Separate detection of NAA and NAAG using MEGA-PRESS at 3 Tesla

R. A. Edden[1,2], M. G. Pomper[1], and P. B. Barker[1,2]

[1]Russell H Morgan Department of Radiology, The Johns Hopkins University School of Medicine, Baltimore, Maryland, United States, [2]FM Kirby Research Center for Functional Brain Imaging, Kennedy Krieger Institute, Baltimore, Maryland, United States

Introduction

Hydrolysis of N-acetylaspartyl glutamate (NAAG) to N-acetyl aspartate (NAA) and glutamate, as regulated by glutamate carboxypeptidase II, is a strategically important reaction in the brain, involving two neurotransmitters. However, except at very high fields and/or under conditions of exceptionally good field homogeneity (1, 2), conventional *in vivo* MRS can only readily measure the sum of NAA and NAAG, not the individual components. In this abstract, it is demonstrated that the MEGA-PRESS sequence (3) can be used to selectively edit the 2.6 ppm resonances of either NAA or NAAG with high specificity.

Theory

Because of the structural similarity between NAA and NAAG, the spectra from these 2 compounds are almost identical, particularly at lower field strengths. However, the ^{2}CH resonance of the aspartyl moiety in NAA is approximately 0.23 ppm upfield from the corresponding resonance in NAAG (4). Although these resonances are difficult to observe *in vivo*, their coupling to the aspartyl $^3CH_2$ resonances (at approximately 2.5 to 2.7 ppm) can be used for spectral editing (e.g. using the MEGA-PRESS sequence).

To Select:	NAA	NAAG
Editing Pulse On:	4.38	4.61
Editing Pulse Off:	4.84	4.15

Table 1. Editing pulse frequencies

MEGA-PRESS editing for a target spin system involves recording one experiment with an editing pulse applied to the passive spins of interest and one with the pulse applied elsewhere. The offset of the editing pulse in the second experiment should be chosen so as to subtract co-editing signals. In the case of NAA and NAAG, this may be achieved by using the editing frequencies listed in Table 1 (and graphically indicated in Figure 1)

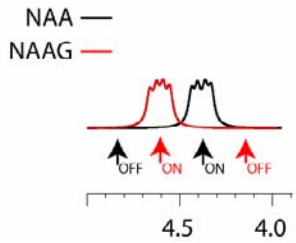


Figure 1. Demonstration of the editing frequencies for exclusive detection of NAA *or* NAAG. Arrows mark editing frequencies (black for NAA; grey for NAAG). The 'OFF' frequency is chosen so the two frequencies are symmetrically placed around the spins to be excluded from editing.

Material and Methods

Two MEGA-PRESS experiments (optimized for NAA *or* NAAG) were performed on two phantoms (30 mM NAAG *or* NAA) and on healthy human volunteers, using a Philips Intera 3T system with a six channel SENSE receive head coil. RF pulses were transmitted on the body coil. Phantom measurements of a 3x3x3 cm^3 voxel in 2 minutes and 3x3x5 cm^3 *in vivo* measurements of centrum semiovale (CSO) white matter were performed in a total scan time of 17 minutes (TR = 2s, TE = 140 ms, TE1 = 26 ms, TE2 = 114 ms). To minimize spatial modulation effects, high-bandwidth (2.2 kHz) frequency-modulated, slice-selective refocusing pulses were used. Gaussian editing pulses (Table 1) of length 40 ms were used (bandwidth 30 Hz).

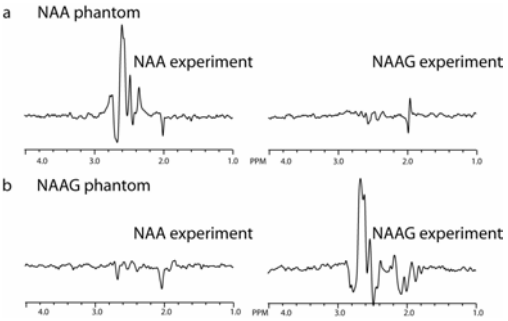
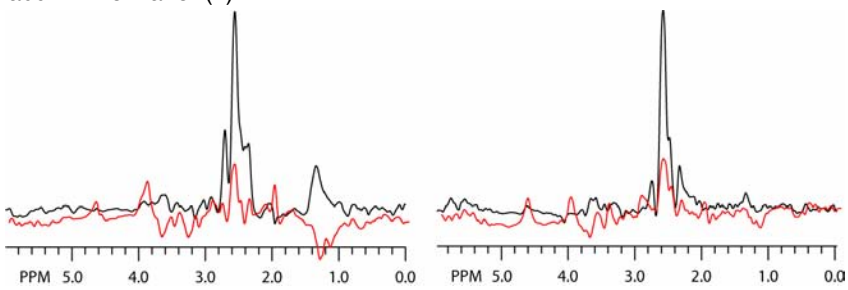


Figure 2. Phantom demonstration of the selectivity of NAA/NAAG detection. a) experiments performed on an NAA phantom optimized for NAA (left) and NAAG (right). b) same experiments performed on NAAG phantom.

Results

Figure 2 shows results of the phantom experiments, and indicate good selectivity of detection for both NAA and NAAG, with "cross-talk" of less than 10%. *In vivo* experiments in two healthy volunteers are shown in Figure 3 (normalized to the NAA signal intensity) demonstrate a very consistent ratio (3.2:1 and 3.0:1) of NAA to NAAG, similar to that reported in the literature for normal adult white matter (1).



Discussion

The experiments performed here demonstrate, for the first time, the possibility of separately determining NAA and NAAG on a clinical MR system (3T) with high selectivity. Previous attempts to measure NAA and NAAG have focused on curve-fitting the overlapping N-acetyl resonances at 2.0 ppm, which are only 0.037 ppm different (1, 4, 5). Although the resonances used for editing in the MEGA-PRESS experiments performed here are only approximately 0.2 ppm different in frequency (i.e. similar to the bandwidth of the MEGA editing pulse), good editing selectivity is achieved by placing the "on" and "off" frequencies of the editing pulse symmetrically around the ^{2}CH resonance of the unwanted compound. A similar approach has been previously used for GABA editing with reduced macromolecule contamination (6). The method shows promise for the quantitative determination of NAA and NAAG in many neurological and psychiatric disorders.

References

(1) Pouwels, PJ and Frahm, J, NMR Biomed 1997; 10(2):73-8, (2) Tkac, I, Andersen, P, *et al.*, Magn Reson Med 2001; 46(3):451-6, (3) Mescher, M, Merkle, H, *et al.*, NMR Biomed 1998; 11(6):266-72, (4) Govindaraju, V, Young, K, *et al.*, NMR Biomed 2000; 13(3):129-53, (5) Tkac, I, Henry, PG, *et al.*, Magn Reson Med 2004; 52(3):478-84, (6) Henry, PG, Dautry, C, *et al.*, Magn Reson Med 2001; 45(3):517-20.

*Supported by NIH P41 RR15241, MGI Pharma and Philips Medical Systems.