Improvement of the Spectral Resolution for Glutamate and Glutamine in the Human Brain at 4.7 T by using a Localized 2D Constant Time COSY

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

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

Introduction

While glutamate (Glu) is the major excitatory neurotransmitter, glutamine (Gln) exists mainly in astrocyte and has an important role for glutamate/glutamine cycle (1). Thus, the *in vivo* detection of Glu and Gln is one of important subjects. However, it is still challenging, because of their close ^{1}H chemical shifts (δ_H) and J_{HH}. Although they could be resolved at 7T, they could be a little overlapped even at 4T (2).

While the difference of δ_H between Glu-4 and Gln-4 is about 0.1 ppm, it corresponds to 20 Hz at 4.7T. Thus, they could be resolved when J_{HH} is decoupled. Although constant time PRESS (CT-PRESS) could detect Glu-4 by decoupled J_{HH}, Gln could not be detected (3). While 2D CT-COSY also decouples J_{HH}, Glu and Gln could be resolved at 4.7 T.

In this work, we demonstrate the improvement of the spectral resolution for Glu and Gln in phantom experiments at 4.7 T by using 2D CT-COSY. We also demonstrate localized 2D CT-COSY spectra in the human brain.

Methods

Phantom experiments were performed on a Varian INOVA spectrometer (Varian, Palo Alto, CA) interfaced to a 4.7T magnet with 310-mm horizontal bore size (JASTEC, Kobe, Japan). Volunteer studies were performed on a whole body 4.7 T INOVA spectrometer (Varian, Palo Alto, CA). A sine coil with 50-mm diameter was used for phantom experiments and a volume TEM coil with 300-mm diameter for volunteer studies.

In phantom experiments, three kinds of spherical phantoms with 40-mm diameter were used. One was filled with 50-mM glutamate, another 50-mM glutamine, and the other 50-mM glutamate and 50-mM glutamine. For each phantom, the three kinds of spectra were obtained by the following protocol. First, water linewidth was adjusted to about 7 Hz which can be achieved in a human brain after shimming. Then, those spectra were obtained by using a one pulse sequence, a 2D COSY sequence and a 2D CT-COSY sequence. VAPOR (4) was used for water suppression in each sequence. The sequence conditions were as follows: number of data points (np) = 4000 and the spectral width (sw) = 5000 Hz for the one pulse sequence; sw in both F_1 and F_2 = 2000 Hz, np = 1024 in t_2, and 256 t_1 increments for 2D sequences. While Gaussian function with 0.3 s (gf = 0.3 s) was used for a 1D spectrum, Gaussian function (gf = 0.05 s) for F_2 and shifted Gaussian function (gf1 = 0.05 s and gfs1 = 0.064 s) for F_1 were used for 2D spectra. In the CT-COSY, constant time tc was set to 0.1 s. 2D spectra were displayed in magnitude mode.

For volunteer studies, a localized CT-COSY sequence (5) was used. Spectra were obtained from a parieto-occipital region (27 ml). The conditions were as follows: np = 4096 in t_2, 144 t_1 increments, sw in F_1 = 1000 Hz, sw in F_2 = 2000 Hz, and tc = 0.1s. To minimize sw in F_1, the receiver frequency was shifted to 1.67 ppm upfiled from the water ^{1}H resonance. The three datasets were acquired as following conditions: TR = 3.5 s and number of traces (nt) = 2, TR = 3.5 s and nt = 4, and TR = 1.9 s and nt =8. 2D raw data were zero-filled to 1024 in t_1, and shifted sine-bell functions were used for both directions (sb = 0.05 s, sbs = -0.04 s, sb1 = 0.072 s and sb1 = -0.01 s). Magnitude display was used for all spectra.

Results & Discussion

Figure 1 shows the spectra obtained from the mixed phantom. One is a 1D spectrum obtained by the one pulse sequence. Another is a maximum intensity projection onto F_1 on a 2D COSY spectrum. The other is that on a 2D CT COSY spectrum. While Glu-4 and Gln-4 are overlapped in the spectrum by the one pulse and the projection on the COSY spectrum, they can be resolved in the projection on the CT-COSY spectrum.

For the volunteer studies, all three datasets were accumulated. Figure 2 shows this accumulated 2D localized CT-COSY spectrum. Figure 3 shows a F_1 cross section through the CT COSY spectrum at δ_H of Gln-4 (2.45 ppm). In the 2D spectrum, the diagonal peak of Glu-4 at 2.35 ppm and that of Gln-4 can be resolved. The cross peak between Glu-3 at 2.1ppm and Glu-4 and that between Gln-3 at 2.1ppm and Gln-4 can be also resolved. The cross peak between GABA-3 at 1.9 ppm and GABA-4 at 3.01 ppm can be also detected.

Conclusions

A localized 2D CT-COSY allows us to resolve glutamate and glutamine in the human brain at 4.7 T even in a magnitude mode. It can also detect GABA. Therefore, this method has a potential for *in vivo* detection of excitatory and inhibitory neurotransmitters.

References

1. Magistretti, P. J. et al., *Science*, 283, 496, 1999
2. Tkáč, I. et al., *Magn. Reson. Med.*, 46, 451, 2001
3. Dreher, W et al., .Magn. Reson. Imag., 17, 141, 1999
4. Tkáč, I. et al., *Magn. Reson. Med.*, 41, 649, 1999
5. Chung, H et a l., Proc. Intl. Soc. *Mag. Reson. Med.*, 11, 1143, 2003

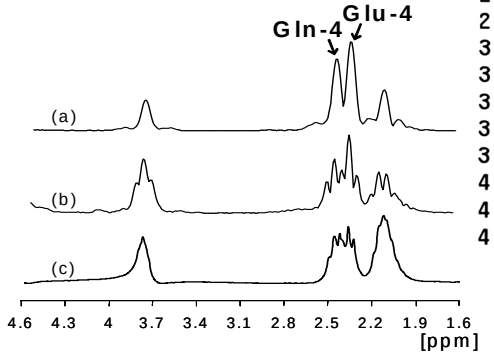

Fig. 1. Mixed phantom spectra. (a) CT-COSY, (b) COSY and (c) 1D spectrum.

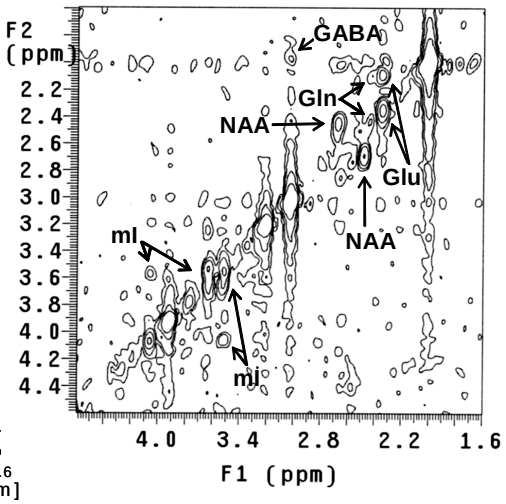

Fig. 2. A localized 2D CT-COSY spectrum obtained from a human brain.

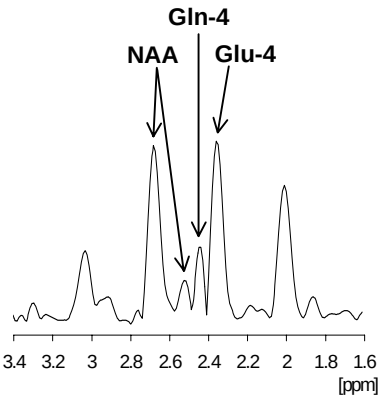

Fig. 3. A F_1 cross section through the spectrum shown in Fig. 2 at Gln-4 frequency.