Influence of regional macromolecule baseline on the quantification of neurochemical profile in rat brain

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Introduction

Prior knowledge of the macromolecule baseline is important for the accurate quantification of metabolite concentrations from *in vivo* ^{1}H NMR spectra acquired at short echo times (TE) [1]. Macromolecules may be altered due to pathology [2]. In contrast, regional alterations of macromolecule baseline in rat brain have not been studied, although the neurochemical profile varies strongly with cerebral regions [3]. Thus, the aim of this study was to measure the macromolecule baselines in different cerebral regions of healthy rats and to evaluate the effects of potential differences on the quantification of metabolites.

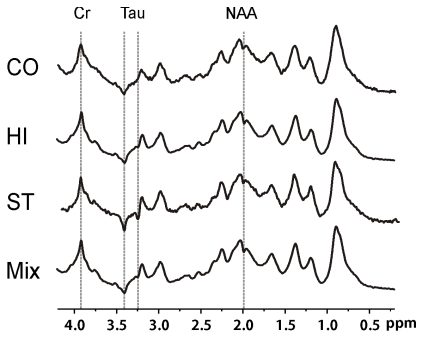

Figure 1. Metabolite-nulled spectra of cortex, hippocampus, striatum and mixed structures. Dotted lines indicate the residual signals of metabolites.

Methods

Experiments. All MRS experiments were performed on a 9.4T/31 cm magnet (Varian/Magnex). ^{1}H *in vivo* NMR spectra were acquired in five rats from four different volumes of interest (VOI) including hippocampus (HI, VOI=12µl), striatum (ST, VOI=15µl), cortex (CO, VOI=9.3µl) and a mixture of brain structures (Mix, VOI=108µl), respectively, using a spin-echo based single voxel localization sequence (SPECIAL [4], TE=2.8ms and TR=4s). For the acquisition of macromolecule baseline in the aforementioned VOIs, metabolite-nulled spectra were acquired *in vivo* using the inversion recovery method achieved by an adiabatic hyperbolic secant RF pulse with an inversion time of 725ms (TE=2.8ms, TR=2.5s). Residual signals of metabolites were removed by HLSVD [5].

Data Analysis. Metabolite concentrations were calculated by LCModel [6] with basis sets containing simulated metabolite spectra using published values of J-coupling constants and chemical shifts [7], and two different macromolecule baselines, *i.e.*, 1) the macromolecules of a specific cerebral region (Mac_CO, Mac_ST and Mac_HI); 2) the macromolecules of a mixed region (Mac_mix). Unsuppressed water spectra served as an internal reference for the absolute quantification of metabolite concentrations.

Results and Discussion

The metabolite-nulled spectra from four different VOIs show minor differences such as varying intensity of two inverted resonances between 3.2 ppm and 3.5 ppm, which are the residual signals of taurine having a higher concentration in the striatum (Fig. 1). As can be seen from Fig. 2a, after removing metabolite residuals, there were slight differences between the specific regional macromolecular spectra and the macromolecular spectrum of mixed brain structures. For instance, the small difference in the broad component at 3.5-4ppm was likely due to the artificial removal of metabolite residuals. The differences in the calculated concentrations of most metabolites were less than 10% when regional specific and mixed macromolecule baselines were used (Fig. 2b). Those metabolites that are less well represented in the spectra, such as PE, NAAG, Asp, Glc and Asc, showed a 10-40% difference, which was comparable to the respective Cramer-Rao Lower Bounds calculated by LCModel (data not shown). A visual inspection of the compared macromolecule baselines (Fig. 2a) suggests that the difference in metabolite concentrations is probably due to the artificial removal of the residual Cr peak at 3.9 ppm and small variability in the phase of the macromolecule spectra.

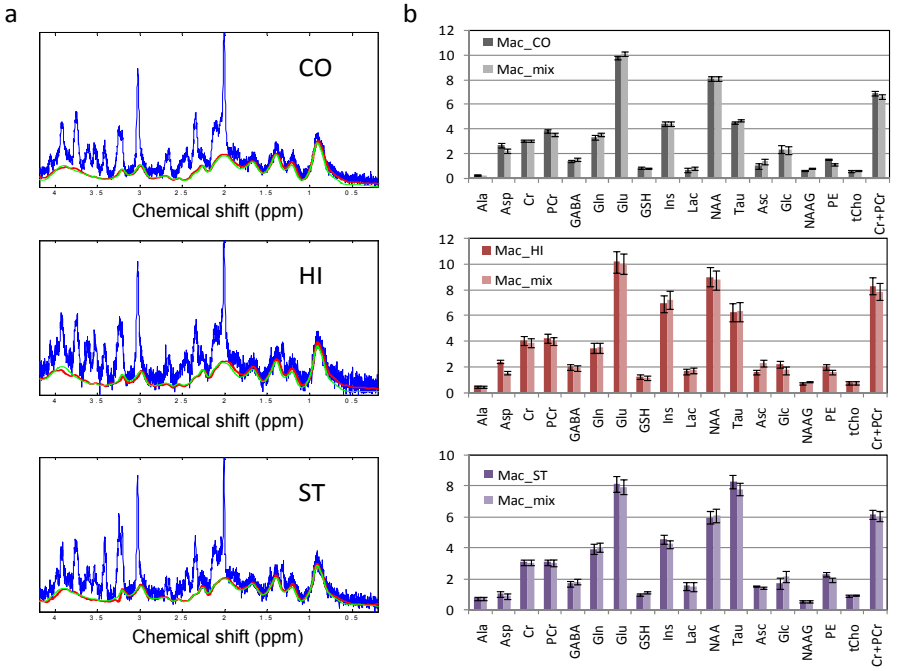

Figure 2. (a). *In vivo* ^{1}H NMR spectra of CO, HI and ST. Two macromolecule baselines (red lines, specific region; green lines, mixed structures) were overlaid for comparison. (b). Metabolite concentrations (mean ± SEM, n=5) obtained using two different macromolecule baselines.

In summary, macromolecule baselines in cortex, hippocampus and striatum show very minor differences relative to that acquired from a large VOI containing various cerebral structures. A slight variability in the shape of the macromolecule baseline introduced by data processing can affect calculated concentrations of those metabolites which are less well characterized in a proton MR spectrum at a level comparable to the respective Cramer-Rao Lower Bounds. We conclude that for most applications, the use of a generic experimental macromolecule baseline provides a sufficiently accurate measurement of the neurochemical profile in rat brain.

References [1] Behar KL et al., Magn Reson Med. 1993. [2] Hwang JH et al., Magn Reson Med. 1996. [3] Tkac I et al., Magn Reson Med. 2003. [4] Mlynarik V et al., Magn Reson Med. 2006. [5] Pijnappel WWF et al. J Magn Reson. 1992. [6] Provencher SW, Magn Reson Med 1993. [7] Govindaraju V et al., NMR Biomed. 2000.
Acknowledgements Supported by Centre d'Imagerie BioMédicale (CIBM) of the UNIL, UNIGE, HUG, CHUV, EPFL and the Leenaards and Jeantet Foundations, and SNF 3100A0-122498.