Group-mean template modelling of NAA- and NAAG-edited MR spectra

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Target audience: Scientists with an interest in quantifying neurotransmitters, particularly NAAG, using edited single-voxel MRS.

Purpose: N-acetyl aspartyl glutamate (NAAG) is the most abundant peptide neurotransmitter in the brain and has been implicated in a number of different disorders (see references in 1). It is difficult to separate NAAG from N-acetyl aspartate (NAA) using conventional 1H-MRS at 3T. However, differentiation of N-acetyl aspartate (NAA) and NAAG is possible through J-difference editing using the MEGA-PRESS sequence[1], by applying editing pulses to aspartyl α-protons (NAA: 4.38 ppm; NAAG: 4.61 ppm) and detecting edited signal from aspartyl β-protons at 2.6 ppm.

Quantification of these edited signals is challenging. Neither the approach taken in the original paper, extracting the peak intensity of the edited signal, nor the simple alternative of integrating the signal, is robust enough for typical *in vivo* data, and model-based fitting of spectra is therefore preferred. Simulations of model spectra rely on accurate characterisation of the spin system, which may not always be available, especially in the case of strongly coupled, multi-spin systems such as NAAG. The acquisition of edited phantom spectra that accurately match in vivo data is also problematic, as pH- and temperature-matched phantoms are required so that the relative frequencies of water and alpha protons are preserved. Therefore in this, abstract, we investigate the possibility of using a model derived from the group-mean spectrum as a model for fitting the 148 individual spectra. *Methods: Acquisition* All data were acquired on a Philips Achieva 3T scanner. Experiments were performed on two 4x3x2.5 cm^3 voxels located in the ACC and the basal ganglia for 62 participants (aged 20-67 years; 32 female; 12 scanned twice). NAAG-suppressed NAA-optimised MEGA-PRESS (with editing pulses at 4.38 ppm and 4.84 ppm) and NAA-suppressed NAAG-optimised MEGA-PRESS (with editing pulses at 4.61 ppm and 4.15 ppm) experiments were performed with TE 140 ms, TR 2 s, 256 transients (experiment time 8 min), spectral width 2 kHz, 2048 data points, and CHESS water suppression. Amplitude modulated slice-selective refocusing pulses with 1.3 kHz bandwidth were used. Short-TE (TE 35 ms) data were also acquired from the same regions and analysed using LCModel[2] to derive total N-acetyl concentration.

Analysis Frequency- and phase-correction of spectra was performed on the basis of the creatine peak at 3 ppm using Gannet (gabamrs.blogspot.com) prior to time averaging. This batch analysis is performed in Matlab, and custom scripts were then written to calculate the group-mean of the NAA and NAAG spectra respectively. A noise-free template model without baseline distortions was then calculated by fitting the mean spectrum using a model consisting of five Gaussian peaks (see Figure 1A) with fitting variables including the frequency, width and amplitude of the Gaussians, and baseline slope and offset (using the nlinfit algorithm) and removing the baseline terms post-fitting. The appropriate template model (i.e. NAA or NAAG) was then fitted to each individual spectrum with variable parameters for the amplitude of the model, and baseline offset and slope. The amplitude parameter for each subject's fitted NAA and NAAG spectra was then combined with the integral ratio of fitted mean spectra and total N-acetyl concentration from short-TE data to calculate the NAA and NAAG concentrations in i.u.

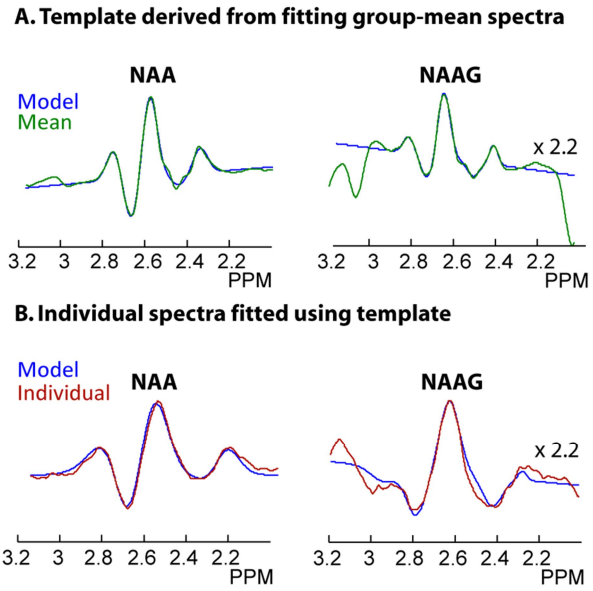

Figure 1: Group-mean spectra are fit to derive the NAA and NAAG model templates (A) that are used to model individual edited spectra (B).

Results: As can be seen in Figure 1A, the group-mean spectra can be modelled to derive a plausible template model. In the case of NAAG, this fitting does not address the non-NAAG signals up- and down-field. Figure 1B shows the fitting of individual spectra. Mean NAAG:NAA ratios were 0.39±0.17 for the ACC region and 0.41±0.19 respectively for the basal ganglia region, which are consistent with prior measures of NAA and NAAG[1]. Mean NAA and NAAG concentrations were 4.57±1.15 i.u. and 1.96±0.92 i.u respectively for the ACC region and 5.24±0.92 i.u. and 2.08±0.78 i.u. respectively for the basal ganglia region. 12 spectra per region were of insufficient quality for good fitting (16%) mainly due either to subject motion or poor SNR and were omitted from the analysis.

Discussion: A data-based modelling procedure was used to quantify NAAG- and NAA-edited spectra, obviating the need for simulating or acquiring basis spectra. This approach is more likely to be effective in large datasets (such as that presented) so that a truly representative template model can be generated.

Conclusion: NAA and NAAG can be distinguished in vivo using MEGA-PRESS editing; however the quantification of these edited spectra remains a relatively undeveloped area. The template-based method of quantifying the in vivo spectra used here improves on previous unsophisticated approaches.

1. RAE Edden et al. MRM 2007; 57(6):977-82. 2. S Provencher et al. NMR Biomed 2001; 14(4):260-4.

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