-processing algorithm to deconvolute overlapping metabolite peaks detected by 1D MRS (LC-Model, MRUI), our preliminary results demonstrate that the cerebral metabolites at low physiological concentrations (0.5-2mM) can be resolved using L-COSY within acceptable range of errors in these measurements. A systematic comparison of these findings with LC-Model processing (4) of 1D MR spectra under identical experimental conditions is under investigation.

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