Edited Detection of GABA in the Human Substantia Nigra

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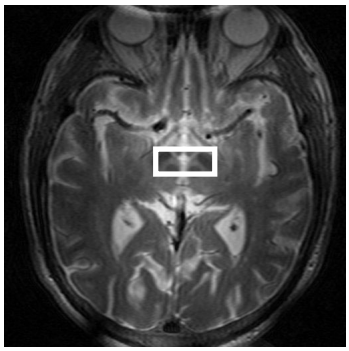
Introduction

The ability to measure the neurochemical profile via ^{1}H NMR spectra in the human substantia nigra (SN) in vivo would be instrumental in elucidating the pathopysiology of Parkinson's disease. GABA is one neurochemical that may be elevated in the SN (1,2). Unresolved GABA resonances in short-echo STEAM spectra from this region make quantitation dependent upon deconvolution software such as LCModel. GABA can be resolved in the presence of broad lines using edited spectroscopy (3, 4). The goal of this study was to compare GABA concentrations quantified using STEAM versus editing in the SN. Because glutamate (Glu) and glutamine (Gln) co edit with GABA (4), their resonances were also utilized to assess accuracy of quantitation.

Methods

Figure 1



Short-echo STEAM spectra and MEGA-PRESS edited spectra (4) were acquired at 4T (TEM volume coil) in vivo from identical volumes of interest (5.3 mL) encompassing the SN (fig. 1). Volunteers were recruited such that age and gender were matched for the two techniques. Shimming (13 Hz ave. line width) was accomplished with FAST(EST)MAP (5). STEAM spectra (TE = 5 ms, TR = 4.5 s, NEX = 400) were acquired and quantified as previously described (2). Subtraction editing (TE = 68 ms, TR = 4.5 s) of the γ-CH_2 resonance (3.0 ppm) of GABA via the coupled β-CH_2 resonance (1.9 ppm) (4) was optimized (fig 2A, 5 mM GABA, 1 mM NAA phantom) with symmetric pulsing for avoidance of macromolecule (MM) contamination (20 ms gaussian editing pulses at 2.0 and 1.4 ppm) and surveillance of B0 drift (< 7 Hz). Under this scheme, Glu, Gln and GSH co edit near 3.76 ppm. A Glx phantom containing 2 mM Gln, 2 mM GSH, 6 mM Glu, and 12 mM NAA was also scanned. A GABA phantom was used to estimate in vivo sensitivity (fig. 2B). The effects of T_2 relaxation on quantitaiton of edited spectra were assumed negligible relative to the measurement error chieved in this study based on prior studies (4).

Results and Discussion

GABA was detected in each volunteer with editing. Figure 2C illustrates the sum of edited spectra (512 scans each, TR = 4.5 sec, TE = 68 ms) acquired from five volunteers. Using the edited NAA and GABA peak heights from the phantom as calibration, the relative signals from the individual edited in vivo spectra indicate an in vivo GABA concentration of 4.0 ± 0.7 mM (mean ± SD, n=5) relative to 11.5 mM NAA, the average NAA concentration measured from the STEAM spectra. Figure 2D illustrates one of the short-echo STEAM spectra measured in this study. The GABA concentration measured with STEAM was 3.6 ± 0.4 mM (mean ± SD, n=4), in good agreement with editing. The edited GABA resonance was distinct from MM contamination up field (2.99 ppm), overruling MM contamination as a major contributor. The sum of the concentrations of Glu, Gln, and GSH in vivo was estimated at 9.1 mM from the edited resonance near 3.76 ppm (Glx, fig. 2C), using the Glx phantom for calibration. This is in good agreement with the 9.7 mM measured with STEAM.

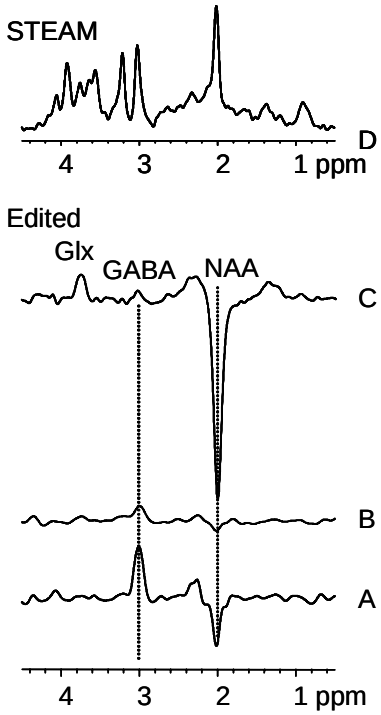


Figure 2. A) Edited phantom spectrum (NEX = 512). B) Subset of A with fewer scans (NEX = 88) to mimic in vivo sensitivity. C) Sum of 5 MEGA-PRESS edited in vivo spectra (NEX = 5 x 512) and D) in vivo STEAM spectrum.

Conclusions

The sensitivity of GABA editing at 4T is sufficient for detection of high GABA (greater than 1.5 mM) levels in this challenging ROI. Edited detection of GABA in a region encompassing the SN affirms the high GABA concentrations measured from STEAM spectra in the same ROI, indicating that LCModel analysis of short echo time STEAM spectra acquired from the SN at 4T provides accurate quantitation of GABA, despite overlapping resonances.

References and Acknowledgments 1) Perry TL, Handbook of Neurochemistry (ed. A. Lajtha), 1, 151, 1982. 2) Oz et al., Proc. Intl. Soc. Magn. Reson. Med., 110, 1, 2004. 3) Hetherington et al, Magn. Reson. Med. 39, 6, 1998. 4) Terpstra et al., Magn. Reson. Med., 47, 1009, 2002. 5) Gruetter et al., Magn. Reson. Med. 43, 31, 2000. NIH P41RR08079, RR008079, MIND inst., KECK fdn.