Sensitivity improvements in peak detection of glutamate, GABA and glutamine in the human brain using ISIS CT-PRESS at 4.7 T

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Introduction

We have reported *in vivo* simultaneous detection of glutamate (Glu), γ-amino butyric acid (GABA) and glutamine (Gln) in the human brain using the localized CT-COSY method at 4.7 T (1). Furthermore, we have developed a quantitation method on 2D CT-COSY spectra and demonstrated quantitation of glutamate and GABA in the human brain (2). However, this method required at least two sets of spectra with different constant times and long measurement time of 40 min for each spectrum was needed. Since diagonal peaks of Glu C4H, GABA C2H and Gln C4H were resolved on the CT-COSY spectra, we thought that CT-PRESS, a spin echo type of CT techniques, had a power of resolution for these metabolites with higher sensitivity. Although GABA could not be resolved on CT-PRESS spectra obtained from the rat's brain even at 4.7 T (3), peak resolution can be improved using appropriate parameters on measurements and post-processing. The purpose of this work is following three items; 1) peak resolution of glutamate, GABA and glutamine by CT-PRESS, 2) sensitivity improvement compared with CT-COSY spectra and 3) peak detection on *in vivo* CT-PRESS spectra of the human brain.

Methods

We developed ISIS version of CT-PRESS, where 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) + $\Delta t_1/2$ – 180° slice pulse (z-direction) – {data acquisition}. This sequence has features to minimize chemical shift displacement errors and obtain a better slice profile, but only along one of two directions defined by two 180° slice pulses in PRESS. It also yields a shortened echo time. Data acquisition was started immediately after crusher gradient for the 180° slice pulse along the z-direction (4). After signal accumulations, a t_1-dependent shift was applied along t_2 to attain constant time condition (4).

First, we performed experiments using two kinds of phantoms containing a brain metabolite mixture. One contained 10 mM NAA, 8 mM Cr, 9 mM Glu, 3 mM Gln and 2 mM GABA. The other contained the same reagents except for GABA. A 200-mL bottle containing one 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. Next, localized CT-COSY signals were also acquired inside the same voxel. Then, the bottle was exchanged for another 200-mL bottle containing the other solution, and the other ISIS CT-PRESS signals were acquired. 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. In all measurements using CT-PRESS, TE1 = 15 ms, TE2 = 36 ms and T_{ct} = 126 ms. In CT-COSY measurements, T_{ct} was set to 110 ms. In all cases, spectral widths along F_1 and F_2 were 1 kHz and 2 kHz, respectively, number of t_1 increments was 150 and number of averages was 2. Shifted Gaussian and Lorentzian windows were applied to time domain data after resolution enhancement along t_1 and t_2. All spectra were displayed in magnitude mode. Relaxation delays were 3 s for phantom measurements and 4 s for volunteer studies. All experiments were performed using a 4.7 T whole-body NMR spectrometer (*INOVA*, Varian). A volume TEM coil was used both for transmitter and receiver.

Results & Discussion

Figure 1 shows CT-PRESS spectra of brain phantoms with GABA (a) and without (b). Figure 1c is a localized CT-COSY spectrum of the same phantom as (a), showing three diagonal peaks of GABA C2H (2.28 ppm), Glu C4H (2.35 ppm) and Gln C4H (2.44 ppm). These three peaks were resolved on spectra by CT-PRESS (Fig. 1a). Absence of signals at 2.28 ppm in Fig. 1b also proved that the peak at 2.28 ppm was originated from GABA C2H. Signal to noise ratio (SNR) of Glu C4H on a CT-PRESS spectrum was 2.24 times higher than that of CT-COSY.

Figure 2 shows a human brain spectrum by CT-PRESS. Three peaks at 2.28, 2.35 and 2.44 ppm were resolved. SNR per unit measurement time ($SNR_{unit\text{-}time}$) of Glu C4H on this spectrum was compared with that obtained in the human brain by CT-COSY with 30-min measurement time (1). $SNR_{unit\text{-}time}$ was improved by a factor of 1.7.

Conclusions

Glutamate, GABA and glutamine can be detected with sensitivity improvements in the human brain at 4.7 T using CT-PRESS. This feature will lead to quantitation in a shortened measurement time.

References

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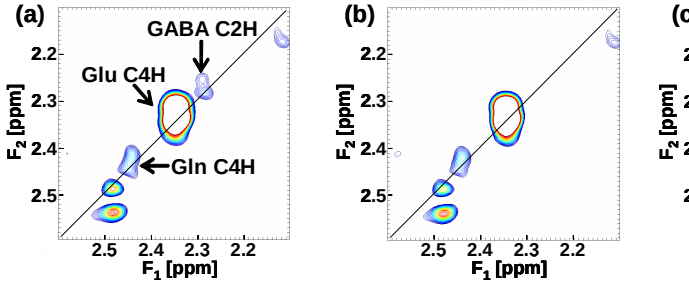

Fig. 1. A CT-PRESS spectrum of a brain phantom (a) with GABA, (b) without GABA, and (c) a CT-COSY spectrum of the same phantom as (a).

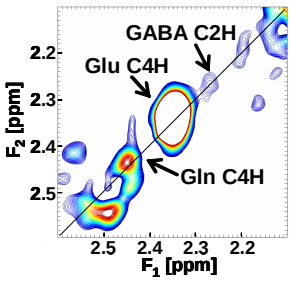

Fig. 2. A CT-PRESS spectrum of the human brain.