High-resolution GABA detection with/without J decoupling using 2D multiple-quantum coherence spectroscopy

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Introduction

Gamma-aminobutyric acid (GABA) is the main inhibitory neurotransmitter in mammalian and human brains. Noninvasive detection of GABA has been of interest in the study of neurological and psychiatric disorders. Proton MR spectroscopy (MRS) offers an useful tool for noninvasively measurement of GABA concentrations in human and animal brains. However, the narrow chemical shift dispersion of metabolites around 3 ppm leads to severe spectral overlap of resonances. Furthermore, inhomogeneous fields due to susceptibility gradients between different structures aggravate the overlapping. Several spectral editing methods including multiple-quantum coherence (MQC)[1] have been proposed to selectively detect GABA from the overlapping with singlets. On the other hand, the zero-quantum coherence (ZQC) was also proposed for high-resolution global detection for *J*-coupled metabolites under magnetic field gradients[2]. In the current work, double/zero quantum coherences are used not only for selective GABA detection, but also for linewidth reduction via fast 2D spectroscopy. *J* decoupling is also achieved for better detection and quantification.

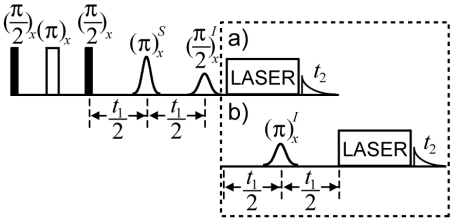

Fig.1 Proposed 2D modified MQC sequence with (a) and without J splitting (b).

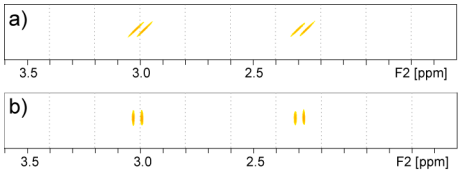

Fig.2 2D GABA MQC spectra before (a) and after (b) shearing.

Methods

The proposed pulse sequence is depicted in Fig. 1, which can be described by the shift operators:

$$I_z + S_z \xrightarrow{\text{DQC prep.}} I_+S_+ \xrightarrow{(\pi)^S} I_-S_+ \xrightarrow{(\pi/2)^I} I_-S_z ,$$

where *I* denotes GABA-H3 (1.89 ppm), and *S* denotes GABA-H2 (2.28 ppm) or GABA-H4 (3.01 ppm).

The intra-molecular multiple-quantum coherence periods not only eliminate overlapping resonances such as creatine (Cr), but also achieve different tilt angles between chemical shift alignment and inhomogeneous broadening. A potential problem of GABA detection using 2D MQC is the coupling to passive spins. It leads to multiplicity patterns, which is undesired particularly under inhomogeneous fields because the broadened peaks may overlap each other. A selective π pulse for the *S* spins sandwiched by split t_1 periods is utilized to refocus the *J* couplings between *I* and *S* spins. It can be seen that the chemical shift evolutions of *I* spins are also refocused. As a result, a coarse sampling rate can be used for the indirect dimension, only a slightly higher than the inhomogeneous broadened frequency, in order to speed up the 2D acquisition.

A typical 2D spectroscopy from the sequence is illustrated in Fig. 2a, which can be sheared along the F2 dimension (Fig. 2b) to obtain a high-resolution projection spectrum. A normal *J* coupling is obtained due to the *J* evolution in the detection period. A decoupled version is also designed for signal intensity enhancement. It is achieved when the tilt angles of inhomogeneous broadening and *J* splitting coincide. A selective refocusing pulse on the S spins and t_1 manipulation is utilized (Fig. 1b). As a result, both inhomogeneous broadening and *J* multiplets align along the F2 axis. Sparse sampling on the indirect dimension can also be used, if followed by the fold-over correction[3].

All experiments were performed on a 9.4 T Bruker scanner, using a volume coil as transmitter and a surface coil as receiver. A modified sinc RF profile (14 ms) was used for the selective π pulse for the *S* spins, while a gauss profile (20 ms) was used for excitation/refocusing of the *I* spin. Spatial localization was achieved by LASER pulses. Repetition time was 3 s and 16 averages were acquired for each increment. A 2D data set with 1200×30 points was acquired with spectral widths of 4000 Hz × 100 Hz in $F_2 \times F_1$ dimensions.

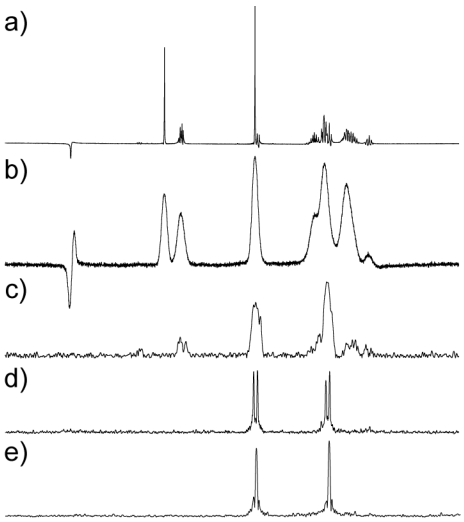

Fig. 3 LASER localized spectra of the Cr, Glx and GABA phantom: (a) under homogeneous fields, (b) under deliberately de-shimmed fields, (c) with DQF editing for GABA and 2D MQC spectra for GABA detection with (d) and without (e) J splittings. 16 averages for (a) ~ (c). 16 averages and 30 increments for (d) and (e).

Results and discussions

A solution phantom containing 10 mM Cr, 5 mM GABA, 15 mM glutamate (Glu) and 10 mM Glutamine (Gln) was used for demonstration. Fig.3a shows a typical 1D spectrum from the phantom under homogeneous fields (linewidth ~1 Hz), and Fig.3b illustrates the broadening of the peaks when the shimming coils were detuned (linewidth ~28 Hz). The single-shot double-quantum filter edited spectrum (Fig.3c) eliminates the singlets but the line broadening and co-edited resonances of Glx remain. Fig. 3d and 3e recover the spectral resolution to 4 and 6 Hz, respectively, using the proposed sequence, demonstrating the effectiveness of the technique to achieve high-resolution even under inhomogeneous fields. In addition, the co-edited resonances are better suppressed in these two spectra.

Quantification of the high-resolution MQC spectrum can be easily achieved by one dimensional analysis approaches such as LCModel[4]. The proposed method can also be potentially used for the detection of other *J*-coupled metabolites such as NAAG, which may result in a shaper linewidth and a better separation with NAA. Optimization of the technique for in vivo studies is under development.

Acknowledgments

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Reference

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