Simultaneous Detection of Glutamate, GABA and Glutamine in the Human Brain at 4.7 T by using a Localized 2D CT-COSY with an ISIS Pulse

H. Watanabe[1], N. Takaya[1], F. Mitsumori[1]

[1]National Institutes for Environmental Studies, Tsukuba, Ibaraki, Japan

Introduction

While glutamate (Glu) is a major excitatory neurotransmitter, γ-amino butyric acid (GABA) is a major inhibitory neurotransmitter. Glutamine (Gln) exists mainly in astrocyte and has an important role for glutamate/glutamine cycle (1). Thus, *in vivo* detection of Glu, GABA and Gln is one of important subjects for ^{1}H MRS. We have demonstrated *in vivo* detection of these metabolites in the human brain by using a localized 2D CT-COSY at 4.7 T (2).

This sequence uses 90 degree, 180 degree and 90 degree pulses as slice selective pulses. Compared to 90 degree pulses, the band width for 180 degree pulses is narrower because of RF power limitation. This causes slice displacement error due to chemical shift dispersion and it is a critical problem especially at high field. The slice profile of 180 degree pulse is also worse than that of 90 degree pulse.

In this work, we propose a localized 2D CT-COSY with an ISIS pulse for one direction to overcome that. We demonstrate the improvement of slice displacement and profile in phantom experiments. We also demonstrate simultaneous glutamate, GABA and glutamine detection *in vivo* in the human brain by using the proposed method.

Methods

The localized 2D CT-COSY sequence with an ISIS pulse uses two slice selective pulses of 90 degree and a non-selective 180 degree pulse in the CT-COSY part. By using an ISIS pulse for the slice selection of the other axis as a preparation pulse, spatially 3D localization is possible. Water signal inside the spatially 2D localized column selected by two slice selective pulses in the CT-COSY part is suppressed by VAPOR (3) in this sequence. Thus, water signal is more suppressed compared to the 3D localization by using three ISIS pulses for all 3D axes. Since an ISIS pulse is a preparation pulse, long pulse duration may be used. Thus, an adiabatic pulse with a wide bandwidth can be used. As a result, the slice displacement and the slice profile improve compared to a previously reported method (2). By using a non-selective 180 degree pulse in the CT-COSY part, refocus and inversion features may also improve.

Phantom experiments and volunteer studies were performed on a whole body 4.7 T *INOVA* spectrometer (Varian, Palo Alto, CA). A volume TEM coil with 300-mm diameter was used.

In phantom experiments, a spherical phantom filled with saline was used. Volume size was set to 30 x 30 x 30 mm^3. By applying a read gradient, the slice profile was measured by using water signal without water suppression pulse. First, carrier frequency of an ISIS pulse was set to water resonance. Second, that frequency was shifted upfield by 200 Hz which is equal to the difference between Cr resonance of 3 ppm and NAA resonance of 2 ppm at 4.7 T. Water signals were measured by applying the proposed sequence and the original sequence (2). Hyperbolic secant pulse with duration of 7 ms was used for the ISIS pulse. The bandwidth was 2800 Hz. For the reported sequence, a universal rotator pulse with duration of 4 ms was used for the slice selective pulse of 180 degrees. The bandwidth was 1240 Hz.

For volunteer studies, localized 2D CT-COSY signals with an ISIS pulse were acquired from a parieto-occipital region (27 ml). The duration of the ISIS pulse was set to 7 ms as in the phantom experiments. To minimize slice displacement error due to chemical shift dispersions, the carrier frequency of slice selective pulses was set to the Cr resonance of 3 ppm. The sequence conditions were as follows; np = 4096 in t_2, 150 t_1 increments, sw in F_1 = 1000 Hz, sw in F_2 = 2000 Hz, TR = 3 s and Tct = 0.11 s. 4 phase cycles were used and total acquisition time was 30 min. Acquired raw data sets were zero-filled to 1024 in t_1, and Gauss function of 0.05 s in t_2 and that of 0.1 s shifted by 0.03 s were applied. 2D spectra were displayed in the magnitude mode.

Results & Discussion

Figure 1 shows the slice profiles with the proposed method and the original method. Slice profile of the proposed method is better than that of the original method. The slice displacement of the proposed method is about 2 mm due to the frequency shift of 200 Hz, compared to that of about 5 mm with the original method. It means that the slice displacement error between Cr and NAA can be two times better improved by using this method.

Figure 2 shows a CT-COSY spectrum of the human brain and a diagonal spectrum obtained by a proposed method. Diagonal peaks of glutamate-4, glutamine-4 and GABA-2 are resolved. A cross peak between glutamate-4 and glutamate-3 is also detected.

Conclusions

A localized 2D CT-COSY with an ISIS pulse allows us to detect glutamate, GABA and glutamine in the human brain. This method can improve the features of the slice selected by an ISIS pulse.

References

1. Magistretti, P. J., Pellerin, L., Rothman, D. L., Shulman, R. G., *Science*, 283, 496, 1999
2. Watanebe, H., Takaya, N., Mitsumori, F., Proc. Intl. Soc. *Mag. Reson. Med.*, 12, 113, 2004
3. Tkáč, I., Starčuk, Z., Choi, I.-Y., Gruetter, R., *Magn. Reson. Med.*, 41, 649, 1999

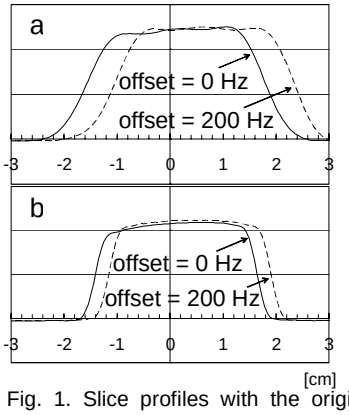
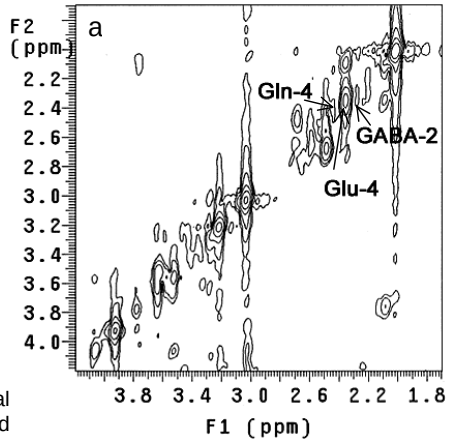


Fig. 1. Slice profiles with the original method (a) and with the proposed method (b).



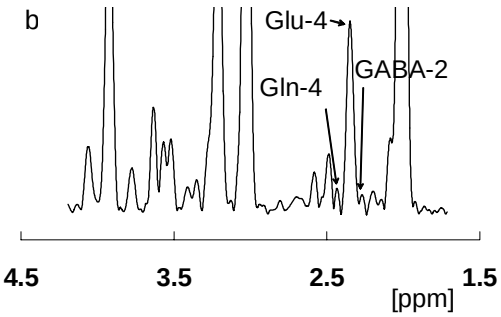


Fig. 2. Human brain 2D spectrum obtained by a localized 2D CT-COSY with an ISIS pulse (a) and a diagonal spectrum (b).