Reproducibility of In Vivo GABA Quantification in Anterior Cingulate at 3 Tesla

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Introduction

GABA (γ-aminobutyric acid (NH_2-$^{\alpha}CH_2$-$^{\beta}CH_2$-$^{\gamma}CH_2$-CO_2H) is the major inhibitory neurotransmitter in the human brain, and its concentration is of interest in many diseases and disorders. The detection of the GABA resonance is complicated by overlap with other resonances from other, higher concentration metabolites. Editing sequences such as MEGA-PRESS[1] have been introduced which allow the detection of GABA. The goal of this work was to evaluate the reproducibility of GABA measurement in the frontal lobe (anterior cingulate) on a clinical 3 T system using MEGA-PRESS editing and compare it with previously reported repeatability of 38%[2].

Methods

Sixteen healthy volunteers were examined twice using a 3 T whole-body Siemens Trio system. Radiofrequency excitation was accomplished with a TEM coil (MR Instruments Inc.) tuned to 123.2 MHz. GABA-edited spectra were acquired using a MEGA-PRESS sequence with VAPOR water suppression from a 27 mL voxel placed over anterior cingulate, as identified on PD-weighted TSE scout scans. A selective 180° pulse (SLR, 45 Hz FWHM) was applied alternatively at 1.9 ppm, the resonance frequency of β-CH_2, and 9 ppm. Edited metabolite-nulled spectra were acquired (T_{IR} = 928 ms) to assess the contribution of macromolecules to the peak observed at 3 ppm.

The edited spectra were analyzed using LCModel[3]. The basis set was built from MEGA-PRESS edited spectra measured using GABA, *N*-acetylaspartate (NAA), glutamate (Glu) phantoms and from sum of 32 MEGA-PRESS macromolecule spectra. GABA was quantified relative to NAA with the assumption that the concentration of NAA is 10 mM.

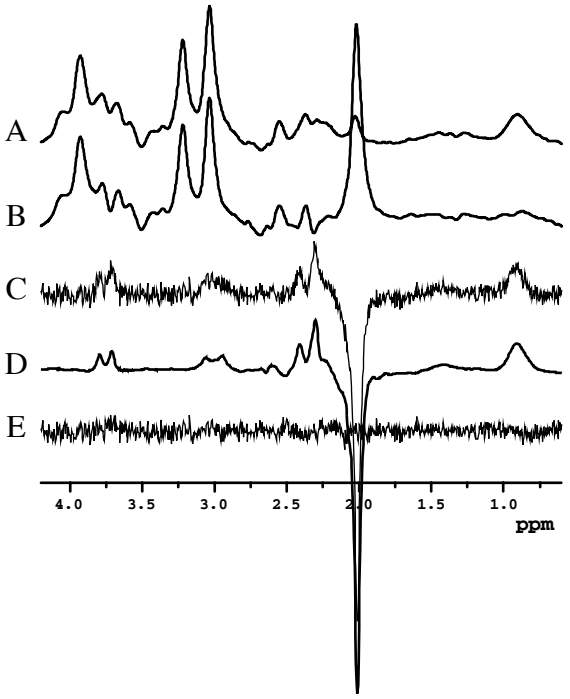

Figure 1. *In vivo* MR spectroscopy of GABA using MEGA-PRESS. Subspectra acquired **A.** in the presence of the frequency-selective pulse and **B.** in the absence of the editing pulse (T_R = 2.5 s, T_E = 68 ms, N_{EX} = 128 each). **C.** Difference spectrum resulting from subtraction of B from A. **D.** Fit of C. performed with LCModel analysis. **E.** Residual from LCModel analysis. Spectra A and B are shown with line–broadening of 3 Hz and spectrum C without any line-broadening.

Results and Discussion

Figure 1 shows *in vivo* spectra from a single subject (a) subspectrum acquired with the selective pulse applied at 1.9 ppm, (b) subspectrum acquired with the selective pulse applied at 9 ppm, (c) difference spectrum resulting from subtraction of (b) from (a), (d) fit from LCModel analysis, and (e) residual.

After LCModel analysis, data with CRLBs higher than 25% for the concentration of GABA were removed. Based on this criteria, data from three subjects were removed leaving thirteen in the analysis. CRLBs for the concentration of GABA for rest of the data were 19 ± 3%. The concentration of GABA averaged over thirteen subjects was 1.14 ± 0.16 mM for the first scan and 1.18 ± 0.15 mM for the second scan. Figure 2 shows Bland-Altman[4] plot for data from thirteen subjects. The mean of the difference was -0.044 ± 0.22 mM, with coefficient of repeatability of 0.44 mM.

Also as a measure of reproducibility, the intra- and inter-subject variability was calculated and expressed as a coefficient of variation (CoV = SD divided by the mean of the test and retest measurement). The mean of intra-subject CoV was 8% (range: 3% to 24%), and the inter-subject CoV was 9% (calculated by taking the average of GABA concentration from two scans and calculating the mean and standard deviation for thirteen subjects and then dividing SD by the mean).

Previously reported intra-subject repeatability of GABA measurement was 38% at 1.5 T using PRESS-localized double quantum filter[2]. In this study, the intra-subject repeatability was 16% if calculated the same way as in Ref. 2. The reproducibility of GABA at 3 T is good and is comparable to reproducibility of NAA at 1.5 T[5].

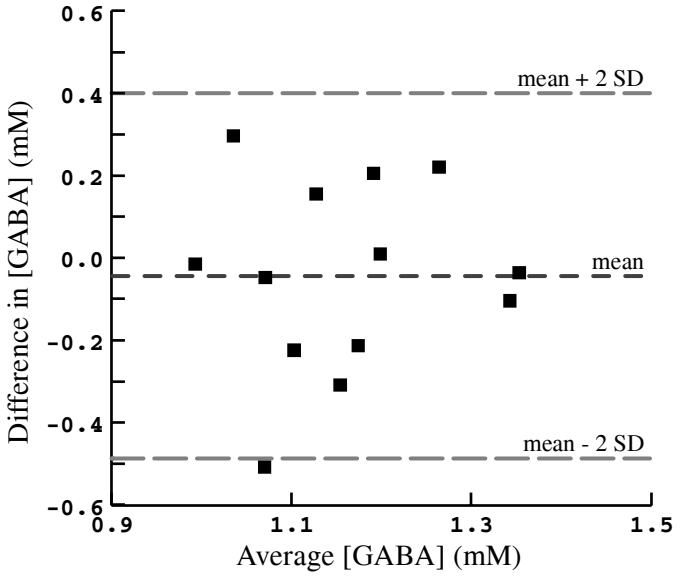

Figure 2. Bland-Altman plot for the concentration of GABA. Mean of the difference was -0.044 mM and the coefficient of repeatability was 0.44 mM.

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