Measurement of N-acetylaspartylglutamate in Human Brain by Difference Editing at 7.0 Tesla

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INTRODUCTION

N-acetylaspartylglutamate (NAAG) is structurally similar to N-acetylaspartate (NAA) and glutamate (Glu). Due to its relatively low concentration (0.5 – 2 mM) and the overlap with abundant multiplets of NAA and Glu, NAAG in human brain is difficult to measure. The most prominent peak is a singlet of the acetyl protons at 2.04 ppm [1], but this signal overlaps with the NAA singlet at 2.01 ppm. The estimation of this NAAG singlet is further complicated by the overlap with the C3-proton multiplets of Glu, glutamine, glutathione and the NAAG Glu moiety at ~2 ppm. Excellent shimming enabled measurement of the NAAG singlet at 2T [2]. A difference editing (MEGA) [3] approach to measure NAAG at 3T has been reported recently [4], which utilized the spectral difference between the aspartyl (Asp) groups of NAAG and NAA. Editing approach for NAAG measurement is relatively new. Here, we report measurements of NAAG and NAA in the human frontal brain by the difference editing at 7T.

METHODS

Difference editing (MEGA) was employed for measurement of NAAG and NAA in human brain at 7T (Philips Medical Systems, Cleveland, OH, USA). The C3 proton resonances (~2.5 ppm) of the NAAG and NAA aspartyl groups were edited using a 20-ms Gaussian radio-frequency (RF) pulse (truncated at 10%; bandwidth = 57 Hz) to selectively excite their coupling partners at 4.61 and 4.38 ppm, respectively. Symmetric carriers of the editing 180° pulse were applied in alternate scans to cancel the residual contamination signal completely. Namely, the carrier was set at 4.61 and 4.15 ppm for NAAG editing, and 4.38 and 4.84 ppm for NAA editing. Single-voxel localization was obtained with an 8.8-ms amplitude/frequency-modulated 90° RF pulse (BW = 4.7 kHz) and two 12-ms amplitude-modulated 180° RF pulses (BW = 1.4 kHz) at B_1 = 15 μT. Density matrix simulation was used for echo time optimization, incorporating the shaped RF and gradient pulses. Published chemical shift and coupling constants [1] were used. *In vivo* tests of the editing sequences were conducted on the medial prefrontal and left-frontal cortices of a healthy volunteer (see Fig. 2). The voxel size was 25×30×30 mm^3 for both regions. A quadrature birdcage head RF coil with 16 reception channels was used for RF transmission and reception.

RESULTS AND DISCUSSION

The numerical simulation indicated that the NAAG edited signal amplitude is maximum at TE = 107 ms. Fig. 1 shows calculated spectra of NAAG and NAA at this echo time for a concentration ratio of [NAAG]:[NAA] = 1:4, for 90°-acquisition and difference editing. The peak amplitude of the edited signal at ~2.5 ppm was 57% and 61% with respect to 90°-acquisition for NAAG and NAA, respectively. With the application of the symmetric carriers, the contamination of NAA in NAAG editing was < 4%, while NAAG contamination to NAA editing was negligible (< 1%).

Fig. 2 presents *in vivo* difference edited spectra obtained from the human prefrontal and left-frontal lobes. The *in vivo* spectral patterns of the edited NAAG and NAA signals are in good agreement with the calculation. The peak area of the NAA edited signal was ~10% relative to the PRESS singlet at 2.0 ppm, as predicted by the simulation. The NAAG-to-NAA edited peak area ratio was measured as 0.11 and 0.26 for the prefrontal and the left frontal, respectively. Assuming identical T_1 and T_2 between NAAG and NAA, the NAAG concentration was estimated to be 1 and 2.3 mM for prefrontal and left-frontal, respectively, with reference to NAA at 9 mM. This regional difference in NAAG levels is in agreement with the previously reported difference in NAAG level in gray and white matter [2]. Further *in vivo* studies for measurement of NAAG in human frontal brain are currently underway.

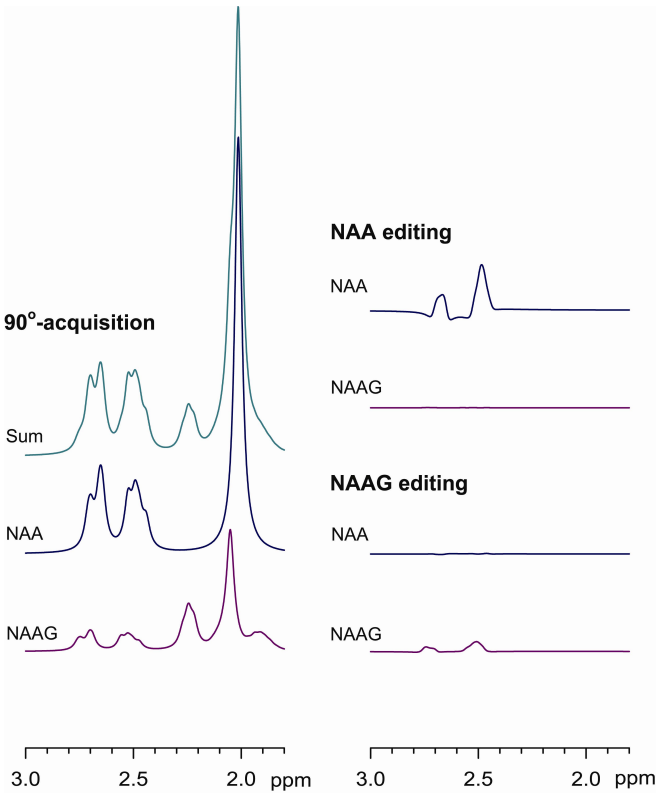

FIG. 1. Calculated spectra of NAAG and NAA, for 90°-acquisition and difference editing at 7T, for an NAAG-to-NAA concentration ratio of 1/4. Spectra are broadened to 0.04 ppm (12 Hz).

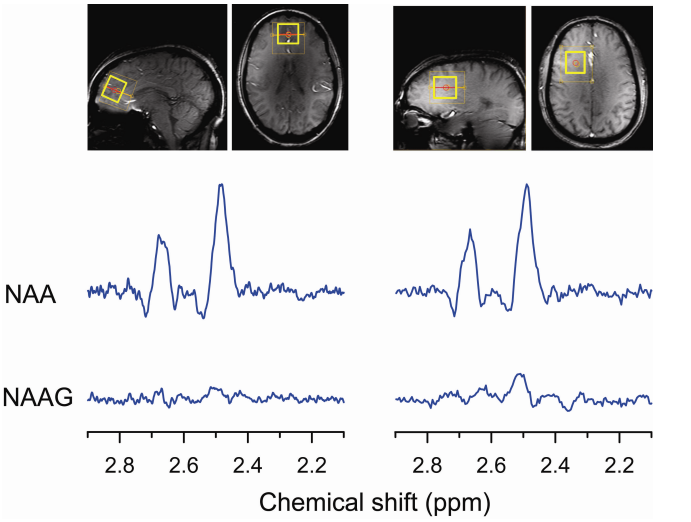

FIG. 2. *In vivo* difference-edited brain spectra of NAA and NAAG, obtained from the medial prefrontal and the left-frontal brain. The spectra were apodized with a 1-Hz exponential function. TR = 2.5 s. TE = 107 ms. NEX = 128 (NAA) and 512 (NAAG). The voxel size was 25×30×30 mm^3.

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