Precision of metabolite concentrations obtained by LCModel as a function of the signal-to-noise ratio in rodent brain

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Introduction

The quantitative analysis of in vivo proton MR spectra is usually performed either in the time domain or in the frequency domain. One of the frequently used software packages using frequency-domain fitting is LCModel (1), which analyzes the spectrum as a linear combination of a basis set of measured or simulated model spectra. A measure of the reliability of each single concentration measurement are the Cramer-Rao lower bounds (CRLBs) (2), which closely mimic standard deviations (3). The CRLBs depend on the quality of the spectrum, in particular on the linewidth and the signal-to-noise ratio (3,4). In our study we examined CRLBs of metabolite concentrations calculated by LCModel for various signal-to-noise ratios.

Methods

Spectra were obtained from the brain of four adult rats and three adult mice anesthetized by isoflurane. The measurements were done on an actively shielded 9.4 T/31 cm INOVA imaging spectrometer (Varian/Magnex Scientific) using the SPECIAL spectroscopy sequence (5) with TR of 4 s and TE of 2.7 ms. This technique provides short-echo-time spectra with ~2-fold increase in signal intensity compared to STEAM. A 14 mm diameter two-loop quadrature coil was used both for RF excitation and signal reception. Field homogeneity was adjusted using FASTMAP resulting in the water linewidth of 13-15 Hz (5). VOIs had nominal sizes of about 50 µl for rats and 22 - 27 µl for mice and were localized to striatum or hippocampus. In total, 240 or scans were collected in 15 or 20 separate blocks, each of them consisting of 16 scans. Concentrations of metabolites and the CRLBs were calculated by LCModel 6.1-4 from spectra obtained by averaging of 16, 32, 64, 96, 128, 160 and 240 (320) scans, using the signal of total creatine as a reference. The peak signal-to-noise ratio in these spectra varied from about 10 to about 40(Fig. 1).

Results

The graphs in Fig. 2 show mean CRLB values obtained from four rats as a function of the number of scans. Three groups of metabolites can be recognized. The CRLBs of strongly represented NAA, Glu, Tau, Ins, Cr, PCr and Gln (green lines in Fig. 2) were low except for spectra with the lowest SNR values, and decreased only slightly with the number of scans. Quantification of metabolites such as Lac, PE, GABA, GSH, Asp (blue lines) benefited from increased SNR achieved at longer measurement times. However, their CRLBs did not decrease substantially for scan numbers larger than 128. The third group of weakly represented metabolites included Glc, PCho, GPC (GPC+PCho is well represented), NAAG, βHB, Ala and Asc (red lines), which were not usually detected at low SNR and were quantified with larger CRLBs only in spectra with the largest numbers of scans. The classification between the second and the third groups depended on actual metabolite concentrations. The data from mice gave similar results. Due to lower SNR nearly the constant CRLB values were reached for more than 160 scans.

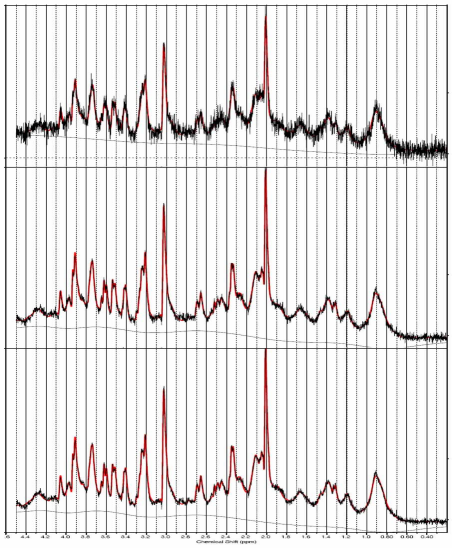

Fig. 1. LCModel output for the spectra of rat brain acquired with 16, 128 and 240 scans, respectively (from top to bottom).

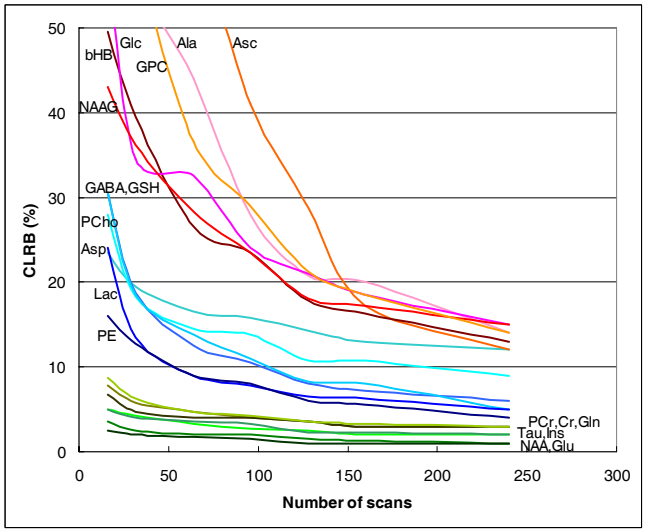

Fig. 2. Dependence of CLRB (the mean of 4 rats) on the number of acquisitions

Discussion

This study on purely experimental data suggested that strongly represented metabolites having large and distinct spectral lines are reliably quantified even from spectra with relatively low SNR ≈ 10 – 20. Less abundant metabolites and those having their spectral lines overlapped with dominant resonances require higher SNR ≈ 20 – 30 for reliable quantification. An increase of SNR over this value using extensively long measurement time brings almost no improvement in the precision of the concentration estimates, as judged from the CRLB. The third group contains compounds, which are usually quantified with other similar metabolites (NAAG with NAA, PCho with GPC) or are poorly defined in the spectrum (Asc, Glc) or have low concentration (Ala, βHB).

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