Single-shot 3D localized Multiple Quantum Spectroscopy of GABA in the Human Brain *In Vivo* with Two Double-Band Pulses for Enhanced Selectivity

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INTRODUCTION

Reliable detection of *in vivo* GABA signals using ^{1}H NMR spectroscopy faces various technical challenges. Among them, effective suppression of water as well as overlapping signals from Cr, macromolecules (MM) and reduced glutathione (GSH) is very important. When using multiple quantum (MQ) filtering methods, the suppression of signals can be made easier since they cannot form J-coupling based MQ coherence. Unlike Cr or water signals, signals from J-coupled molecules such as MM and GSH can be coedited by conventional spectrally non-selective or semi-selective MQ filtering methods. However, when the MQ filtering techniques are combined with a doubly selective pulse, which selects only GABA-3 and -4 for MQ preparation, the contribution of MM and GSH signals to the GABA signal can be made minimal in each single scan (1). The purpose of this study was to improve the selectivity of the MQ filtering method for *in vivo* GABA measurements in the human brain at 3 Tesla using a single-shot 3D localized sequence with two double-band spectrally selective refocusing pulses.

METHODS

The pulse sequence is composed of MQ coherence preparation, conversion of MQ coherence into observable single quantum (SQ) coherence, DQ gradient filtering. Two double-band spectrally selective 180° pulses set at 3.0 ppm and 1.9 ppm were used (Fig. 1). The first one was located in the MQ preparation period in-between the two slice-selective 90° (five-lobe sinc pulse, 4 ms) pulses. The second one was located in the rephasing period in-between a semi-selective 90° (90° on GABA-3, 0° on GABA-4) and FID acquisition. The semi-selective 90° pulse was spatially selective and spectrally semi-selective. It consists of two 45° slice-selective universal rotator pulses to enable single-shot 3D localization (2). All experiments were performed on a 3 Tesla SMIS system using a helmet coil. A spherical phantom containing 20 mM GABA, 10 mM Cr, 30 mM glutamine (Gln), 40 mM acetate and 10 mM NAA was used. For *in vivo* measurements (n=3), the volume of interest was placed in the fronto-parietal region of the human brain.

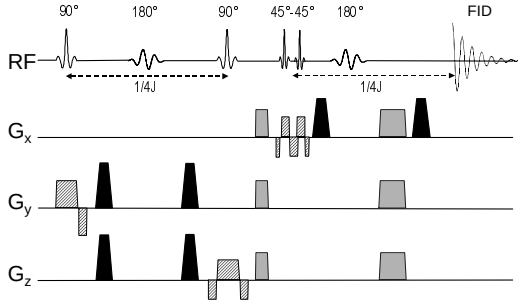

Fig. 1 Single-shot 3D localized MQ filtering sequence.

RESULTS AND DISCUSSION

A phantom PRESS spectrum (TE = 68 ms, Fig. 2A) shows a relatively high water signal after CHESS water suppression and GABA signal was not discernible under the Cr signal at 3.03 ppm. Figure 2B-D show MQ filtered GABA spectra, which were line-broadened to match *in vivo* linewidth. When a non-selective 180° pulse was used during MQ preparation, limited suppression of other signals and reduced intensity of the GABA signal were observed (Fig. 2B) compared to Fig. 2C using the double-band selective pulse during MQ preparation and Fig. 2D using two double-band selective pulses during MQ preparation and refocusing periods, respectively. When the two double-band selective pulses were used (Fig. 2D), all residual unwanted signals were further suppressed by the 2nd double-band pulse and its crusher gradients because only the signals originated from the GABA-3, 4 will pass this step with full yield. Fig. 3 demonstrates *in vivo* detection of GABA in the human brain using the two double-band pulse MQ method. A clear GABA doublet with frequency separation of 13.5 Hz was observed in all subjects indicating minimal contamination from other resonances such as Cr, GSH and MM. A very clean water suppression was also observed as expected. Both the 90° slice-selective universal rotator pulse for converting GABA-3, 4 antiphase SQ into MQ and the spectral-spatial 45°-45° pulse for conversion of GABA-3, 4 MQ into SQ achieve localization using the DQ filtering gradients. With limited strength of the DQ filtering gradients degraded outer volume suppression can be expected. We, therefore, tentatively assign the signals at ~2 ppm to Glx (see Fig. 2D) and possibly DQ filtered lipids from outer volume. The preliminary estimated GABA concentration was ~0.7 mM using the external reference method.

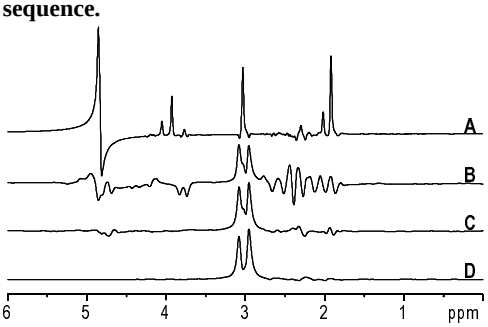

Fig. 2 Comparison of the selectivity of GABA using MQ methods. (A) PRESS (TE=68 ms) spectrum (B) non-selective 180° (C) one double-band selective 180° (D) two double-band selective 180° sequence.

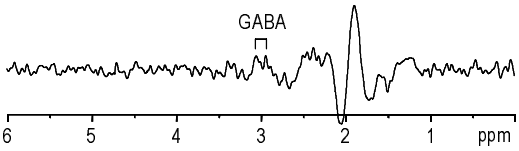

Fig. 3 MQ GABA spectrum of the human brain *in vivo* using two double-band selective MQ method. (TE = 68 ms, tr = 2 s, nt = 640).

In conclusion, we have demonstrated that it is feasible to use a combination of slice-selective 90° pulse, a slice-selective universal rotator 90° pulse and a spectrally semi-selective and slice-selective 90° pulse composed of universal rotator 45° pulses for single-shot spatial localization in MQ filtering. Two double-band spectrally selective refocusing pulses can enhance GABA selectivity with excellent suppression of tissue water. Further optimization of the outer volume suppression and DQ filtering gradients should reduce the signals observed around 2 ppm although they do not interfere with GABA measurements at 3.0 ppm.

REFERENCES:

1. Choi et al, *Proc ISMRM* **11**: 433 (2003); Shen et al. *MRM* **47**: 447 (2002). 2. Shen et al. *JMR* **163**:73 (2003).

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