New In Vivo Spectral Editing in the Human Brain Based on Doubly Selective Homonuclear Hartmann-Hahn Match

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INTRODUCTION

To detect low concentration metabolites with J-coupled spins such as γ-aminobutyric acid (GABA), a range of spectral editing techniques have been proposed that all are based on pulse-interrupted free-precession of J-coupling interactions to differentiate the signal of interest (e.g., GABA) from overlapping resonances (e.g., macromolecules, creatine, glutathione). When the spectral selectivity is critically dependent on the bandwidth and profile of the selective editing pulse, sizable sensitivity loss during the editing process is inevitable. The purpose of this study was to develop a fundamentally different method, the Hartmann-Hahn transfer, for reliable *in vivo* measurement of GABA in the human brain with superior sensitivity and spectral selectivity. The Hartmann-Hahn method achieves spectral selectivity via the Hartmann-Hahn match, which can be made far more selective than conventional editing pulses.

METHODS

Eleven healthy subjects were studied (32 ± 8 years old, mean ± SD). The pulse sequence consists of the water suppression and the Hartmann-Hahn transfer parts. The water suppression part was specially designed to presaturate both water at 4.65 ppm and signals at ~3 ppm simultaneously using optimized double-band frequency selective pulses. The selective homonuclear Hartmann-Hahn match was created by doubly selective spin-locking of the C4 and C3 methylene protons of GABA at 3.02 ppm and 1.89 ppm, respectively. Localization was achieved using a slice-selective 90^o pulse before spin-lock along the y-axis and two slice-selective 180^o refocusing pulses after the spin-lock along the x- and z-axes (all pulses were optimized five-lobe sinc, 2.4 ms). *In vivo* GABA concentration was estimated by the external reference method. All studies were performed on a 3 T SMIS system using a circularly polarized ^{1}H RF coil. The volume of interest was positioned in the fronto-parietal region of the human brain (27 – 43 ml).

RESULTS AND DISCUSSION

Excellent spectral selectivity by the doubly selective Hartmann-Hahn transfer is demonstrated in Fig. 1. The GABA spectra were first acquired from a GABA only solution phantom (Fig. 1A) and then lysine was added to the GABA solution to mimic the chemical shift and J-coupling properties of macromolecules overlapping with the C3 and C4 methylene protons of GABA (Fig. 1B). The PRESS spectrum from a mixture of GABA and lysine shows overlapping resonances of GABA and lysine at around 3.0 ppm and 1.7 - 1.9 ppm (Fig. 1B left). In contrast, the spectrum acquired using the doubly selective homonuclear Hartmann-Hahn transfer method clearly demonstrated the superior spectral selectivity, showing excellent suppression of lysine at ~3.0 ppm without spectral subtraction (Fig. 1B right). In addition, the selective Hartmann-Hahn transfer process generates a GABA C4 triplet with a large fraction of the central peak retained providing a significant sensitivity gain over the theoretical maximum editing yield of 50% for the C4 methylene protons of GABA by all previously proposed GABA editing methods (e.g., 1, 2).

Figure 2 shows the measurements of GABA in the human brain *in vivo* with the distinctive NAA singlet. An individual trace of the GABA spectrum was acquired with an average of 4 transients for individual frequency drift correction based on the frequencies of the NAA signal. Excellent suppression of water at 4.65 ppm and Cr at 3.03 ppm to the noise level was also achieved. The selective homonuclear Hartmann-Hahn transfer spectrum at the metabolite null was shown in Fig. 2B (TR/TIR = 2000/644 ms, VOI = 27 ml, NT = 1024). No distinctive residual macromolecule signals were found at around 3.0 ppm, consistent with the phantom results shown in Fig. 1. The *in vivo* GABA triplet showed an excellent match with that of *in vitro*, indicating minimal contamination from other sources. The linewidth of the phantom spectrum was line-broadened to match that of the *in vivo* spectrum (TR = 2 s, VOI = 27 ml, NT = 1024). The estimated concentration of GABA was 0.7 ± 0.2 μmol/g (mean ± SD, n = 12).

This method provides a sensitivity enhancement of over the upper limit achievable using conventional GABA editing methods as well as excellent suppression of overlapping macromolecules at ~3.0 ppm in a single shot.

REFERENCES

1. Choi et al, *MRM* **51**: 1115 (2004). 2. Shen et al. *MRM* **47**: 447 (2002).

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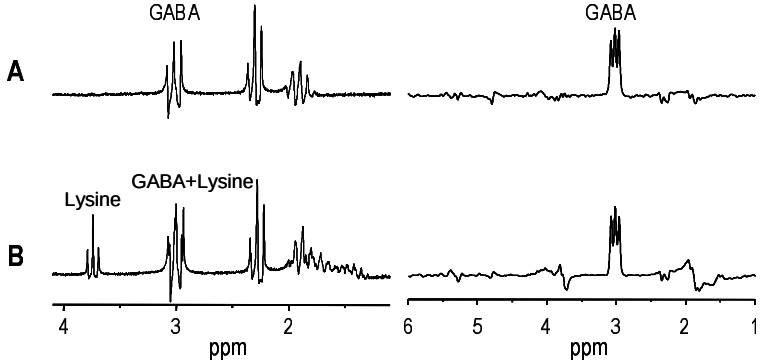

Fig. 1 Excellent spectral selectivity of GABA by the selective Hartmann-Hahn match. PRESS spectra (left, TE = 26 ms, TR = 4 s) and Hartmann-Hahn transfer spectra (right, TE = 14.5 ms, TR = 2 s) from a 10 mM GABA phantom (A) and the GABA phantom after adding 10 mM lysine (B).

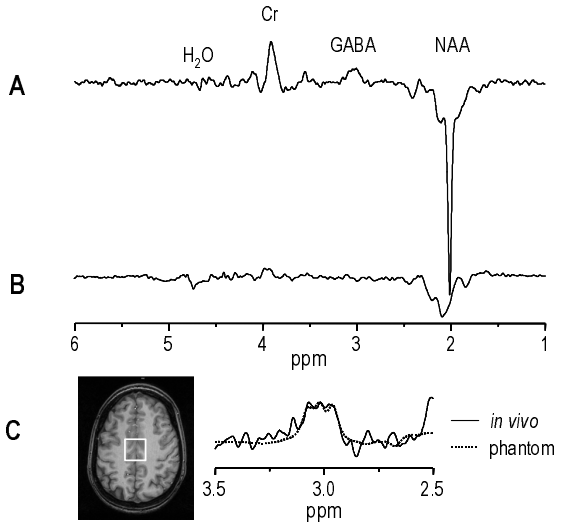

Fig. 2 *In vivo* GABA spectra in the human brain using the doubly selective Hartmann-Hahn transfer method. (A) *In vivo* GABA and (B) the corresponding metabolite-nulled spectra. (C) MRI with VOI (left) and an excellent match between *in vivo* and *in vitro* spectral patterns of GABA (right).