In Vivo Evaluation of the Concentration of Macromolecule Species involved in GABA Editing

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INTRODUCTION

γ-Aminobutyric acid (GABA) can be detected noninvasively in human brain by proton NMR spectroscopy. Spectral editing is commonly used to overcome the spectral overlap of this low-concentration metabolite. The C4 proton resonance at 3.01 ppm has been targeted in majority of editing studies. A primary concern in this editing is the partially-coedited macromolecule (MM) signal. The degree of MM contamination depends on the spectral selectivity of the editing RF pulse and the echo time of the sequence. Precise evaluation of MM contamination is important for correct interpretation of the edited signal. Metabolite-nulling inversion recovery is often used for estimating the MM contribution. However, the resulting signal, typically at the noise level, does not measure the MM contamination accurately because the fully-edited GABA signal itself is not far greater than the noise level. Furthermore, it cannot be entirely rejected that, as the GABA T_1 is unknown, the residual signal, if any, includes or is a GABA signal arising from a recovery delay improperly set for GABA. Such uncertainty can be clarified if the concentration of the MM species involved in the GABA editing is known. Here, we present an evaluation of the MM concentration and its contamination to GABA editing by selective detection of GABA and MM in the human brain *in vivo*. This strategy can be similarly applied to other types of GABA editing.

METHODS

In addition to our previously-reported double-quantum (DQ) filter for GABA measurement [1], we have designed another DQ filter for selective detection of MM, Fig. 1. The MM species may be modeled as a four-spin system, *i.e.*, two spins resonating at 3.01 ppm, the other two at 1.71 ppm, and their coupling strength of 7.8 Hz, [2]. The GABA and MM filters include 28.6-ms and 30.3-ms long dual-band 180° (D180) pulses that excite, respectively, 3.01 and 1.89 ppm, and 3.01 and 1.71 ppm, Fig. 2(a). At TE_1 = 49.4 ms, the 28.6-ms D180 generates maximum GABA target antiphase coherence of 0.93, but little (0.07) MM coherence that will be coedited. The 30.3-ms D180 gives maximum MM target antiphase coherence of 0.99 at TE_1 = 48.4 ms, but much less coherence of GABA (0.15). It is predicted that the GABA and MM signals edited by the two filters are proportional to these calculated coherences. The total echo times of the filters, TE_1+TE_2, were equal (82 ms). The mixing time TM was 9 ms. Experiments were carried out at 3.0 T in an 80-cm bore magnet (Magnex Scientific PLC), interfaced to a SMIS console. A 28-cm diameter quadrature birdcage coil was used for RF transmission and reception. The sequence was tested on a 30×25×30 mm^3 voxel of a 6-cm diameter spherical phantoms (pH = 7.1) with GABA and Cr at 8 and 80 mM, respectively. *In vivo* tests were conducted on two healthy subjects. A 30×25×30 mm^3 voxel was positioned in the prefrontal cortex. The density-matrix simulation was programmed with Matlab.

RESULTS AND DISCUSSION

Fig. 3 presents GABA phantom spectra obtained with the GABA and MM filters. The GABA filter gives a normally-edited GABA peak. A small GABA signal is detected following the MM filter because the GABA 1.89 ppm resonance is partially affected by the 30.3-ms long D180 of the MM filter. The area ratio of the two GABA peaks is 0.16, as predicted from the GABA antiphase coherence calculation in Fig. 2(b), *i.e.*, 0.15/0.93. The good agreement between calculation and experiment for GABA implies that the edited MM signal is determined by the calculated coherences. Fig. 4 shows *in vivo* prefrontal spectra obtained from the GABA and MM filters. The edited peak area ratio between the filters is measured as 1.0±0.2 (mean±SD, n = 2). Incorporating the experimentally-obtained equality with the ratio of the calculated coherences in Fig. 2(b), the MM contribution to the GABA DQ filter output is estimated as 6±1%, irrespective of relaxation times and concentrations of GABA and MM. The filtered signal intensity depends on the concentration and the relaxation times. Assuming that the MM signal has relaxation times 5 times shorter than GABA, the MM to GABA concentration ratio is estimated to be 6±1 (mean±SD). This result agrees well with an MM-to-Cr concentration ratio of ~0.8 which can be derived from the MM-to-Cr 3.0-ppm signal ratio of ~0.25, found in published short-TE spectra with and without metabolite-nulling [2].

REFERENCES

1. C. Choi *et. al.*, Magn Reson Med **54**, 272 (2005).
2. K. Behar *et. al.*, Magn Reson Med **32**, 294 (1994).

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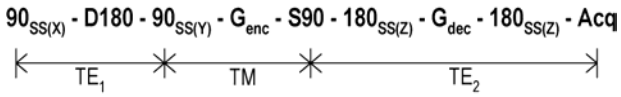

FIG 1. Overview of the DQF sequence. Localization is obtained with the first and second 90° pulses, and a pair of adiabatic 180° pulses during TE_2. The dual-band 180° RF pulse (D180) prepares the target antiphase coherences for GABA or MM filtering. S90 (9ms-long, Gaussian) is a single-band 90° pulse, tuned to 1.89 and 1.71 ppm for GABA and MM measurements, respectively. The decoding gradient G_{dec} is twice the encoding gradient G_{enc}.

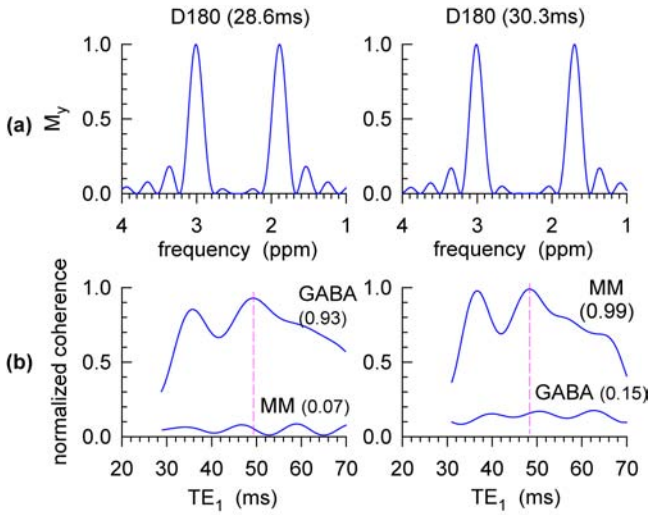

FIG 2. (a) Refocusing profiles of the D180 pulses of DQ filters for detection of GABA and MM. The 28.6-ms long D180 of the GABA filter is tuned to 3.01 and 1.89 ppm, and the 30.3-ms long D180 of the MM filter is tuned to 3.01 and 1.71 ppm. (b) Plot of the antiphase coherences responsible for the DQ filtered signal of GABA and MM versus TE_1. The number in the bracket is the GABA or MM coherence at TE_1 = 49.4 (left) and 48.4 ms (right), indicated by vertical dashed lines.

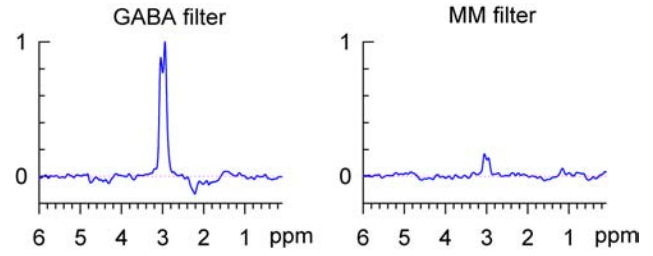

FIG 3. GABA phantom spectra, obtained with the GABA and MM filters. The experimental GABA peak area ratio (0.16) confirms the calculated GABA target coherence ratio, 0.15/0.93, in Fig. 2(b).

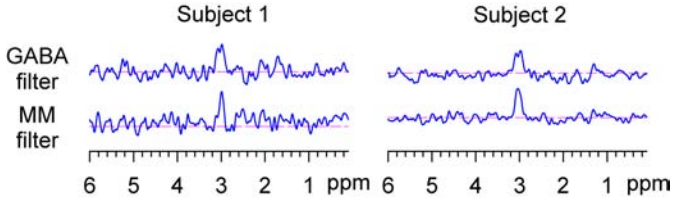

FIG 4. *In vivo* prefrontal DQ filtered spectra from two subjects, obtained with the GABA and MM filters. TR = 2.4 s. NT = 512. The peak area of the edited signal from the two filters is observed to be equal.