Glycine Tissue Level in Medulla Oblongata Measured in vivo with ^{1}H MRS at 9.4 T in Rat Brain

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Introduction: In the central nervous system, glycine has a dual role as inhibitory neurotransmitter activating glycine receptors [1] and as co-agonist for glutamate excitatory transmission through *N*-methyl-D-aspartate receptors [2]. The medulla oblongata (MO) is the part of the brainstem which regulates autonomic functions, such as heart beat, breathing and blood pressure. In the MO, glycine is present in particularly high concentration [3], but it has never been quantified *in vivo* and in a noninvasive way. Recently, detection of glycine in rat brain *in vivo* has been reported, using a spin echo coherence excitation with the optimized echo time (TE) of 20 ms [4]. The aim of the present investigation was i) to measure the *in vivo* neurochemical profile in the MO by localized ^{1}H NMR spectroscopy, with particular focus on glycine quantification, and ii) to compare the neurochemical profile in MO with that in hippocampus, striatum and cortex.

Method: Experiments were performed on a 9.4T/31cm horizontal-bore MR scanner (Varian/Magnex). Spectra of a VOI in the MO, hippocampus, striatum and cortex, of five male Sprague Dawley rats were acquired using a localized MR spin echo sequence (SPECIAL, [5]) at a very short TE of 2.8 ms (for assessment of the neurochemical profile) and at TE of 20 ms (for glycine detection). A homemade ^{1}H quadrature surface coil (17 mm diameter) was used as a transceiver. Shimming was achieved by FASTMAP [6]. Spectral data analysis was performed with LCModel [7]. For quantitation of short TE spectra (TE=2.8ms), water was used as an external reference. Regional glycine concentrations were obtained from spectra acquired at TE=20ms using regional total Cr concentration obtained at TE=2.8ms as the internal reference, considering similar metabolites T_2 range at 9.4 T [8].

Results and Discussion: The ^{1}H spectrum obtained in MO (Figure 1) suffered from lower SNR (due to a large distance of the VOI from the surface coil), and broader linewidth (caused by motion and susceptibility effect of the surrounding sinuses), compared to spectra from hippocampus, striatum and cortex. The water linewidth was 15-17 Hz in MO and 10-12 Hz in the other regions. Seventeen metabolites were quantified with CRLB lower than 25%. Glycine was detected in the spectra of TE=20 ms with CRLB below 20%. Moreover, glycine was detected in MO at the short TE of 2.8 ms, with CRLB 5-6%, due to its high concentration. Glycine concentration in MO was 3.3 ± 0.6 µmol/g (n=5) which was three-fold higher compared to the other three brain regions (Figure 2A), and was in accordance with previous *in vitro* studies [3]. Comparing the neurochemical profile in MO with the other three regions (Figure 2B), it was also noticed that glutamate, glutamine and taurine concentrations have a significant decrease in the MO. These results are also in excellent agreement with *in vitro* studies [9].

We conclude that the neurochemical profile of 17 metabolites including glycine can be quantified *in vivo* in the rodent MO at 9.4 T. Compared to other measured regions (hippocampus, striatum and cortex), MO shows a three-fold higher glycine concentration, as well as a significant decrease in glutamate, glutamine and taurine levels.

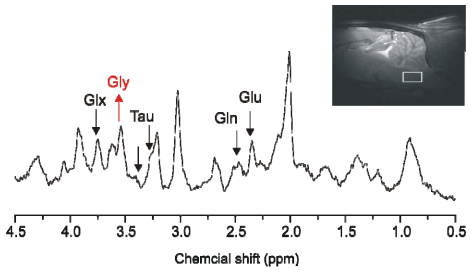

Figure 1. ^{1}H NMR spectrum in medulla oblongata (VOI=32 µL, TE=2.8 ms).

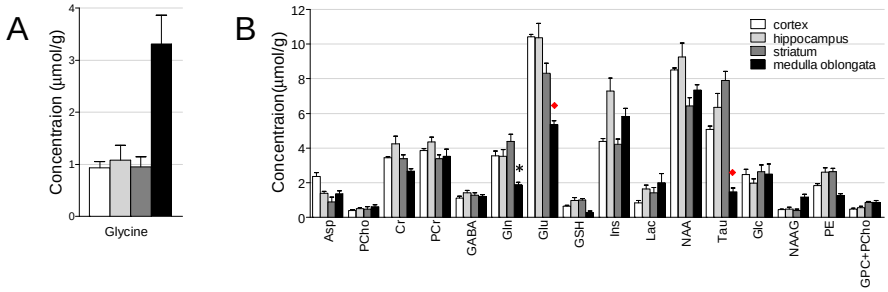

Figure 2. Glycine (A) and other metabolite (B) concentrations in cortex, hippocampus, striatum and medulla oblongata. Data shown as mean±SEM of 5 different rats. * P<0.01, ◆ P<0.001 different from the other three regions, compared with two-way ANOVA followed by Bonferroni's post-test.

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