# Localized *in vivo* $^1$H NMR Spectroscopy of the Rat Brain at 16.4T

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## Introduction

Localized *in vivo* $^1$H NMR spectroscopy has allowed detection and quantification of nineteen cerebral metabolites in the rat brain at 9.4T and at 14.1T [1]. It would be promising to explore the further possibility of quantifying additional metabolites by utilizing advantages of ultra-high fields. Here, we report results of $^1$H NMR spectroscopy of the rat brain *in vivo* at 16.4T, demonstrating the possibility to acquire an enhanced neurochemical profile with reliable quantification of additional metabolites, acetate and ethanolamine.

## Methods

All experiments were performed on a 16.4 T/26 cm Bruker BioSpec MRI scanner (Bruker BioSpin GmbH, Ettlingen, Germany) operated with Paravison version 5.0. Eleven Sprague-Dawley rats weighing 229 ± 14 g were measured under isoflurane anesthesia. Body temperature was monitored and maintained at 37 ± 0.5 $^0$C by an electric heating pad during the measurements. A quadrature surface coil with two geometrically decoupled single-turn coils was employed for transmit and receive. The volume-of-interest (5.2 x 2.5 x 5.2 mm$^3$) was placed in a brain region including the cortex, hippocampus and corpus callosum. Localization was achieved with an ultra-short TE STEAM sequence with the following parameters: TR 6000 ms; TE 1.7 ms; TM 20 ms; 2048 complex data points; 512 averages. The static field inhomogeneities were corrected with FASTMAP [2], yielding a linewidth of 18 ± 5 Hz (0.026 ppm) of the tCr methylene signal *in vivo* in a 68 µl voxel. For acquiring a metabolite-nulled spectrum, a TI of 710 ms combined with a reduced TR of 2500 ms and increased averages of 1280 was applied. Residual metabolite contributions were eliminated with the HLSVD algorithm [3]. Each macromolecular component was parameterized [4] and implemented in LCModel [5] to determine macromolecular components. To prove the assignment of an acetate signal at 1.9 ppm, a supplementary measurement with acetate infusion was performed according to a reported bolus-variable rate [6]. Numerically calculated metabolite spectra were generated with a home-made Matlab program (MathWorks, Natick, MA, USA) and employed as a basis set in LCModel analysis. Absolute concentrations were calculated with reference to tCr assumed to be 8.5 µmol/g [7].

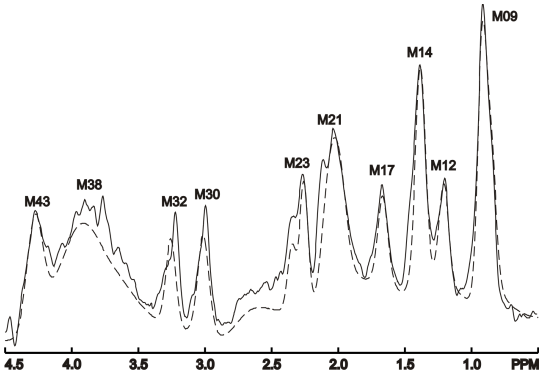


**Figure 1.** Macromolecular spectra: Measured metabolite-nulled spectrum and simulated macromolecular components (dashed line) in LCModel.

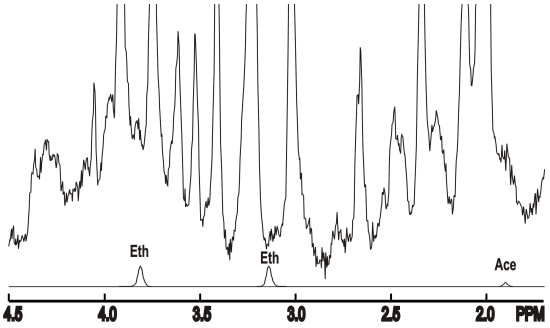


**Figure 2.** Localized *in vivo* $^1$H NMR spectrum of the rat brain at 16.4T (upper row). Only Fourier-transform and phase correction were applied. Fitting results of acetate and ethanolamine from LCModel analysis (bottom row).

## Results and Discussion

Fig. 1 shows close agreement between two fitted macromolecular spectra in LCModel, one based on the measured macromolecular spectrum and the other based on the parameterized macromolecular components (dashed line). A representative *in vivo* $^1$H MR spectrum demonstrated sufficient spectral resolution to detect and quantify more than 20 metabolites (Fig. 2). In an acetate infusion experiment, a significantly elevated level of acetate (1.21 µmol/g, CRLB 9%) was represented with maintaining stable quantification of two overlapping metabolites, GABA (0.93 µmol/g, CRLB 9%) and NAAG (0.76 µmol/g, CRLB 14%). The addition of acetate and ethanolamine in the basis set showed no noticeable differences ensuring independent quantification of these two metabolites (Fig. 3). In this study, an improved neurochemical profile was achieved and quantified at ultra-high field by minimizing TE, adjusting field inhomogeneities, including macromolecular components in the analysis and using a precise quantification algorithm. This will expand the scope and possibilities of localized *in vivo* $^1$H NMR spectroscopy substantially.

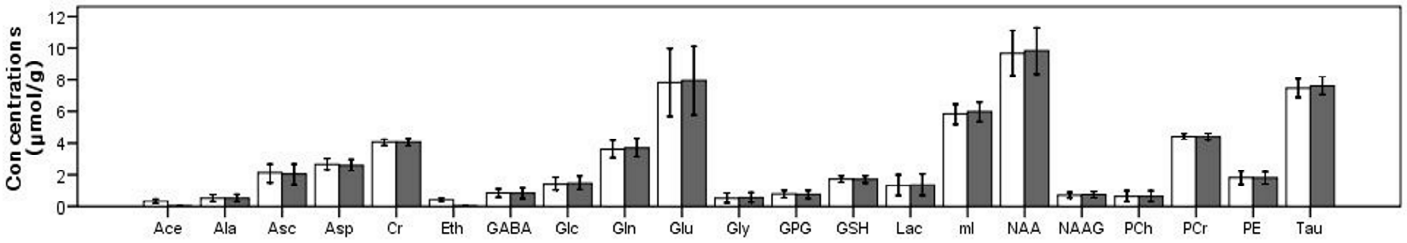


**Figure 3.** Comparison of metabolite concentrations as found with (white) and without (gray) acetate and ethanolamine included in the basis set. Error bars represent standard deviations.

**References** [1] Mlynárik V. et al., JMR 2008;194:163-168. [2] Gruetter R. MRM 1993;29:804–811. [3] Pijnappel WWF. et al., JMR 1992;97:122-134. [4] Seeger U. et al., MRM 2003;49:19-28. [5] Provencher SW. MRM 1993;30:672-679. [6] Patel AB. et al., PNAS 2005;102:5588-5593. [7] Pfeuffer J. et al., JMR 1999;141:104–120.