Simultaneous detection of multiple quantum filtered GABA and single quantum creatine in the human brain in vivo using a single shot, two-echo acquisition scheme

I-Y. Choi[1], S-P. Lee[1], H. Merkle[2], J. Shen[3]

[1]Medical Physics, The Nathan Kline Institute, Orangeburg, NY, United States, [2]NINDS, NIH, Bethesda, MD, United States, [3]NIMH, NIH, Bethesda, MD, United States

INTRODUCTION

The multiple quantum (MQ) filtering techniques have several unique features compared to many other spectroscopic techniques for reliable detection of GABA. However, conventional MQ filtering methods lack internal reference signals since MQ filtering eliminates all singlets such as Cr (3.03 ppm) or NAA (2.01 ppm), which often serves as a marker for the internal concentration reference, a reference for the phase originated from frequency shift due to B_0 drift and/or subject's movement during measurements in ^{1}H MRS. The purpose of this study was (a) to develop a single shot, two-echo method for simultaneous detection of MQ filtered GABA and single quantum (SQ) Cr to overcome the shortcomings of conventional MQ filtering techniques and (b) to quantify *in vivo* GABA signals using the interleaved SQ Cr signal as an internal concentration reference.

METHODS

Ten healthy subjects were studied (34 ± 9 years old, mean ± SD) with several of them being studied multiple times. The pulse sequence consists of two parts: the MQ filtered GABA acquisition part and the SQ Cr acquisition part with no further relaxation delay for Cr. The three-dimensional localized MQ sequence part uses a double-band frequency selective 180° pulse during MQ preparation period for the improved selection of GABA-4 (3.0 ppm) and GABA-3 (1.9 ppm) (1). The SQ Cr sequence part is composed of water suppression interleaved with outer volume suppression, followed by a localized PRESS sequence. *In vivo* GABA concentration was estimated by both the external and internal reference methods. The external reference method compares the signal intensity of GABA with that measured from a GABA solution phantom. For the internal reference method, the *in vivo* GABA-to-Cr concentration ratio was obtained by comparing the signal intensity of GABA with that of Cr from the simultaneously measured *in vivo* MQ GABA and SQ Cr spectra using the two-echo MQ method. All studies were performed on a 3 Tesla SMIS system using a helmet coil. The volume of interest was positioned in the fronto-parietal region of the human brain.

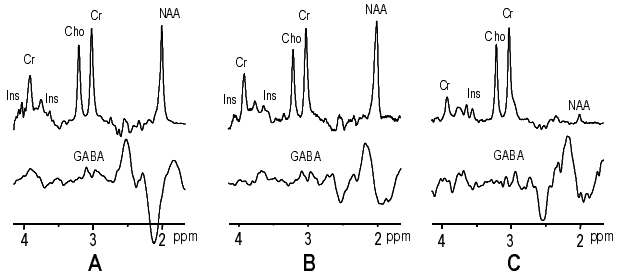

Fig. 1 Consistent observation of GABA doublet in simultaneous measurements of MQ GABA and SQ Cr in the human brain *in vivo* at 3 Tesla.

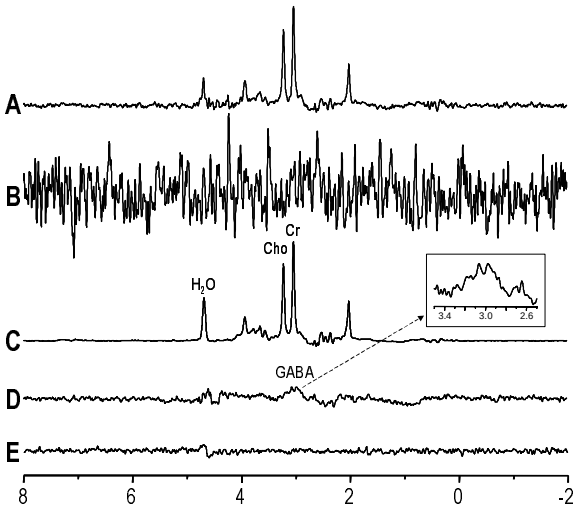

Fig. 2 MQ GABA and SQ Cr spectra in the human brain *in vivo* using the two-echo MQ method. (TE = 68 ms, tr = 2 s, nt = 8 for (A) & (B), nt = 1024 for (C) & (D)).

RESULTS AND DISCUSSION

Using the single shot two-echo method, the individual traces of the SQ Cr and MQ GABA spectra were acquired simultaneously (Fig. 1 & 2). The observed pattern of GABA doublet was consistent among all subjects with a frequency separation of 13 ± 1.2 Hz (mean ± SD, n=17). When the SQ Cr and MQ GABA (Fig. 2A & 2B) measurements were performed using an average of 4 or 8 transients, the MQ GABA signals were not discernible from the noise while the SQ Cr signal was clearly visible. This simultaneously measured Cr singlet served not only as an internal concentration reference but also as a navigator for correction of frequency drifts in each single acquisition. Figures 2C and 2D show the averaged spectra (NT = 1024) after individual frequency drift correction based on the frequencies of each SQ Cr spectrum. The zeroth-order phase of MQ GABA was corrected based on that of SQ Cr from the interleaved Cr spectra. The zeroth-order phase difference between MQ GABA and SQ Cr was the same among all subjects. In addition, improved selectivity of MQ GABA using the double-band frequency selective pulse was illustrated by the excellent suppression of overlapping signals from Cr. Contamination from overlapping macromolecules were also negligible using this method as shown in a metabolite-nulled spectrum (Fig. 2E). GSH was not selected by the double-band pulse. The GABA-to-creatine ratio was 0.09 ± 0.03 (mean ± SD, n=17) and the estimated concentration of GABA in the fronto-parietal region of the human brain *in vivo* was 0.66 ± 0.19 (mean ± SD, n=17) using the internal reference method and 0.69 ± 0.18 μmol/g (mean ± SD, n=17) using the external reference method.

In conclusion, this study demonstrates for the first time single shot, three-dimensionally localized simultaneous ^{1}H NMR spectroscopy of MQ filtered GABA and SQ Cr in the human brain *in vivo* with minimal sensitivity reduction. The proposed method should be applicable for other J-coupled metabolites and can be adapted to chemical shift imaging (2) to assess regional heterogeneity of the metabolites' distribution in health and disease.

REFERENCES

1. Choi et al, *Proc ISMRM* **11**: 433 (2003). 2. Choi et al, *Proc ISMRM* **11**: 522 (2003); Shen et al. *MRM* **41**: 35 (1999).

This work is supported by NIH grant 8R01EB00315 and R03AG022193.