Quantification of glycine in the human brain by PRESS at 3T

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INTRODUCTION

Glycine (Gly) in the human brain is difficult to measure reliably by standard short-TE ^{1}H-MRS approaches at intermediate field strengths, due to its relatively low concentration and the spectral overlap with *myo*-inositol (mI) at normally much higher concentrations. The J coupling effects between the mI resonances can be exploited for detection of the Gly singlet. Prior studies include 2D J-resolved MRS at 3T [1], TE-averaging at 4T [2], and long-TE triple refocusing at 3T [3]. Although these methods provide Gly measures with improved selectivity, the methods all require modifications to the standard sequences and/or post-data processing. Given that PRESS and STEAM sequences are readily available in most clinical MR scanners, direct measurement of Gly by these standard methods may greatly facilitate clinical applications of ^{1}H-MRS. Here, we present the feasibility of an optimized long-TE PRESS method for differentiation between Gly and mI in the human brain at 3T.

METHODS

PRESS subecho time dependence of the mI coupled resonances was investigated for Gly detection at 3T, with numerical simulations that include the 3D volume localization by the shaped RF and gradient pulses. Spectra of Gly and mI were calculated for TE_1 and TE_2 in 20 – 200 ms. Published chemical shift and J coupling constants were used in the simulation [4]. Single-voxel localization was obtained with a 9.8-ms 90° RF pulse (BW = 4.2 kHz) and a 13.2-ms 180° RF pulse (BW = 1.3 kHz). Experiments were carried out on a whole-body 3T scanner (Philips Medical Systems). A body coil was used for RF transmission and an 8-channel phased-array coil for reception. The optimized PRESS echo time was validated in phantoms. *In vivo* tests of the PRESS sequence were conducted on five healthy volunteers. Written informed consent was obtained prior to the scans. Following the survey scans, T_1w images (MP-RAGE) were acquired with 1×1×1 mm^3 spatial resolution. MRS data were acquired from a 2×2×2 cm^3 voxel in the right parietal cortex, with TR = 2 s, TE = 160 ms, sw = 2.5 kHz, and 2048 sampling points. FIDs were recorded in 32 blocks, each with 4 averages (scan time 4.3 min). An unsuppressed short-TE water signal was acquired with STEAM (TE, TM) = (18, 21) ms and TR = 20 s. Data were corrected for frequency drifts and eddy current artifacts during the post-data processing. LCModel software [5] was used for spectral analysis. The GM, WM, and CSF fractions within the voxel were obtained from the MP-RAGE images. For each subject, the Gly concentration was evaluated relative to the brain water using [Gly]/[water] = S_{Gly}/S_{water}. The water concentration within the voxel, [water], was obtained using the GM/WM segmentation results and published GM/WM water concentrations [6]. The relaxation effect adjusted Gly signal, S_{Gly}, was obtained using T_1 = 1.5 s and T_2 = 200 ms. The water signal, S_{water}, was obtained from LCModel analysis of the STEAM water signal, incorporating the STEAM-to-PRESS volume localization ratio.

RESULTS and DISCUSSION

Figure 1 shows the J coupling effects on the composite signal of mI and Gly. The simulations indicated that the mI multiplet at (TE_1, TE_2) = (60, 100) ms exhibits a narrow peak at 3.62 ppm and low amplitude at the 3.55 ppm Gly resonance, permitting detection of both Gly and mI with optimum selectivity. This theoretical spectral pattern was well reproduced in *in-vitro* spectra, Fig. 2 (left). For [mI]/[Gly] = 5, Gly was not readily detectable in a short-TE STEAM spectrum, but the small Gly singlet was clearly revealed in the optimized-PRESS spectrum, Fig. 2 (right). For *in vivo*, for an 8 ml volume with TR = 2 s, Gly was measurable with CRLB below 20% when NSA (number of signal averages) was greater than 50, as shown in Fig. 3. The CRLB was further decreased with increasing NSA and eventually became 8% at NSA > 110. The CRLB of mI was less than 20% for NSA ≥ 8. The mI concentration estimate was varied at small NSAs and became constant after NSA ~ 80. From the PRESS spectra with NSA = 128 from the five normal subjects, the Gly and mI concentrations in the right parietal cortex were estimated to be 0.6±0.1 mM and 4.3±0.4 mM (mean±SD), with mean CRLBs of 9±1% and 5±1%, respectively.

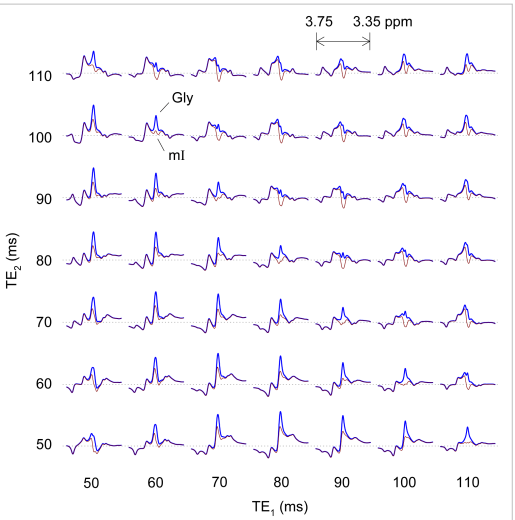

FIG. 1. Calculated PRESS spectra of mI+Gly (blue) and mI (brown), at 3T, are displayed *vs.* subecho times TE_1 and TE_2 for 50 – 110 ms. The spectra are scaled for a mI-to-Gly concentration ratio of 5. The spectral range is 3.75 – 3.35 ppm. Spectra, calculated without T_2 relaxation effects , were broadened to singlet linewidth of 3 Hz.

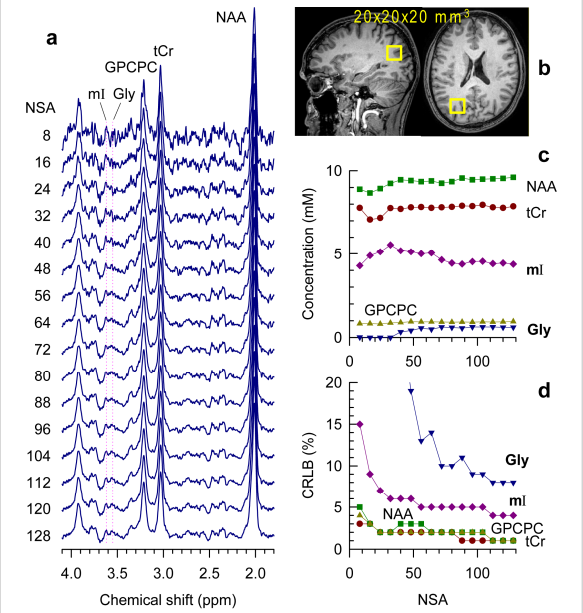

FIG. 3. (a) *In vivo* brain spectra are presented *vs.* number of signal averages (NSA). Vertical dotted lines are drawn at 3.55 and 3.62 ppm. (b) Voxel (20×20×20 mm^3) positioning in the right parietal cortex. Concentration estimates (c) and CRLB (d) are plotted *vs.* NSA for Gly, mI, tCr, NAA, and GPCPC. Data were acquired with TR = 2 s and PRESS (TE_1, TE_2) = (60, 100) ms.

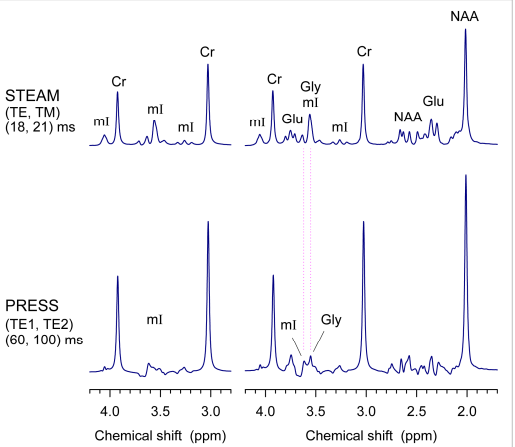

FIG. 2. *In vitro* spectra at PRESS (TE_1, TE_2) = (60, 100) ms, obtained from a phantom with mI (25 mM) and Cr (40 mM) (Left), and another with Gly, mI, Cr, NAA and Glu at a concentration ratio of 1:5:8:10:10 (Right), at 3T, are shown together with short-TE STEAM spectra. Singlet linewidth is 3 Hz. Vertical dotted lined are drawn at 3.55 and 3.62 ppm.

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