Phasing and curve fitting of highly resolved 2D constant time PRESS spectra for quantitation of glutamate, GABA and glutamine

Hidehiro Watanabe[1], Nobuhiro Takaya[1], and Fumiyuki Mitsumori[1]
[1]*Center for Environmental Measurement and Analysis, National Institute for Environmental Studies, Tsukuba, Ibaraki, Japan*

Target audience: Basic scientists or clinicians interested with either development or applications in magnetic resonance spectroscopy, especially with quantitation of glutamate, γ-amino butyric acid and glutamine in brain.

Introduction

While glutamate (Glu) and γ-amino butyric acid (GABA) are major neurotransmitter in human brain, glutamine (Gln) is a precursor and storage form of Glu, which plays an important role in the Glu-Gln cycle. These peaks are overlapped on the conventional *in vivo* ^{1}H spectra due to strong coupling with small chemical shift difference and J_{HH} coupling. This may lead to difficulty of accurate quantitation of Glu, GABA and Gln. Constant time (CT) two dimensional methods have a feature of good peak resolution through ^{1}H decoupling along F_1. We have resolved three diagonal peaks of Glu C4H, GABA C2H and Gln C4H in human brain *in vivo* using two kinds of 2D localized CT methods, CT-COSY (1) and CT-PRESS applied with window of resolution enhancement (2). Curve fitting of these peaks may lead to accurate quantitation of Glu, GABA and Gln. In this work, we first demonstrate phasing of 2D CT-PRESS spectra for higher peak resolution in phase sensitive mode. We also demonstrate curve fitting of these three peak volumes for quantitation.

Methods

Phantom experiments and volunteer measurements were performed on a 4.7 T whole-body MR system (INOVA, Agilent). We used a quadrature volume TEM coil of 300-mm diameter both for transmission and reception. ISIS version of CT-PRESS sequence was used (2). In this sequence water suppression and outer volume suppression are followed by a module for localization; ISIS pulse (x-direction) – 90° slice pulse (y-direction) – 1/2*TE1 – 180° non-slice pulse – 1/2*(TE1+TE2)+Δt_1/2 – 180° slice pulse (z-direction) – {data acquisition}. After signal accumulations, a t_1-dependent shift was applied along t_2 to attain the constant time delay (2). Then, our developed window function of resolution enhancement for shifted echoes was applied to time domain data (2).

In phantom experiments, we used a phantom containing a brain metabolite mixture of 10 mM NAA, 8 mM Cr, 9 mM Glu, 3 mM Gln and 2 mM GABA. A 200-mL bottle containing this solution was placed in a water bath containing 0.9 % dissolved NaCl for mimicking an *in vivo* load and ISIS CT-PRESS signals were acquired inside a voxel within that bottle. In volunteer studies, ISIS CT-PRESS signals were acquired in a 30x30x30 mm^3 voxel in a parieto-occipital region with a measurement time of 20 min. Constant time delay was 123 ms. TE1 was 15 ms and TE2 was 37 ms. Spectral widths along F_1 was 1 kHz and that of F_2 2 kHz. Relaxation delays were 3 s for the phantom experiments and 4s for the volunteer studies.

After reconstruction, phases of three singlets of NAA at 2.01 ppm, Cr at 3.02 ppm and Cr at 3.91 ppm were measured. Phasing of spectra was applied with zero-order and linear phases calculated by linear least square fitting of these three phases. To quantitate Glu, GABA and Gln, the fitting area including diagonal peaks of Glu C4H, GABA C2H and Gln C4H was extracted from 2D CT-PRESS spectra. We then computed the peak volumes of these peaks on phased spectra using the spectral analysis software that we developed on MATLAB 8.3. In this software, three diagonal peaks and multiplet peaks of NAA around 2.4 ppm were curve-fitted with a linear combination model of simulated basis CT-PRESS spectra. A basis spectrum of each metabolite was calculated by the software of GAMMA. Both of real and imaginary data of phased spectra were used for the curve-fitting. To avoid local minimum problems, the following fitting procedure was done. First, parameters of peak volume, line broadening and peak positions of Glu C4H that was a landmark peak were calculated in the landmark area only including GluC4H around 2.35 ppm. Next, peak volumes of Glu, GABA, Gln and NAA were calculated by least squares fitting of the fitting area with other parameters on the magnitude mode spectrum. Then, these calculated parameters were used as initial values of Glu, GABA, Gln and NAA for non-linear least squares fitting of the fitting area.

Results & Discussion

Phantom and human brain spectra were successfully phased (Figs 1a, b and Figs 2a, b). Figures 1b and 2b shows surface plots of these spectra viewed from F_1 axis. Glu C4H, GABA C2H and Gln C4H were well resolved. Figures 1c and 2c show the fit results after the curve fitting. Both of the fit residuals were small (Figs. 1d, 2d). The ratio among three peak volumes of Glu, GABA and Gln in the phantom spectrum was 1: 0.19: 0.32. Although T_2 correction was not done, this ratio was close to that of concentrations of 1: 0.22: 0.33.

Conclusions

2D CT-PRESS spectra are successfully phased by our demonstrated method. Peak volumes of Glu C4H, GABA C2H and Gln C4H are well curve-fitted by the spectral analysis. These are useful for quantitation of glutamate, γ-amino butyric acid and glutamine.

References

1. Watanabe H., Takaya N., Mitsumori F., Simultaneous observation of glutamate, γ-amino butyric acid and glutamine in human brain at 4.7T using localized two dimensional constant-time correlation spectroscopy. NMR in Biomed. 2008;21(5):518-526.
2. Watanabe H., Takaya N., Mitsumori F., Highly resolved ^{1}H spectroscopy of the human brain using ISIS CT-PRESS with resolution enhancement. Magn. Reson. Med. Sci. 2012;11(4):235-241.

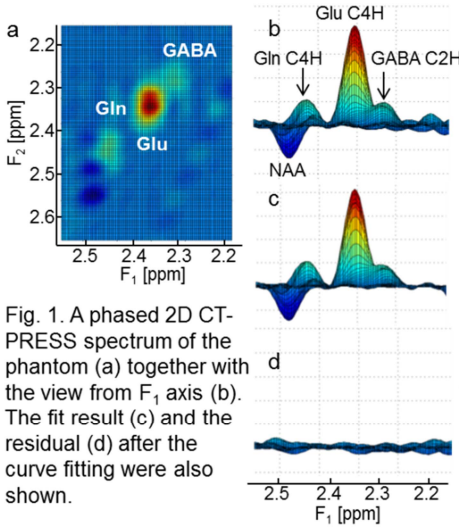

Fig. 1. A phased 2D CT-PRESS spectrum of the phantom (a) together with the view from F_1 axis (b). The fit result (c) and the residual (d) after the curve fitting were also shown.

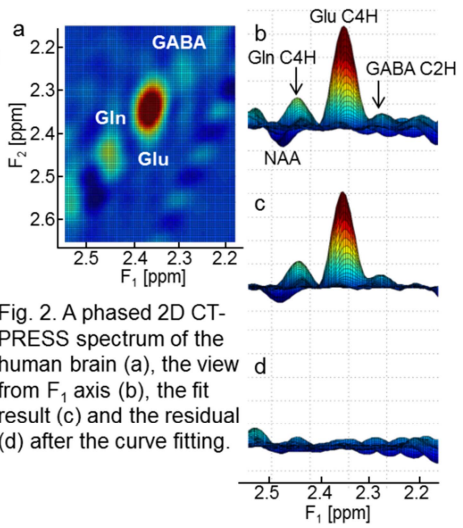

Fig. 2. A phased 2D CT-PRESS spectrum of the human brain (a), the view from F_1 axis (b), the fit result (c) and the residual (d) after the curve fitting.