Measurement of glycine in the human brain by 1H-MRS at 3T

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INTRODUCTION

Glycine (Gly), an inhibitory neurotransmitter and co-agonist at the N-methyl-D-aspartate receptors, has a singlet resonance at 3.55 ppm. Because of its low concentration and the overlapping coupled resonances of *myo*-inositol (mIns) at much higher concentrations, precise measurement of Gly by ^{1}H-MRS remains as a challenge. For intermediate field strengths, following the applications of 2D J-resolved PRESS (point-resolved spectroscopy) at 3T [1] and TE-averaging PRESS at 4T [2], a long-TE triple refocusing method was reported for 3T [3]. Recently, short-TE and optimized long-TE approaches were reported at 7T [4, 5]. Here, we report an optimized long-TE PRESS method for differentiation between Gly and mIns at 3T. Preliminary *in vivo* results from healthy volunteers are presented.

METHODS

Differentiation between the Gly and mIns signals at ~3.55 ppm using a standard PRESS sequence has been explored at 3T. Subecho time dependence of the mIns coupled resonances was investigated, with density matrix simulations, for TE_1 and TE_2 in 20 – 200 ms. The simulation indicated that the Gly and mIns signals at ~3.55 ppm can be separated using a subecho time pair, (TE_1, TE_2) = (60, 100) ms. The simulations were undertaken incorporating the slice selective RF pulses of the PRESS sequence; a 9.8-ms 90° RF pulse (bandwidth = 4.2 kHz) and a 13.2-ms 180° RF pulse (bandwidth = 1.3 kHz). Preliminary *in vivo* tests of the sequence were carried out on a Philips whole-body 3T scanner (Philips Medical Systems). A body coil was used for RF transmission and an 8-channel phased-array coil for reception. Six healthy volunteers were employed in the study. Single-voxel localized ^{1}H spectra were obtained from two brain regions (voxel size 30×30×30 mm^3); occipital cortex (3 subjects) and parieto-temporal lobe (3 subjects). Data were acquired in sixteen blocks, each with 4 averages. The data were corrected for frequency drift and residual eddy current effects individually prior to the summation of the data. LCModel software [6] was employed to analyze the spectra, using numerically simulated model spectra of twenty metabolites as basis functions. Published chemical shift and J coupling constants were used in the simulation [7].

RESULTS and DISCUSSION

Figure 1 presents numerically-calculated spectra of brain metabolites at a physiological concentration ratio [7] for PRESS (TE_1, TE_2) = (60, 100) ms at 3T. The mIns multiplet is reduced due to the J evolution effects (Signal reduction ratio relative to 90°-acquisition for the localized volume being ~8). Although the residual mIns multiplet exhibits amplitude (at 3.62 ppm) ~1.3 times greater than the Gly singlet for [Gly]:[mIns] = 1/8, the multiplet exhibits a decreasing pattern towards the Gly resonance, thereby allowing detection of the 3.55-ppm Gly singlet, as indicated in the sum spectra. Figure 2 displays a stack of *in vivo* spectra obtained from two brain regions as indicated in the images. The spectra all exhibit a spectral pattern at 3.5 – 3.6 ppm similar to the mIns-Gly composite signal shown in Fig. 1. The multiplets in 2 – 3 ppm are also as predicted by the simulation. Figure 3 presents a spectral analysis result from LCModel (for the spectrum from subject 1 in Fig. 2). An LCModel fit using a basis function without Gly is also shown for comparison. While an LCModel fit with Gly in the basis function gives noise-level residuals at ~3.55 ppm, a fit without Gly exhibits large residuals at the Gly resonance. This incomplete basis function is also reflected as a distortion in the baseline at ~3.55 ppm. The large residuals and baseline distortion from the fit without Gly in the basis function were observed consistently in all spectra, indicating that a signal at 3.55 ppm is primarily attributed to Gly. With LC model fitting, [Gly]/[Cr] and [mIns]/[Cr] were estimated to be 0.08±0.01 and 0.70±0.07 (mean±SD, N = 3) for the occipital lobe, and 0.07±0.01 and 0.81±0.21 (N = 3) for the parietal lobe, respectively. A mean Cramér-Rao lower bound (CRLB) of Gly was 9±1% for the six spectra. Compared to a prior long-TE (200 ms) triple refocusing study at 3T, which gave CRLB of Gly at 13% [3], the CRLB of Gly in this study is notable since the scan time is 5-fold shorter for a similar voxel size (*i.e.*, 2 min vs. 10 min). This is likely due to the multi-channel reception of MR signals (high-SNR performance) and in part due to slightly reduced T_2 signal loss (TE = 160 ms). Further, the Gly CRLB of 9% in the present study at 3T is quite comparable to those of prior 7T studies (*i.e.*, 7%) [4, 5].

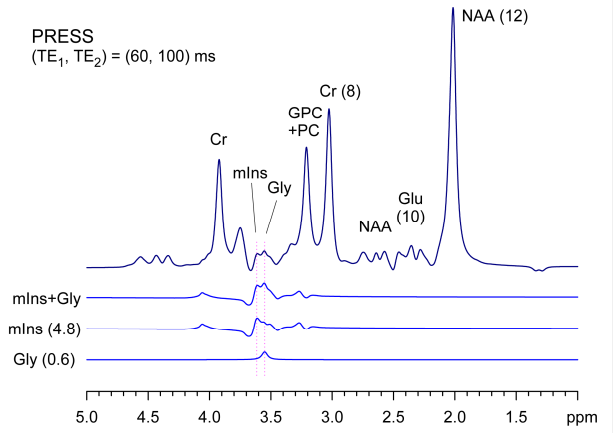

FIG 1. Density-matrix simulated spectra of brain metabolites at a physiological concentration ratio (as indicated in brackets) for PRESS (TE_1, TE_2) = (60, 100) ms at 3T. Spectra of mIns and Gly are shown at the bottom. Spectra are broadened to 7 Hz. Vertical lines at 3.55 and 3.62 ppm indicate Gly and mIns peaks, respectively.

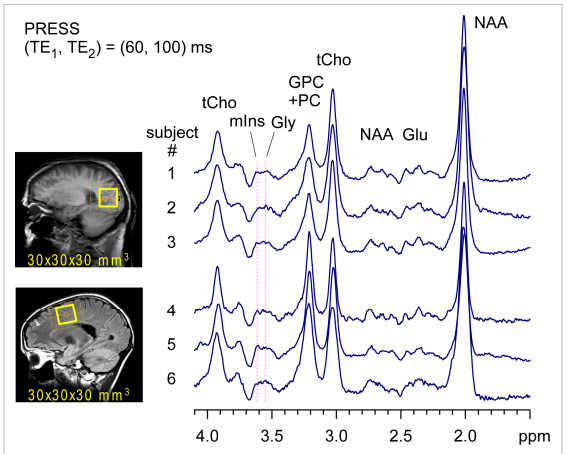

FIG 2. A stack of in vivo brain spectra obtained with PRESS (TE_1, TE_2) = (60, 100) ms at 3T are shown together voxel positioning. TR = 2 s. NEX = 64.

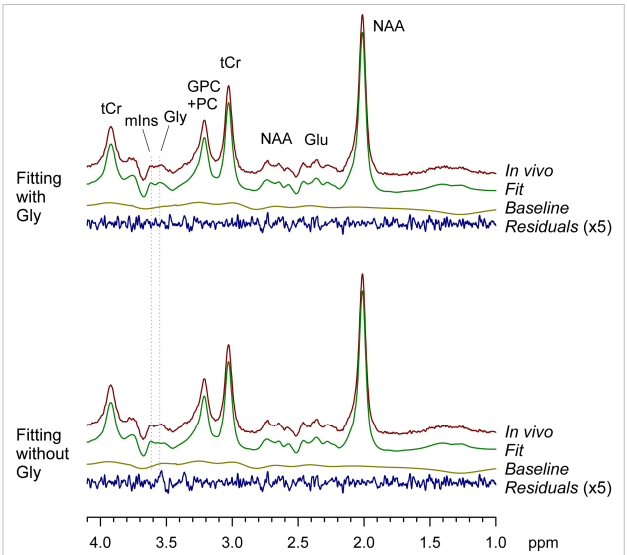

FIG 3. Illustration of LCModel analysis results (for the spectrum from subject-1 in Fig. 2) obtained using a basis set with and without Gly. The fit without Gly results in increased residuals and distorted baseline at ~3.55 ppm. The residuals are 5-fold magnified.

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