Optimized detection of glutathione in the human brain at 3T using MEGA-PRESS

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Introduction

Glutathione (GSH) is believed to play an important role in the brain as an antioxidant, but is difficult to measure by MRS *in vivo* because of its relatively low intensity and overlap with other, more intense, resonances. Therefore, most attempts to measure GSH have used spectral editing techniques, based on either difference spectroscopy[1] or multiple-quantum filtering. In this abstract, it is demonstrated that, because of the finite bandwidth of the slice-selective refocusing pulses, *in vivo* detection of glutathione using the MEGA-PRESS[2] editing sequence is significantly affected by spatially-dependent J-modulation effects. It is shown that an appreciable increase in sensitivity can be gained by using high-bandwidth pulses, and the optimal echo-time for GSH detection is also investigated.

Material and Methods

MEGA-PRESS experiments were performed on a phantom (100 mM GSH) and on a healthy human volunteer, using a Philips Intera 3T system with a six-channel SENSE receive head coil. RF pulses were transmitted on the body coil which has a maximum RF field of 14 μT (≈ 600 Hz). Phantom measurements of a 3x3x3 cm^3 voxel were performed in 2 minutes; *in vivo* measurements were performed of a 4.5x4.5x4.5 cm^3 voxel located in the posterior white matter in a total experiment time of 17 minutes (TR = 2s, TE = 140 ms, TE1 = 26 ms, TE2 = 114 ms). Measurements were performed using either conventional 9-lobe sinc-Gauss slice-selective refocusing pulses of bandwidth 600 Hz, or numerically optimized FM refocusing pulses ("fmref07"[3]) of bandwidth 2.2 kHz. 2D PRESS-MRSI was performed to demonstrate the spatial evolution of the modulation due to J-coupling (matrix size 20x20; FOV 80x80 mm^2; voxel 55x55x20 mm^3). Phantom measurements were also acquired at a range of echo times (68-160 ms) using a 5-lobe sinc-gauss refocusing pulse and the fmref07 pulse (100-160 ms).

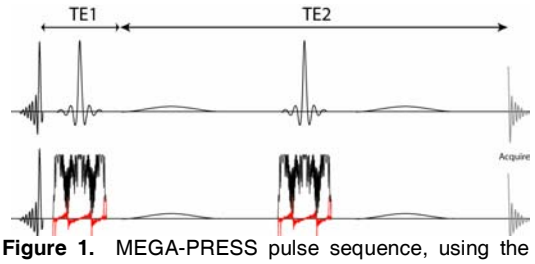

Figure 1. MEGA-PRESS pulse sequence, using the sinc-gauss (top) and fmref07 pulse (below, frequency modulation in red).

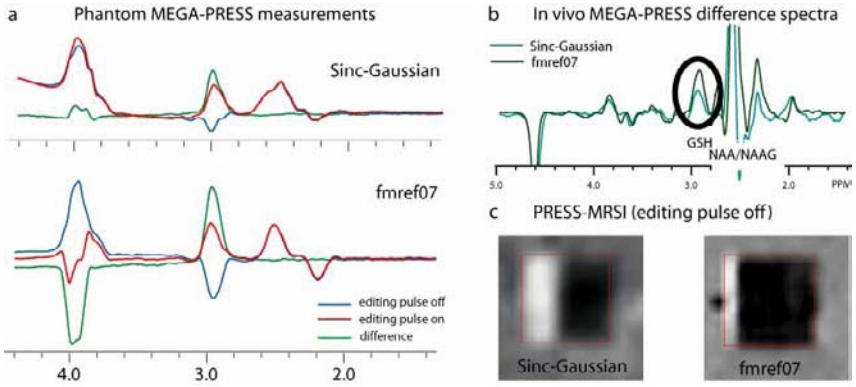

Figure 2. MEGA-PRESS of glutathione. Phantom (a) and in vivo measurements (b) show a similar improvement in signal intensity, using high-bandwidth refocusing pulses. MRSI of the 'editing pulse off' experiment (c) shows the spatial origin of the signal loss.

Results

The phantom single-voxel measurements (Figure 2a) clearly demonstrate that the edited difference signal is appreciably larger (47%) in the fmref07 experiment (lower spectrum). They also show that the signal loss primarily occurs in the 'editing pulse off' experiment. Phantom MRSI results are shown in Figure 2c, explaining the almost total cancellation of signal in the sinc-gauss experiment, since almost half the voxel contains un-modulated signal. *In vivo* results in Figure 2b show a 44% increase in edited signal intensity (as well as significant co-editing with NAA/NAAG). Investigation of the optimum echo time (Figure 3) appears to favour echo times of 120-140 ms (in contrast to Terpstra et al.[1] using 68 ms at 4 T).

Discussion

The GSH peak detected at 2.9 ppm consists of two unresolved doublets, both coupled to the methine proton at 4.5 ppm. Successful editing of this resonance with MEGA-PRESS requires the subtraction of one scan in which the signal is inverted due to J-coupling from a second in which it is not. Spatial variation of J-coupling effects at high fields using PRESS is well known for compounds such as lactate, but is less recognized for other compounds. Because the chemical shift difference of the coupled GSH resonances is quite large, significant losses in the MEGA-PRESS editing sequence will occur (~40% under the conditions used here). This abstract shows that these losses can be significantly reduced by the use of high-bandwidth frequency-modulated refocusing pulses. An alternative approach to this problem would also be to use the IVS method[4], which uses saturation pulses to eliminate regions of the voxel with unwanted modulation patterns. The experiments performed here also confirm that, with appropriate refocusing pulses, the optimum TE for MEGA-PRESS GSH editing is in the range of 120-140 ms, as expected (1/J) for a 7 Hz coupling constant.

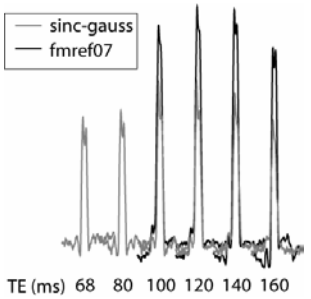

Figure 3. Variation of signal intensity with echo time.

References

1. Terpstra M, Henry P-G & Gruetter R Magn Reson Med 50, 19-23 (2003). 2. Mescher M, Merkle H, Kirsch J, Garwood M, & Gruetter R. NMR Biomed 11(6), 266-272. (1998), 3. fmref07 pulse designed by Jim Murdoch, Philips Medical Systems. 4. Edden RAE, Schär M, Hillis AE & Barker PB Magn Reson Med 56 (4), 912-917 (2006). *Supported by NIH P41 RR15241 and Philips Medical Systems.