Proton NMR detection of glycine in rat brain at 9.4 T

G. Gambarota[1], L. Xin[1], I. Kohler[1], V. Mlynárik[1], and R. Gruetter[1,2]

[1]Laboratory for functional and metabolic imaging (LIFMET), Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland, [2]Departments of Radiology, Universities of Lausanne and Geneva, Switzerland

Introduction

Glycine is a neurotransmitter that is difficult to measure in vivo, despite ~ mM concentrations [1]. Using TE-averaged PRESS its detection has been recently reported in healthy human subjects [2], but its detection in animal model has remained elusive. MRS in animal studies is typically performed at high field strengths ($\geq$ 7 Tesla), where substantial increases in SNR and spectral resolution are expected to allow its detection without editing or TE-averaging. We hypothesized that, by a proper choice of echo time, it might be possible to detect glycine at 9.4 T in rat brain in vivo.

Methods

The spin system of glycine consists of a singlet at 3.55 ppm overlapped by a strong signal from the M_2 protons (3.52 ppm) of the AM_2N_2P spin system of *myo*-inositol [3]. As TE increases, the J-coupling introduces a dephasing in the M_2 resonance of *myo*-inositol which can be exploited for detecting the singlet of glycine. To minimize the overlap with glycine, the spectrum of *myo*-inositol was simulated as a function of TE, using simulations based on the density matrix formalism. Experiments were performed on a 9.4T/31cm horizontal-bore MR scanner (Varian/Magnex). Spectra of a VOI in the hippocampus of five healthy male Sprague Dawley rats were acquired using SPECIAL [3] at a very short TE (2.8 ms) and at TE = 20 ms. Metabolite concentrations and Cramer-Rao lower bounds (CRB) were determined by spectral data analysis performed with LCModel [5], using total creatine as an internal reference for quantitation.

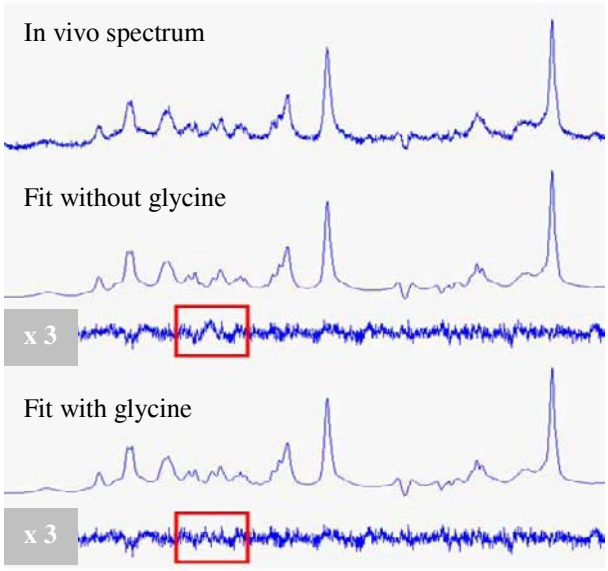

Figure 1. In vivo proton MR spectrum (TE = 20 ms) and LCModel fits. Below each fit the residual (enlarged 3 times) is shown. The box highlights the residual at the resonance frequency of the glycine singlet.

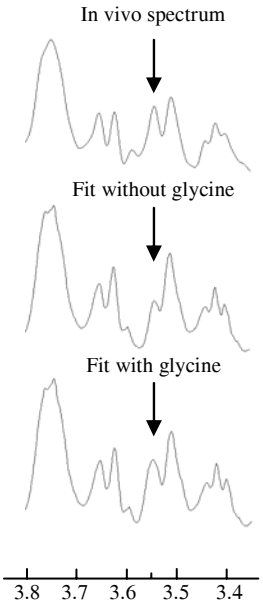

Figure 2. Zoom in the region at 3.55 ppm of an in vivo proton MR spectrum (**top**) and LCModel fits without (**middle**) and with (**bottom**) glycine in the basis set. The arrow indicates the 3.55 ppm resonance frequency.

Results and Discussion

At TE = 20 ms, the signal intensity of the M_2 protons of *myo*-inositol showed a ~ 50 % decrease due to J-modulation (data not shown). The spectral fit to the basis set without glycine displayed a considerable residual with positive amplitude at 3.55 ppm (**Figure 1, middle**). The inclusion of glycine in the basis set minimized the residual at 3.55 ppm to the noise level (**Figure 1, bottom**). The improvement of the fit is also shown in **Figure 2**, where the arrow indicates the resonance frequency of glycine. Glycine concentration was 1.1 ± 0.1 mM with an average CRB of 8.6 ± 1.5 % (**Table**). These values are in agreement with reported values of glycine concentrations in healthy human brain (~ 1 mM). For the very short TE spectrum, the mean CRB of glycine was 33%. This is in line with previous studies performed at TE ~ 1-2 ms, where glycine was not consistently detected [6]

Conclusions

In the present study we show that it is possible to detect glycine at 9.4 T, in rat brain in vivo, at a short TE of 20 ms without 2-D spectroscopy or editing methods such as TE-averaging. The ability to detect glycine with this approach has the advantage of experimental simplicity, since it is based on a spin-echo based sequence and no additional pulses or complex gradient schemes are needed to edit the glycine resonance.

	Concentration (mM)	CRB (%)
#1	1.13	8
#2	1.04	11
#3	1.00	8
#4	1.25	7
#5	1.20	9

References

[1] Eulenburg V et al., Trends Biochem Sci. 2005;30:325-333. [2] Prescot AP et al., Magn Reson Med. 2006;55:681-686. [3] Govindaraju V et al., NMR Biomed. 2000;13:129-53. [4] Mlynárik V et al., Magn Reson Med. 2006;56:965-970. [5] Provencher SW, Magn Reson Med 1993;30:672-679. [6] Pfeuffer J et al., J Magn Reson. 1999;141:104-120.

Acknowledgements. Supported by Centre d'Imagerie BioMédicale (CIBM) of the UNIL, UNIGE, HUG, CHUV, EPFL and the Leenaards and Jeantet Foundations.