# Quantitation of Glutamate and GABA in the Human Brain *in vivo* using Localized 2D Constant Time COSY at 4.7 T

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## Introduction

Glutamate (Glu) and γ-amino butyric acid (GABA) are major neurotransmitters (excitatory and inhibitory, respectively) in the human brain. Thus, *in vivo* quantitation of glutamate and GABA is one of significant subjects for $^1$H MRS. We have demonstrated *in vivo* peak detection of glutamate and GABA in the human brain using localized 2D CT-COSY at 4.7 T shown in Fig.1 (1). For the absolute quantitation using 2D CT-COSY spectra, the following two difficulties must be overcome; $T_2$ decay during the constant time delay, $T_{ct}$, and the peak volume calculation on the 2D spectra. In this work, we will propose a quantitation method with $T_2$ correction and the peak volume calculation. We validated this method in the phantom experiments and demonstrated *in vivo* quantitation of glutamate and GABA in the human brain.

## Methods

On the localized 2D CT-COSY spectra of the human brain, three peaks related to glutamate and GABA were resolved; the diagonal peaks of Glu C4H at 2.34 ppm and GABA C2H at 2.28 ppm, and the cross peak between Glu C4H and Glu C3H (1). We used two diagonal peaks of Glu C4H and GABA C2H for quantitation here.

First, four spectra with $T_{ct}$ of 110 ms, 130 ms, 150 ms and 270 ms were obtained from the human brain. For the evaluation of glutamate, the 3 dimensional peak of Glu C4H on each spectrum was fitted by that in a 50 mM glutamate phantom obtained with $T_{ct}$ of 130 ms. Then, the peak volume ratios were calculated. Difference of coil-loading factors between the human brain and the phantom was corrected using an internal water reference method. Next, $T_2$ correction was performed. In the localized CT-COSY sequence, the signal intensities are modulated due to $^1$H-$^1$H coupling, $J_{HH}$, in addition to $T_2$ decay. We calculated this dependence function, $f(T_{ct})$, using GAMMA simulation (2) with the reported values of the chemical shifts and $J_{HH}$ (3). Then, the net signal intensities were proportional to a function, $A^*e^{-Tct/T2} * f(T_{ct})$. Thus, $T_2$ was calculated by curve-fitting using this function. Then, glutamate concentration was obtained using calculated peak volume ratios and $T_2$. Quantitation of GABA was also done using this procedure.

All experiments were performed using a 4.7 T whole-body NMR spectrometer (*INOVA*, Varian). First, for validation of this protocol, we did phantom experiments using a 10 mM glutamate phantom. Next, human volunteer studies were performed. The volume of interest was 36 ml and was set inside the parieto-occipital lobe.

## Results & Discussion

In the 50 mM phantom experiments, the measured signal intensities of Glu C4H were well fitted by the proposed function, $A^*\exp(-T_{ct}/T_2)^*f(T_{ct})$ (Fig. 2 (a)). The calculated $T_2$ value was 580 ms. In validation experiments using the 10 mM glutamate phantom, the calculated concentration was 9.62 mM.

In the human volunteer studies, $T_2$ value of Glu C4H was calculated as 117 ms (Fig. 2 (b)). By our proposed quantitation method, concentrations of glutamate and GABA in the human brain were calculated as 11.7 mM and 0.95 mM, respectively. Those two values were in good agreement with the previously reported values.

## Conclusions

Glutamate and GABA in the human brain were quantitated by the proposed method with $T_2$ correction and peak volume calculation. The calculated concentrations were within the previously reported values.

## References

1. Watanebe, H., Takaya, N., Mitsumori, F., Proc. Intl. Soc. *Mag. Reson. Med.*, 13, 2496, 2005.
2. Smith, SA., Levante TO., Meier BH., Ernst RR., *J Magn. Reson.* Ser A, 106:75-105, 1994.
3. Govindaraju, V., Young, K., Maudsley, AA., *NMR Biomed.*;13(3):129-153, 2000.

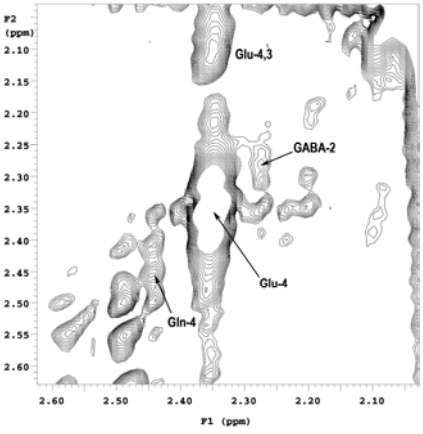


Fig. 1. A localized 2D CT-COSY spectrum obtained from the human brain.

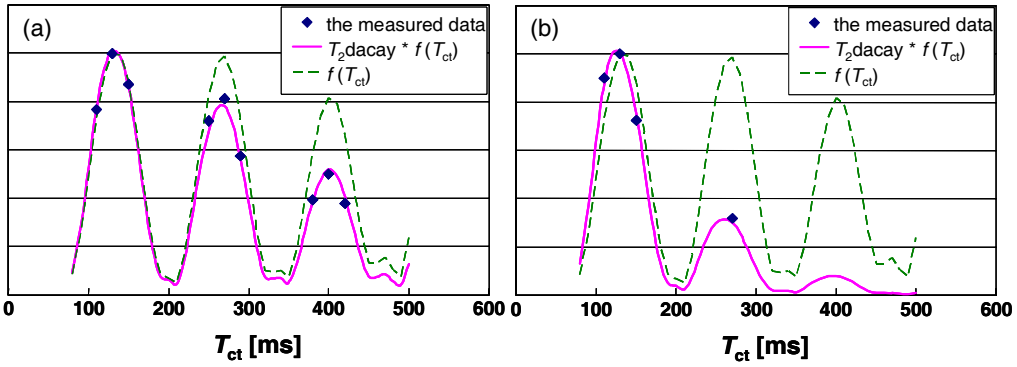


Fig. 2. The measured signal intensities of Glu C4H were well fitted by a function of $A^*\exp(-T_{ct}/T_2)^*f(T_{ct})$. The function, $f(T_{ct})$ is a $T_{ct}$ dependence function due to $J_{HH}$. (a): the 50 mM glutamate phantom data, (b): the human brain data.