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Processing of NAA and NAAG edited spectra acquired using the MEGA-PRESS sequence

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In the present work we used a MEGA-PRESS sequence to separately measure the contributions of NAA and NAAG in human brain spectra during a functional experiment using visual stimulation. The paradigm used consisted of one off block of 5min20s followed by an on block and another off block, both with 10min40s, tested on 8 healthy subjects. Visual stimuli consisted of a radial black-white checkerboard flickering at 8 Hz. Because resulting NAA/NAAG peaks at 2.5ppm are small and have undefined shapes, the pre-processing and quantification steps are complex. The phase and frequency corrections seemed to work for some spectra within a scan but not for all, and therefore a possible solution might be to perform case-to-case corrections. Averaging spectra over subjects seemed to give an acceptable SNR for the NAA experiment, but not for the NAAG experiment, for which the 2ppm residue stayed as visible as the peak of interest at 2.5ppm. Specific frequency corrections for this experiment have to be investigated more thoroughly. Quantification with AMARES resulted in large quantification errors, which did not allow assessment of possible stimulus-associated changes. These errors were expected due to the undefined shape problem.

I. INTRODUCTION

The metabolites N-acetyl-aspartate (NAA) and N-acetyl-aspartyl-glutamate (NAAG) are responsible for the most prominent peak of in vivo MR spectra of the human brain located at 2ppm, with contributions to it of around 10:1 (NAA:NAAG). Although the role of these metabolites in the central nervous system is not thoroughly understood, it is well-known that NAA is associated to neuronal integrity [1], and NAAG has been pointed as responsible for the vascular hyperemic response that originates the BOLD signal [2]. Separate measurement of NAA and NAAG using MRS is difficult due to the large superposition of their spectra, but they have been separated at a post-processing stage with LCModel [3]. Using this approach in a functional MRS (fMRS) experiment with visual stimulation our group found interesting changes of these metabolites with stimulus (20% NAA decrease and 200% NAAG increase) [4]. Recently Edden et al. used a MEGA-PRESS sequence to edit NAA and NAAG in MR spectra [5]. We thus designed an fMRS experiment using MEGA-PRESS to further evaluate the separate contributions of these metabolites.

II. OBJECTIVE

To develop processing approaches to quantify NAA and NAAG in MEGA-PRESS fMR spectra.

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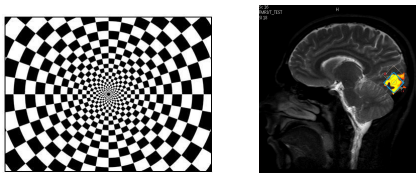
III. MEGA-PRESS SEQUENCE

The MEGA-PRESS experiment used to separate NAA from NAAG [5] consists of applying 2 editing pulses in an interleaved way (i.e., one to odd and the other to even spectra). One pulse targets the resonance of interest and the other can be, in principle, applied anywhere in the spectrum. Thus subtraction of odd from even spectra should yield zero everywhere but on the resonance of interest. In the present case, the resonances of interest were the NAA and NAAG peaks located around 4.5ppm. Although we cannot see the effect of the editing pulses at those resonances due to the water peak, they are coupled to other peaks at around 2.5ppm. Therefore the result of the experiment should yield a peak at around 2.5ppm (which would be a NAA or NAAG peak, depending on the targeted resonance at $\sim$4.5ppm).

IV. METHODS

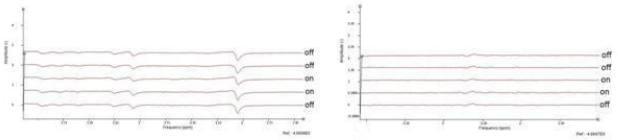
The fMRS protocol was 1 baseline block (5'20", 20 spectra), 1 block on (10'40", 40 spectra) and 1 block off (10'40", 40 spectra), and visual stimuli consisted of radial black-white checkerboard flickering at 8 Hz (Fig. 1-a). Data were acquired at 3.0T with MEGA-PRESS, TR/TE = 2000/140ms, 2048 data points, 2000Hz spectral width, 8 averages and voxel size $3\times3\times2$cm^3. Before the fMRS scan an fMRI protocol was performed and the MRS voxel was positioned on the right occipital lobe over the activated area (Fig. 1-b). The protocol was run twice, to obtain NAA spectra (suppressing NAAG) and vice-versa. Eight healthy subjects (mean age 29 ± 7, range 21-40 years, 63% women) participated on this study. The project was approved by the local Ethics Review Board, and all subjects gave written consent. The last two spectra of the baseline block, and the first and last two spectra of the on and off blocks were eliminated to avoid between-blocks cross-talk.

All spectra were phase and frequency corrected. Odd spectra were then subtracted from corresponding even spectra resulting in spectra with an NAA or NAAG peak at ∼2.5 ppm, with null NAA residue at 2ppm if the editing worked properly. Next spectra were averaged in 4'48"-blocks for every subject. The resulting spectra were then aligned among subjects, based on the peak at ∼2.5ppm, and then averaged over subjects, giving 5 spectra (at 5 time points). These were quantified with AMARES [6].

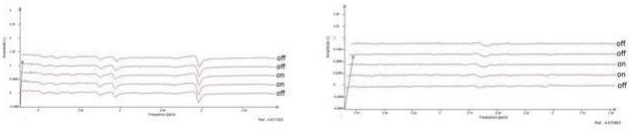


(a) (b)

Figura 1: (a) Visual stimulus used. (b) MRS voxel was positioned over the fMRI activated area.



(a) NAA experiment.

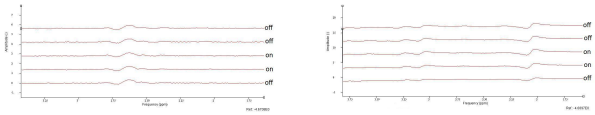


(b) NAAG experiment.

Figura 2: Hard-phase correction of the NAA peak at 2ppm for one subject (left) and spectrum of same subject without phase-correction (right).

V. RESULTS

For the phase correction step we attempted two different approaches: a zero-order phase correction; and a hard-phase correction of the NAA peak at 2ppm. None of these gave good results, since the resulting NAA residue at 2ppm for any of the methods was larger than if no correction was applied, therefore we chose not to apply the initial phase correction (Fig. 2). For the frequency correction we also attempted two approaches: aligning all spectra with respect to the first spectrum of each subject; or aligning odd spectra with respect to the first, and then applying this same correction to the corresponding even spectra (to avoid misaligning spectral pairs). The latter approach gave the best results, but still resulted in non-zero residues at 2ppm for some spectra, more accentuated for the NAAG experiment. As expected, the over-subjects spectral average resulted in an increase of SNR. It also resulted in practically null residue at 2ppm for the NAA experiment (Fig. 3-a); however, for the NAAG experiment the residue at 2ppm also increased, staying with a peak height of about the same size as the NAAG peak at ∼2.5ppm (Fig. 3-b). Finally, quantification with AMARES resulted in large quantification errors, which did not allow assessment of possible stimulus-associated changes.



(a) NAA experiment. (b) NAAG experiment.

Figura 3: Over-subjects averaged spectra for the NAA and NAAG experiment.

VI. CONCLUSIONS

Processing of NAA/NAAG MEGA-PRESS edited spectra is difficult since the resulting NAA/NAAG peaks at ∼2.5ppm are small and have undefined shapes, which makes the processing and quantification steps more complex. Indeed, the phase and frequency corrections seemed to work for some spectra within a scan but not for all, and therefore a possible solution might be to perform case-to-case corrections. Averaging spectra over subjects seemed to give an acceptable SNR for the NAA experiment, but not for the NAAG experiment, for which the 2ppm residue stayed as visible as the peak of interest at ∼2.5ppm. Specific frequency corrections for this experiment have to be investigated more thoroughly. The large quantification errors found with AMARES were expected due to the undefined shape problem, since this method uses either Lorentzian or Gaussian lineshapes. We are next looking into developing a specific quantification methodology for these spectra.

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