Regional Variations of Metabolite Concentrations in the Rat Brain Assessed with *in vivo* ¹H MR Spectroscopy at 16.4T

S-T. Hong[1], D. Z. Balla[1], G. Shajan[1], C. Choi[2], and R. Pohmann[1]
[1]High-Field Magnetic Resonance Center, Max-Planck Institute for Biological Cybernetics, Tuebingen, Baden-Wuerttemberg, Germany, [2]Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, Texas, United States

Introduction

In vivo ¹H NMR spectroscopy provides a neurochemical profile containing invaluable information associated with energy metabolism, membrane metabolism, antioxidants and osmolytes [1]. Postnatal and regional changes in metabolite concentrations were reported in the rat [2] and the mouse brain [3], even in the very small region of the hypothalamus [4]. All these results demonstrated different metabolite concentrations in specific brain regions. The purpose of this study was 1) to demonstrate acquisitions of spectra in different brain regions at 16.4T 2) to investigate the anatomical distribution of cerebral metabolites.

Methods

Five Sprague-Dawley rats (193 ± 5.2 g) were measured under isoflurane anesthesia. All experiments were performed on a Bruker console (Bruker BioSpin GmbH, Ettlingen, Germany) interfaced to a 16.4 T/26 cm horizontal magnet (Magnex Scientific, Abingdon UK). An ultra-short TE STEAM sequence (TR = 5000 ms, TM = 20 ms, TE = 1.7 ms, 2048 complex data points) was applied to maximize observable metabolites by reducing T_2 relaxation and J-modulation. Three volumes-of-interest, hippocampus (7.0 x 2.0 x 3.0 mm^3), thalamus (6.5 x 3.5 x 2.5 mm^3) and striatum (7.7 x 3.0 x 3.0 mm^3) were selected based on MR images acquired with a RARE sequence. Different number of averages, 320 in hippocampus and 256 in thalamus and in striatum, were applied. An automatic shimming method (FASTMAP) [5] resulted in an average linewidth (tCr methylene signals) of 20 Hz in hippocampus, 23 Hz in thalamus and 23 Hz in striatum, respectively. Measurement time was 22 min in thalamus and striatum and 27 min in hippocampus. Correction of frequency shifts was not necessary based on a prior frequency drift measurement (17 Hz/h). Quantitative analysis was done with LCModel [6] containing a basis set composed of simulated metabolites and macromolecular components. Statistical analysis was performed with SPSS software (SPSS 15.0 for Windows, SPSS Inc., Chicago, IL USA). The MANOVA was used to determine regional differences, setting statistical significance at $p < 0.05$.

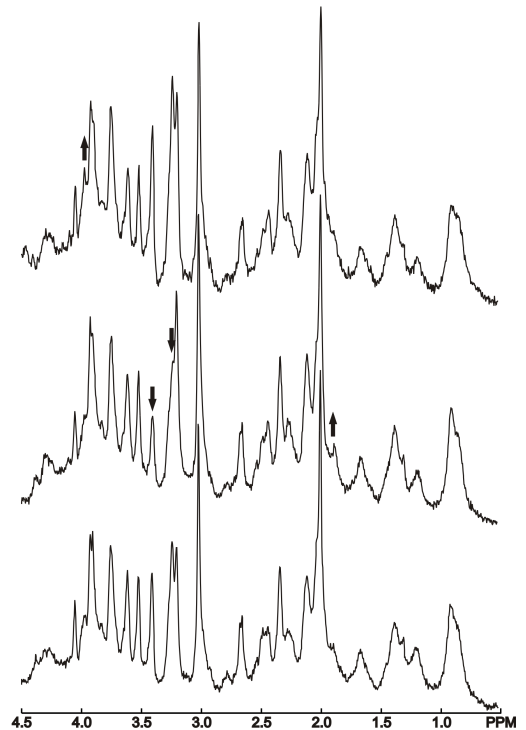

Figure 1. *In vivo* ¹H NMR spectra of the hippocampus (bottom row), thalamus (middle row) and striatum (top row) of the rat brain obtained with an ultra-short STEAM sequence. Eddy current correction, Fourier-transformation and phase correction were applied.

Results and Discussion

Representative *in vivo* ¹H MR spectra from different brain regions, hippocampus, thalamus and striatum, are shown in Fig. 1. All metabolites were quantified with CRLBs below 50% except one case, glycine in striatum (54%) among a total of 15 spectra (3 brain regions x 5 rats), implying stable and high data quality. Remarkable spectral differences were increased PE in striatum, increased GABA and substantially decreased Tau in thalamus, marked with arrows in Fig. 1. All metabolites except Asp and NAA showed statistically significant variations, summarized in Fig. 2. Precise measurements of metabolic variations in different brain regions were achieved by fully making use of advantages of the ultra-high field strength. Different anatomical distribution of metabolites was reflected with specific alterations of metabolites in particular regions. Accurate detection of changes in the order of below 0.5 μmol/g in the rat brain *in vivo* would expand possibilities of using *in vivo* ¹H NMR spectroscopy in pre-clinical research.

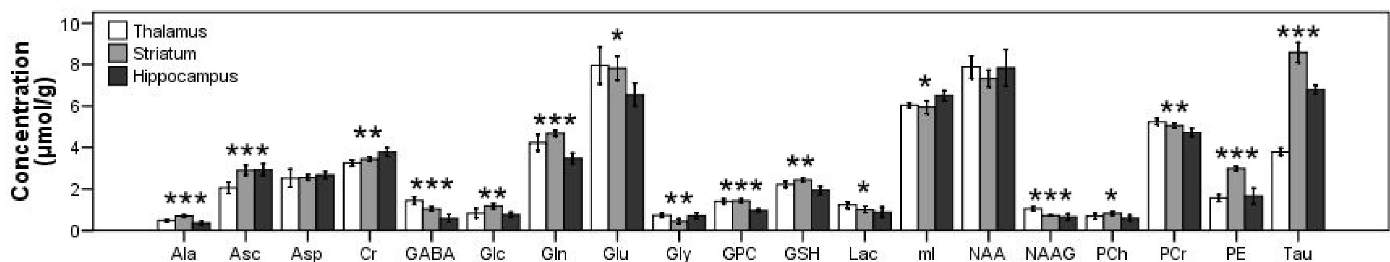

Figure 2. Concentrations of cerebral metabolites in thalamus (white), striatum (gray) and hippocampus (black) quantified in LCModel. Error bars represent standard deviations. Statistical significance was expressed as $*P < 0.05$, $**P < 0.005$ and $***P < 0.0005$.

References

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