In Vivo GABA Detection with Improved Selectivity and Sensitivity by Localized Double-Quantum Filter Technique at 4.1T

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Abstract
γ-aminobutyric acid (GABA) is difficult to be detected with conventional single quantum technique. Using a highly selective read pulse, DANTE, and at the facility of increased sensitivity and chemical shift resolution at high field 4.1T, GABA editing by Double Quantum Filter (DQF) with robust suppression of Creatine (Cr) and Glutathione (GSH) was achieved. Furthermore, GABA DQF editing spectra were acquired with echo time (TE=77ms), macromolecular signals that could contaminate to GABA editing were found to be negligible.

Introduction
GABA plays a key role in maintaining the normal function of human brain. It is important to detect GABA in vivo to better understand the regulating mechanism of GABA in brains and improve the management of various neurological diseases. Due to the low concentration of GABA and overlapping with other signals from Cr, GSH and macromolecules, it is difficult to detect GABA signal by conventional MRS methods (1,2). Here, we present our work on the DQF acquisition of GABA signal in human brain with elimination of the contamination of Cr, GSH and macromolecules at high field 4.1 T with a high selective read DANTE pulse.

Methods
All experiments were performed at a 4.1T whole-body imaging/spectroscopy MR system with a transverse electromagnetic head coil operated at 175MHz. The pulse sequence for localized DQF experiments was shown in Fig.1. Briefly, the spatial localization PRESS sequence was modified by adding a rectangular π/2 pulse (230µs), and a read π/2 DANTE pulse train (3) with 8 block pulses separated by 0.6ms to selectively excite the β moiety of GABA. The two delays t1 (1/[4J]=34ms) and tm (3.5ms) were designed for coherence transfer, and multiple quantum coherence (MQC) evolution, respectively. For inversion recovery experiment, a 5ms of hyperbolic secant inversion pulse and following three directions de-phasing gradients were set before PRESS sequence. All vivo spectra were obtained from 18-27ml on the occipital lob of 11 healthy volunteers.

Results
The spectral editing efficiency of DQF and Cr suppression ratio were measured to be 42% and 1250:1 respectively. The contribution of GSH to GABA DQF editing was also absolutely suppressed (spectra of phantom studies were not shown). Spectra acquired with PRESS (TR/TE=3000/30ms, NA=128) and DQF-PRESS (TR/TE =3000 /77ms, NA=256) in a healthy volunteer were shown in Fig. 2(a), and (b) respectively. The spectrum acquired with DQF pulse sequence from another volunteer (Fig. 2c) shows the well-resolved GABA peak with a 13.2 Hz of split, showing excellent of B0 homogeneity. Due to the acquisition of DQF with long TE (requirement of coherence transfer), the signal of macromolecules was substantially reduced because of the T2 effect (4). It was verified by the spectra acquired by normal PRESS with TE=77ms which is the same as that of DQF and inversion recovery. The spectra were shown on Fig3. (b) TIR= 820ms, (c) TIR=912ms and (d) TIR=1112 ms respectively. The normal spectrum acquired by PRESS with TE=77ms was shown in Fig.3 (a). The results clearly show no macromolecule signal at 3.0ppm was detected in Cr nulled spectrum with TE=77ms.

Discussion and Conclusion
This DQF sequence was designed to measure in vivo GABA level with the elimination of Cr and GSH signals by using DANTE, and the elimination of macromolecule signal using long TE (77ms). Due to the high selectivity of DANTE, which excites the β protons of GABA at 1.89ppm but does not excite CH (X) proton of GSH at 4.56ppm, Double quantum coherence of GSH cannot be transferred to single quantum coherence and is de-phased by the coherence selection gradient. The DQF edited spectrum was acquired with long TE (77ms). It means that the signal of macromolecules was reduced by 75% prior to signal acquisition (4). So the signal of macromolecules was not observable in normal PRESS spectra with Cr nulled and TE=77ms. Even if the residual 25% signals could contaminate to GABA editing, it was furthermore reduced and only 10% macromolecules could possibly contribute to GABA editing when taking into account of DQF editing efficiency (42%) in our experiments. Thus the contribution of macromolecules to GABA editing by DQF can be negligible. The mean GABA level was measured to be 1.12±0.15mM in the occipital lobe (in reference to 7.1mM Cr concentration) and is consistent with published data (1,2).

References