Highly accurate quantification of proton MR spectroscopy in rat brain in vivo at 16.4 T

S-T. Hong[1], D. Z. Balla[1], S. Gunamony[1], K. Ugurbil[2], and R. Pohmann[1]

[1]Max Planck Institute for Biological Cybernetics, Tuebingen, Baden-Wuerttemberg, Germany, [2]Center for Magnetic Resonance Research, Minneapolis, Minnesota, United States

Introduction

Localized ^{1}H MR spectroscopy is an efficient tool capable of noninvasively measuring metabolite concentrations in the brain. However, quantification is often difficult due to several inherent limitations of ^{1}H MRS, especially the inherently low signal-to-noise ratio (SNR) and the narrow range of chemical shifts that causes overlap between several adjacent resonances. Higher field strengths alleviate both limitations, allowing the in vivo quantification of additional peaks (including NAA at 4.38 ppm, GPC at 4.31 ppm and PCho at 4.27 ppm) at 14.1 Tesla [1] and 16.4 Tesla [2]. In this study, a magnetic field strength of 16.4 T was used to evaluate the quantification of metabolites from the rat brain with an ultra-short TE STEAM sequence.

Methods

^{1}H NMR Spectroscopy Spectra were acquired from 4 male adult Wistar rats that were anaesthetized by inhalation of 1.5-2 % concentration of isoflurane. All MR experiments were performed on a 16.4 T/26 cm horizontal bore Magnex magnet interfaced to a Bruker Biospec spectrometer with a 12 cm gradient coil (strength: 1000 mT/m, rise time: 212 µs). A home-built surface coil was used for transmitting RF pulses and receiving signals. To achieve an ultra-short TE, Gaussian shaped RF pulses (450 µs) were employed in the STEAM sequence (TR, 4000 ms; TE, 2 ms; 400 averages; 2048 complex data points) with the VAPOR water suppression interleaved with three OVS modules. A 62 µl voxel was positioned inside the brain encompassing the cortex and hippocampus. Field homogeneity was adjusted by calibrating all first- and second-order shim terms with FASTMAP, resulting in a tCr linewidth of 20 Hz (0.0293 ppm) in vivo.

Spectrum Analysis All the acquired spectra were analyzed using LCModel [3]. In vitro spectra were collected from the following 20 metabolites in a buffered solution (pH = 7.2) at a temperature of 37 0C, kept constant by feedback-controlled heating pads: alanine (Ala), aspartate (Asp), Ascorbate (Asc), creatine (Cr), γ-aminobutyric acid (GABA), glucose (Glc), glutamate (Glu), glutamine (Gln), Glycine (Gly), glutathione (GSH), glycerophosphorylcholine (GPC), phosphorylcholine (PCho), myo-inositol (Ins), Histidine (His), lactate (Lac), N-acetylaspartate (NAA), N-acetylaspartylglutamate (NAAG), phosphocreatine (PCr), phosphorylethanolamine (PE), and taurine (Tau). These spectra were used as basis sets for the LCModel quantification of the in vivo data. Metabolite peaks were assigned by fitting with LCModel and verified using literature values [4].

Results

A representative spectrum from a rat brain is shown in Fig 1, demonstrating excellent water suppression and high SNR, which made it possible to quantify, for the first time, the His peaks at 3.11 ppm, 3.22 ppm and 3.97 ppm in vivo, with Cramer-Rao lower bounds of less than 20 % in three of the four examined animals, indicating high quantification reliability. Especially the His peak at 3.11 ppm, which is usually concealed by the Cr-resonance, could be isolated.

Discussion

Due to the increased spectral resolution at the ultra-high field, the minimized J-modulation at the ultra-short echo time, and spectral fittings with LCModel based on basis sets from phantom solutions, the accurate and reliable quantification of in vivo brain metabolite spectra is possible. For the first time, this includes the reliable detection of the signal from His, which serves as precursor for Histamine and is connected to zinc excretion. Further improvements in the quantification accuracy will be possible by further reducing the echo time using asymmetric pulses and by taking account of the macro-molecular peaks in the quantification.

References

[1] Mlynárik V. et al., JMR 2008;194:163-168. [2] Balla DZ et al., ISMRM 2008;3295. [3] Provencher SW. MRM 1993;30:672-679. [4] Govindaraju V. et al., NMR in Biomed 2000;13:129-153.

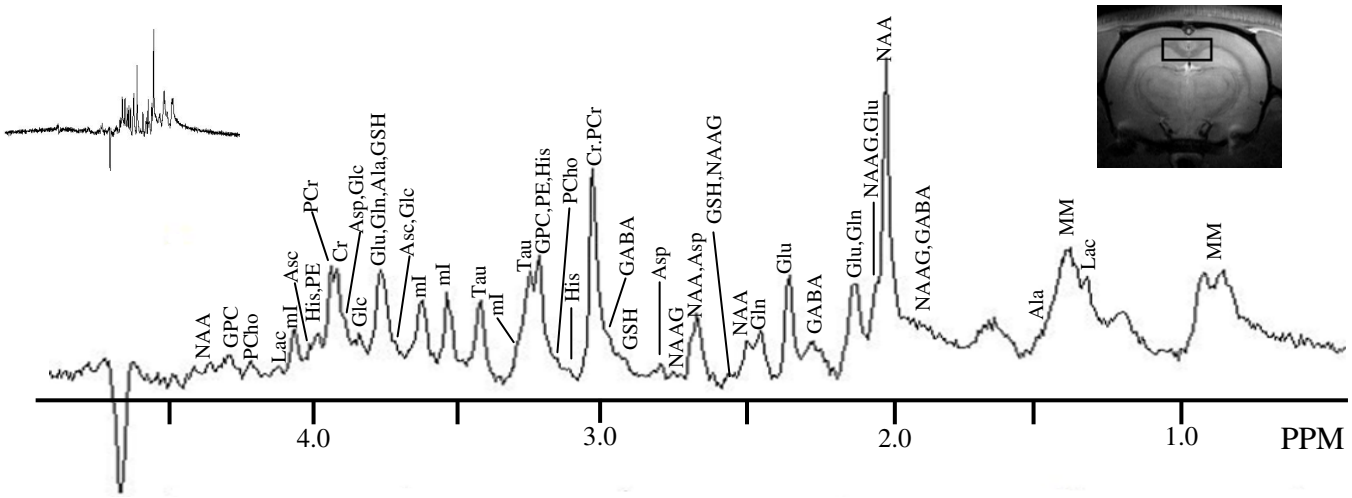

Figure 1. In vivo ^{1}H NMR spectrum acquired at 16.4T using the STEAM sequence with TR = 4000 ms, TE = 2 ms, VOI = 62 µl and 400 averages. The full-range spectrum illustrates excellent water suppression and a flat baseline. The spectrum was processed only with Fourier-transformation and zero-order phase correction; no apodization and baseline correction was applied.