Detection of Glutathione in Human Brain In Vivo by Yield-Enhanced Double-Quantum Filtering at 3T

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INTRODUCTION

Glutathione (GSH) in human brain is difficult to measure by ^{1}H MRS because of its relatively low concentration and the abundant overlapping signals from N-acetylaspartate (NAA), glutamate (Glu), and creatine (Cr), etc. The coupled resonances of the cysteine moiety at ~2.95 ppm have been targeted in several editing approaches [1-3]. The editing yield of prior methods is < 50% with respect to a 90°-acquired signal. The large chemical shift difference between the GSH resonances causes substantial signal loss under the limited excitation bandwidth of the slice-selection RF pulses. Here, we report yield-enhanced GSH double quantum filtering (DQF), achieved with interchange of DQC and ZQC during the encoding period and spatial localization with large-bandwidth adiabatic 180° pulses. A preliminary result from human brain in vivo is presented.

METHOD and MATERIALS

The cysteine moiety of GSH exhibits a multiplet at ~2.95 ppm, arising from scalar coupled resonances at 2.93 and 2.97 ppm. These two resonances are weakly coupled to the 4.56-ppm resonance. Fig. 1 depicts a GSH DQF sequence and the evolution of the target coherences over the sequence. Following the generation of antiphase coherences during TE_1, a 10-ms long single-band Gaussian 90° RF pulse, tuned to 4.56 ppm, was applied at the end of TE_1, converting antiphase coherences to DQC and ZQC equally. Encoding of DQC with a gradient G_1 was followed by a 20-ms-long double-band Gaussian180° pulse, tuned to 4.56 and 2.43 ppm, as shown in Fig. 2. The selective 180° rotation of the 4.56-ppm resonance and null effect on ~2.95 ppm induced interchange between DQC and ZQC. Another encoding gradient G_2 that was equal to G_1 was applied to encode the DQC that has been converted from ZQC. The encoded coherences were then converted to antiphase coherences by the second S90 and decoded with a gradient G_3 (= $2G_1$ = $2G_2$) during TE_2, eventually bringing about a target multiplet at ~2.95 ppm. Suppression of neighboring resonances of NAA and aspartate (Asp) was taken into account in designing the D180 pulse. The bandwidth of this 20-ms long D180 was large (51 Hz at half amplitude), causing partial excitation (60%) of the NAA resonance at 4.38 ppm. The D180 pulse was designed to excite its coupling partners at 2.67 and 2.49 ppm, but have no effect on the GSH 2.93 and 2.97-ppm resonances. The DQC of NAA at the beginning of the TM period were therefore largely preserved, and encoded by both G_1 and G_2, consequently being dephased with the G_3 gradient in TE_2. Potential contamination of the Asp 2.8-ppm resonance was eliminated by excluding its coupling partner (3.89 ppm) from the excitation band of the D180 pulse. RF phase optimization [1] is not required in this editing.

Single-voxel localization was obtained with a 90° RF pulse (3.0 ms; BW = 3.8 kHz) and two pairs of adiabatic 180° pulses (5 ms; BW = 5.0 kHz). The spectral difference between the GSH resonances was ~4% with respect to the refocusing bandwidth of the slice-selection 180° pulse, thereby minimizing signal loss due to the voxel displacement effect.

The DQF sequence was tested on a phantom solution (pH = 7.0) with GSH (37 mM), NAA (33 mM), and Gly (50 mM). In vivo tests were performed on a healthy volunteer (parietal cortex). Spectra were acquired from a 30×30×30 mm^3 voxel, with adiabatic double-echo (NEX = 16) and DQF (NEX = 256) sequences. TR was 2.4 s. Experiments were carried out at 3.0 T in an 80-cm bore magnet, interfaced to a SMIS console. A standard quadrature birdcage head coil was used for RF transmission and reception.

RESULTS and DISCUSSION

Numerical simulation and phantom tests indicated that a DQF GSH signal was maximized at sequence times, {TE_1, TM, TE_2} = {67, 46, 46} ms. Fig. 3 presents a phantom DQF spectrum, together with spectra from a 90°-acquisition and an adiabatic double echo (TE = 113 ms) sequence. In the 90°-acquired spectrum, the area of a GSH multiplet at ~2.95 ppm is 75% with respect to the Gly singlet, reproducing the phantom concentration ratio well. A DQF GSH signal shows peak area 39% relative to the Gly singlet from an identical voxel. DQF editing efficiency versus 90°acquisition is therefore estimated as 55% (= 39/75). This result indicates substantial yield enhancement of the present method, compared with a recent report [3]. Fig. 4 displays in vivo spectra obtained from the parietal lobe of the human brain. The GSH edited peak exhibits area 37% with respect to the Cr 3.02-ppm singlet. Assuming identical T_1 and T_2 between GSH and Cr, GSH concentration is estimated to be 0.8 mM, with reference to Cr at 8 mM. A drawback of the present method is that the Cr singlet resonance is co-edited in a single shot. Since the Cr resonance is not affected by the D180, phase cycling of D180 can be used to cancel the Cr resonance in alternate scans. Elimination of potential Cr contamination is indicated by the complete suppression of the NAA singlet which undergoes similar cancelation. In conclusion, we have demonstrated the feasibility of interchanging DQC and ZQC for signal enhancement in GSH DQF. Further in vivo studies are currently underway.

FIG. 1. Overview of the GSH DQF sequence and the coherence evolution. The first 90° pulse and two pairs of adiabatic full passage (AFP) pulses are slice selective. S90 denotes a single-band 90 pulse tuned to the GSH 4.56-ppm resonance. D180 during TM is a dual-band 180° pulse, tuned to 4.56 and 2.43 ppm. The 180° rotation at 4.56 ppm by D180 interchanges DQC and ZQC of GSH, enhancing the edited signal at ~2.95-ppm, with encoding and decoding gradients, $2G_1 = 2G_2 = G_3$. {TE_1, TM, TE_2} = {67, 46, 46} ms.

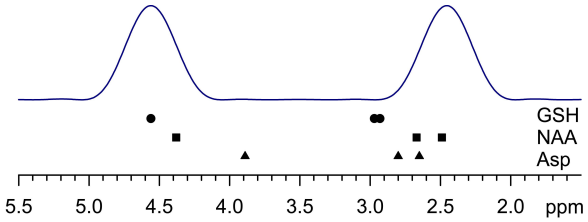

FIG. 2. Excitation profile of D180, and the resonances of the target metabolite (GSH) and interferences (NAA and Asp).

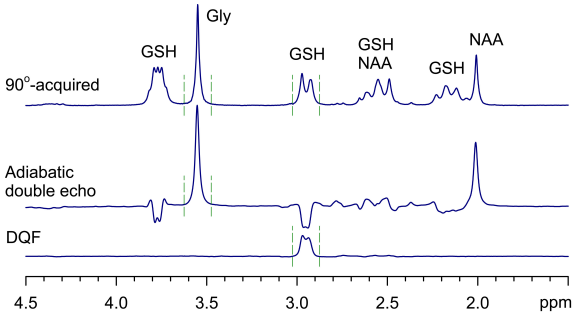

FIG. 3. Phantom spectra following a 90° pulse, an adiabatic double-echo sequence (TE = 113 ms), and a GSH DQ filter. Spectra are broadened to 3 Hz. Spectra are scaled with respect to the Gly signal. Amplitude and area were calculated between vertical dashed lines.

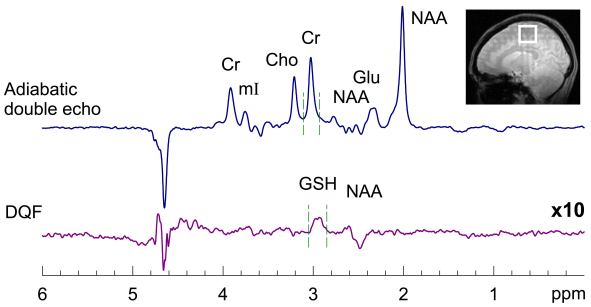

FIG. 4. In-vivo human brain spectra (parietal; 30×30×30 mm^3) following an adiabatic double-echo sequence (TE = 113 ms) and a GSH DQ filter, together with voxel positioning. The DQF spectrum is magnified 10 times. Spectra were filtered with a 3-Hz exponential function. TR = 2.4 s. NEX = 16 (Adiabatic double echo), 256 (DQF). Amplitude and area were calculated between vertical dashed lines.

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