

Investigation of NAA dynamics underlying visual stimulation using MEGA-PRESS

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Introduction

The metabolite N-acetyl-aspartate (NAA), together with N-acetyl-aspartyl-glutamate (NAAG), is 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 NAA in the central nervous system is not thoroughly understood, it is well-known that NAA is associated to neuronal integrity [1]. Separate measurement of NAA from 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 [2]. Using this approach in a functional MRS (fMRS) experiment with visual stimulation our group found 20% decrease of NAA with stimulus [3]. However, possible NAA variations with stimulation are a controversial discussion topic in the literature [4]. Recently Edden et al. used a MEGA-PRESS sequence to edit NAA and NAAG in “static” MR spectra [5]. In this work we designed an fMRS experiment using MEGA-PRESS to further evaluate the individual dynamics of NAA underlying brain activation.

Aim: To investigate possible NAA changes during visual stimulation on healthy subjects using MEGA-PRESS.

Materials and Methods

¹H spectra were acquired in a 3T MR system (Achieva, Philips, The Netherlands) with an 8-channels SENSE head coil. The fMRS paradigm was the same as in [3] [1 **baseline** block (5min20s, 20 spectra), 1 block **on** (10min40s, 40 spectra) and 1 block **off** (10min40s, 40 spectra)]. MEGA-PRESS was used with TR/TE = 2000/140ms, 2048 data points, 2000Hz spectral width, 8 averages and voxel size 3×3×2cm³. The visual stimulus was a black-white radial checkerboard pattern flickering at 8Hz. Before the fMRS scan, T2 images were acquired, followed by an fMRI protocol with the same visual stimulus used for the fMRS experiment. The activation map was superposed on the T2 images, and the MRS voxel was positioned on the occipital lobe over the activated area [3]. The editing pulses were set at 4.38 and 4.84 ppm to obtain NAA spectra (suppressing NAAG) [5]. Nineteen healthy subjects (mean age 26±6, range 20-40 years, 42% 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 apodized (3Hz) and frequency and phase corrected. Odd spectra were subtracted from corresponding even spectra resulting in spectra with an NAA peak at ~2.5ppm. Next spectra were averaged in 4min48s-blocks for every subject, giving 5 spectra (at 5 time points). NAA was quantified by integrating the area under the ~2.5ppm peak for every spectrum. Due to poor data quality, one subject was excluded from the analysis.

Results

Fourteen (out of 18) subjects presented a similar pattern of NAA variation along the acquisition (Fig. 1). For these, NAA decreased with the stimulus (between 15% and 100%), and increased after cessation of the stimulus, returning back to (or showing a trend to return back to) baseline levels in most cases (with the exception of subjects 7, 8, 13 and 14, for whom NAA levels stayed low even after stimulus cessation). The remaining four subjects presented seemingly random variation patterns (Fig. 2).

Discussion

The NAA decrease found in 14 out of 18 subjects falls into a current literature discussion and may have either of (or a combination of) two explanations: 1) the shape of the NAA peak changes due to the BOLD effect (linewidth narrows and amplitude increases [6]) causing a variation of the area under the curve, which does not imply a concentration change [6,7]. However, these effects would amount to ~2% variation [7], while the variations found here range from 15 to 100%. 2) NAA actually decreases, synthesizing NAAG that originates the hemodynamic response [8,9]. These explanations will be further investigated in future work, by attempting to correct the BOLD effects in the spectra, and by attempting to measure individual NAAG changes using a similar experiment.

References

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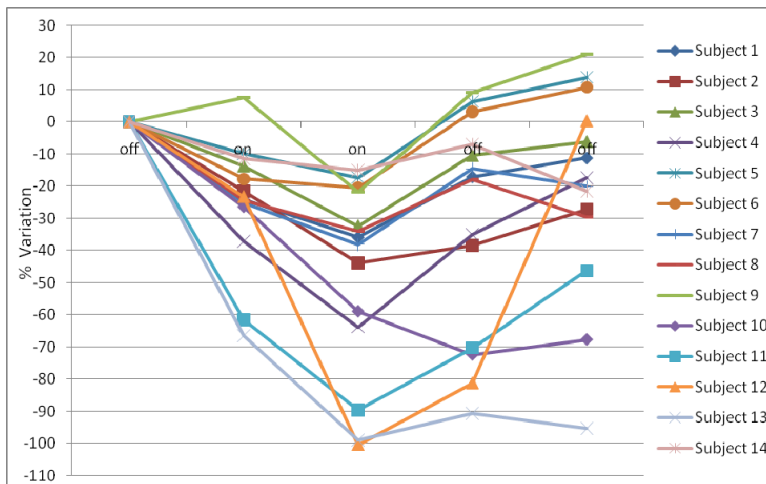


Figure 1. Percentage changes of NAA for 14 subjects.

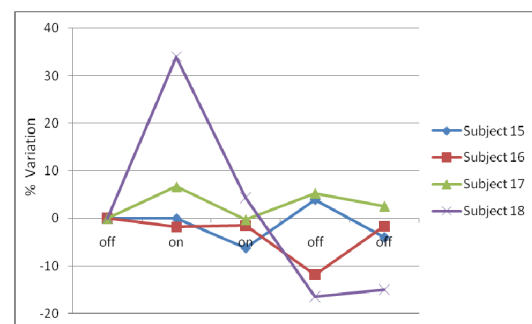


Figure 2. Percentage changes of NAA for the remaining 4 subjects.