Usefulness of LCModel Analysis with an Experimental Basis Set in Brain 1H-MRS at 3T

Hyeon-Man Baek[1,2], Youngjae Jeon[1], Jooyun Kim[1], Mirim Bang[1], Gyunggoo Cho[1], and Chaejoon Cheong[1]

[1]*Center for MR Research, Korea Basic Science Institute, Ochang, Chungbuk, Korea,* [2]*Department of Bio-Analytical Science, University of Science & Technology, Yuseong-gu, Daejeon, Korea*

Introduction

In vivo localized proton single-voxel MR spectroscopy (^{1}H-MRS) is a non-invasive technique that provides information on brain metabolism and physiology, which may be used in diagnosing diseases and monitoring the therapeutic response [1]. Recently, the implementation of short-echo time (TE) MR spectroscopy at 3T has shown that glutamate (Glu), γ-amino butyric acid (GABA), and glutamine (Gln) in the prefrontal region of the brain can be reliably measured with standard single-voxel ^{1}H-MRS, without resorting to editing schemes [2]. However, short-TE spectra introduce specific problems in quantification due to strongly overlapping metabolite resonances and the presence of macromolecules and lipids [3]. In this study, *in vivo* ^{1}H-MRS data and basis sets were acquired in-house on the same scanner. To test the performance of in-house basis sets, Cramer-Rao Lower Bounds (CRLB) were calculated. We also investigate how many and which metabolites can be reliably quantified in human prefrontal cortex using short-echo time (TE) ^{1}H-MRS at 3T.

Materials and Methods

This study included 24 healthy control subjects (mean±SD, 52±8.4 years). Single-voxel ^{1}H-MRS was performed using a PRESS sequence at 3T (e.g., Philips Achieva TX System with a 32-channel receive-only array head coil). The examinations (voxel size, 2×2×2 cm^3) were measured from left prefrontal cortex in healthy subjects. After shimming procedure water suppression was accomplished with "VAPOR" pulses. The acquisition parameters were TR/TE = 2500/35 ms, and 128 acquisitions for averaging. A fully relaxed, unsuppressed spectrum was also acquired to measure the water peak (16 averages). In this study, 16 metabolites used in LCModel method were experimentally measured in-house on the same scanner (e.g., KBSI site). Data shows mean±SD for each group using a two tailed *t*-test with significance threshold of *p < 0.05, **p < 0.01, and ***p < 0.001. For multivariate analysis, partial least squares regression discriminant analysis (PLS-DA) was performed using SIMCA-P 13.0 software (Umetrics Inc.).

Results

LCModel fitting results with (e.g., KBSI, top-left) and without in-house basis sets (e.g., LCModel, top-right) are shown in Figure 1. The upper ppm limit was set at 4.0 ppm. The CRLBs for LCModel spectral fits were less than 10% for the most of metabolites: N-acetyl aspartate (NAA), phosphocreatine plus creatine (PCr+Cr, tCr), choline containing compounds (GPC+PC, tCho), Glu, and myo-inositol (Ins) (CRLB<10%) (Figure 1 (bottom)). Metabolites such as glutathione (GSH) (12 vs. 13%), Gln (26 vs. 26%), aspartate (Asp) (27 vs. 137%), GABA (68 vs. 38%), and Taurine (Tau) (45 vs. 32%) showed high CRLBs in the prefrontal cortex of healthy controls at 3T. However, GABA and Tau could not be reliably quantified (CRLB>30%). Figure 2 shows the spectral fitting results using the upper ppm limit set at 4.2ppm. LCModel fits quantified NAA, tCho, tCr, Glu, Glx, and Ins (CRLB<10%) and GSH (12 vs. 13%), Gln (27 vs. 29%), Asp (20 vs. 40%), GABA (288 vs. 46%), and Tau (95 vs. 182%). The scores plot resulting from applying PLS-DA to the numeric data (e.g., CRLBs and metabolite concentrations (not shown here)) is shown in Figure 3. The two groups (e.g., KBSI vs. LCModel) were not clearly separated. The Asp from LCModel was an outlier in the both PLS-DA plots.

Discussion

In this present study, LCModel with in-house basis sets reliably quantified 8 of 16 metabolites in the prefrontal cortex of healthy subjects at 3T. However, GABA and Tau showed relatively high CRLBs because these two peaks have low-concentration, complex multiplets that severely overlap with other, which make their quantification difficult. So, to detect these small metabolites, one of solutions is to use spectral editing or a based on direct measurement of the metabolite-nulled background signal [4]. There were statistically significant differences in CRLBs between LCMode fitting results with and without in-house basis sets. This means that LCModel using in-house basis sets may be especially useful for short-TE and metabolites characterized by strongly coupled resonances, namely Ins, Glu, Gln, GSH, and Asp. Therefore, it indicates that LCModel analysis with in-house basis sets can be helpful for improving in vivo quantification of metabolite signals with low concentrations.

References

[1] Frey *et al*., Bipolar Disorders 2007;9:119-127. [2] Nery *et al*., J Psychiatric Research 2010;44:278-285. [3] Govindaraju *et al*., NMR Biomed. 2000;13:129-153. [4] Provencher *et al*., NMR Biomed. 2001;14:260-264.

Acknowledgement: This work was supported in part by KBSI- #E34600.

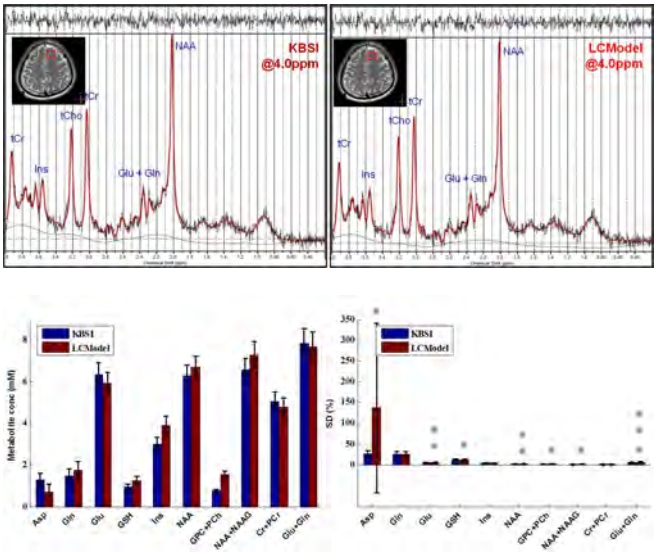

Figure 1. MR spectra from the same subject as analyzed by LCModel with (Top, left) and without in-house basis sets (right). The upper ppm limit was set at 4.0ppm. Metabolite conc. (Bottom, left) and CRLB estimates (right).

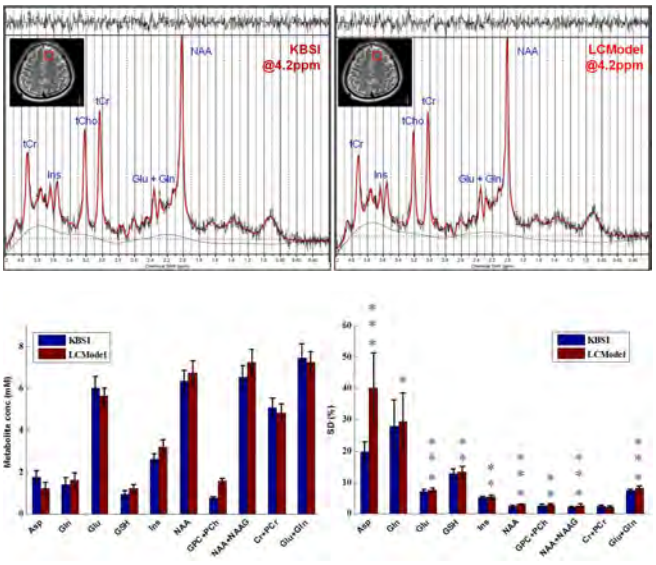

Figure 2. MR spectral fits analyzed by LCModel with (Top, left) and without in-house basis sets (right). The upper ppm limit was set at 4.2ppm. Metabolite conc. (Bottom, left) and CRLB estimates (right).

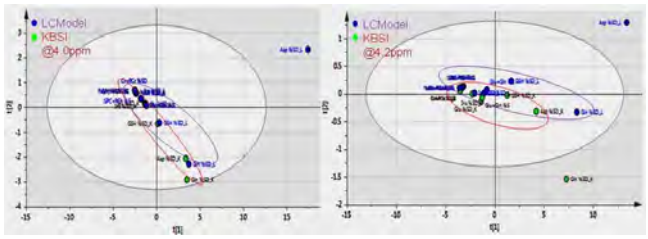

Figure 3. PLS-DA score plot showing a separation in CRLBs between KBSI and LCModel: upper limit of 4.0 ppm (Left) and of 4.2ppm (Right). Asp metabolite was an outlier in the LCModel fits.