In Vivo ^{1}H NMR measurement of glycine in human brain at 7 T at short echo time

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Introduction

Glycine is an amino acid present in mammalian brain, acting as a putative modulator of glutamatergic action and is implicated in several pathologies [1]. The measurement of glycine in brain is hampered by the fact that its resonance at 3.55 ppm overlaps with the much larger resonances of *myo*-inositol. To overcome this problem, editing techniques, such as TE-averaged PRESS or 2D J-PRESS [1, 2], have been used at 3 and 4 T to detect glycine in human brain. However, with increasing B_0, the sensitivity of editing methods including TE-averaged PRESS stands to suffer from the shortened T_2. Previous MRS studies performed at very short TE (1-6 ms) and very high fields (in human brain at 7 T and in rat brain at 9.4 T) reported no detection of glycine [3, 4]. The aim of the present study was to determine if glycine can be measured at 7 T in human brain *in vivo*, without editing or TE-averaging techinques, at short TE.

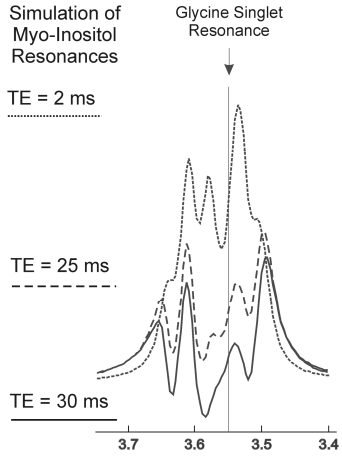

Figure 1. Simulated ^{1}H MR spectra of *myo*-inositol at TE = 2, 25 and 30 ms using SPECIAL excitation at 7 T. At TE = 30 ms, the *myo*-inositol signal substantially decreases due to J modulation, in particular at the resonance frequency of the glycine singlet (3.55 ppm).

Methods

Theory. The glycine singlet at 3.55 ppm is overlapped by the larger signal from the M_2 protons (3.52 ppm) of the AM_2N_2P spin system of *myo*-inositol. To determine the TE where the M_2 amplitude was reduced the most, the spectrum of *myo*-inositol was simulated as a function of TE, for single spin-echo coherence generation, using the density matrix formalism. **Experiments.** Experiments were performed on an actively-shielded 7T/68cm scanner (Siemens/Magnex) with a head gradient insert (41cm, 80mT/m max gradient strength) and a home-built quadrature surface coil of 13cm diameter. After first- and second-order shimming with FASTMAP, spectra of a 2x2x2 cm^3 VOI in the occipital lobe of three healthy volunteers were acquired using SPECIAL [5] with TE of 5.7 and 30 ms (TR = 4 s, 512 ms acquisition time) and with VAPOR water signal suppression and outer volume suppression. Briefly, SPECIAL consisted of a spin-echo sequence with 90º and 180º slice-selective pulses, and the signal localization in the third dimension was achieved by a 1D ISIS approach. Metabolite concentrations and Cramer-Rao lower bounds (CRLB) were determined by LCModel, using a basis set of 21 metabolites and 8mM total creatine as an internal reference.

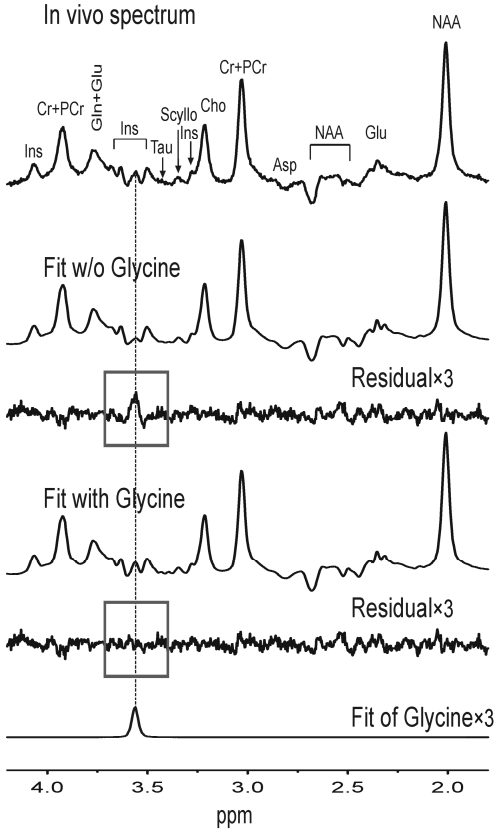

Figure 2. In vivo 7 T ^{1}H MR spectrum (TE = 30 ms, scan time = 4min 16s) and LCModel fits. Below each fit the residual (enlarged 3 times) is shown. The box illustrates elimination of the residual at the resonance frequency of the glycine singlet, when including glycine in the basis set.

Results and Discussion

When using a single spin-echo sequence, *myo*-inositol underwent rapid J-modulation due to its large J-coupling of ~ 10 Hz and, as a result, the M_2 amplitude was strongly reduced, with the strongest suppression at TE = 30 ms (**Figure 1**). The LCModel fit to the basis set without glycine displayed a significant residual with positive amplitude at 3.55 ppm in all subjects (**Figure 2, middle**), which was eliminated when including glycine in the basis set (**Figure 2, bottom**). Glycine concentration was 1.18 ± 0.07 mM with an average CRLB of 10 ± 3 %. For the TE=5.7ms spectrum, the CRLB of glycine was 93% in one subject and > 100% in the other two subjects, in line with previous studies at very short TE, where glycine was not detected [3, 4].

We conclude that it is possible to detect glycine at 7 T in human brain *in vivo*, at a reasonably short TE of 30 ms without editing methods. The current approach is simple (since it is based on a spin-echo sequence, with no additional RF pulses or gradient schemes needed to edit the glycine resonance) and robust (glycine was detected, with low CRLB, in all subjects).

References. [1] Prescot AP et al., Magn Reson Med. 2006;55:681-686. [2] Schulte RF et al., NMR in biomedicine 2006;19:255-263. [3] Tkac I et al., Magn Reson Med. 2001;46:451-456. [4] Pfeuffer J et al., J Magn Reson. 1999;141:104-120. [5] Mlynárik V et al., Magn Reson Med. 2006;56:965-970. **Acknowledgements**. Supported by Centre d'Imagerie BioMédicale (CIBM) of the UNIL, UNIGE, HUG, CHUV, EPFL, the Leenaards and Jeantet Foundations and SNF grant No. 3100A0-116220.