Evaluation of Sensitivity and Reliability of Functional MR Spectroscopy Using Virtual Titration

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Introduction

Functional magnetic resonance spectroscopy (fMRS) has been used to investigate the activation-related metabolic changes of neurons following stimulation [1]. One of the most critical challenges in fMRS is the extremely tiny signal change, no matter originating from blood-oxygenation level dependent (BOLD) line narrowing [2] or stimulation-induced alteration in metabolite concentrations [3]. Thus a reliable fMRS quantification method should ideally be sensitive to the tiny signal change, so as to yield accurate results to resolve discrepant conclusions [2,3]. In this study, we used the virtual titration method [4] to investigate the ultimate sensitivity level of ^{1}H spectroscopy at 3.0 Tesla. We further performed fMRS visual stimulation tests to examine the quantitative level of concentration changes in N-acetylaspartate (NAA).

Materials and Methods

A total of 13 spectra, 4 obtained in the frontal lobe and 9 in the occipital lobe, were used in this study for virtual titration. These spectra were acquired from healthy subjects without history of neurological diseases on a 3T Siemens Magnetom Trio system (Erlangen, Germany) using a PRESS sequence with the following parameters: voxel size = 8 cm^3, TE = 30ms, TR = 3000ms, and 128 signal averages. The virtual titration method includes the following steps. First, every in vivo spectrum was analyzed using LCModel [5], with NAA signal extracted and compared with the NAA basis spectrum to obtain the acquisition condition parameters, including frequency drifts, phase alteration, relaxation line broadening, field inhomogeneity, and so forth [5]. The basis NAA spectrum was then modified to mimic the same acquisition conditions in vivo. Afterwards, the modified NAA basis was adjusted to designated levels to simulate concentration changes, and was then added back to the in vivo spectrum. The added NAA concentrations were 0.01%, 0.02%, to 20%, relative to the original NAA concentration. Finally, the modified spectra were re-analyzed using LCModel to examine the resultant concentration changes in NAA. Spectra showing Cramér-Rao Lower Bounds (CR-SD) higher than 10% for NAA, suggesting poor acquisition conditions, were removed due to unreliable detection of NAA. Following virtual titration investigation, five subjects were included in fMRS experiments, which used interleaved visual stimulation of 32 scans of activation and 32 scans of resting state repeating four times. The acquisition parameters were the same as above and these acquired spectra were analyzed by LCModel after 32 scan average (96 sec).

Results

One spectrum in frontal and two in occipital were excluded for their high CR-SD values of NAA. For the remaining 10 cases, estimated NAA concentration changes versus the added NAA concentrations demonstrated strongly linear correlation, all showing Pearson's correlation coefficients $R^2 > 0.99$. One representative case is shown in Fig.1. Note that the slope of the regression line (1.03) was close to the ideal unity. The average regression slope for the 10 cases was 0.993±0.073 (mean ± standard deviation). The estimation errors, derived as the difference between the concentration changes analyzed using LCModel and the added NAA concentrations, were within ±0.2% (Fig.2). The imprecision level, reflected in the error bars of Fig.2, seemed to increase at large values of added NAA concentrations. From our fMRS data, the average concentration difference of NAA between the activation state and the resting state is 2.7% increase (not shown).

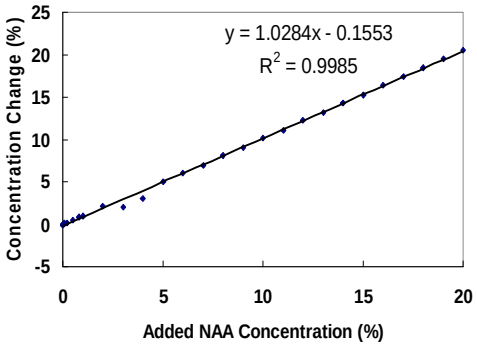

Figure 1. Concentration change versus added concentration for NAA in one representative spectrum. Both of the horizontal and vertical axes are expressed in percentage units of the original NAA concentration.

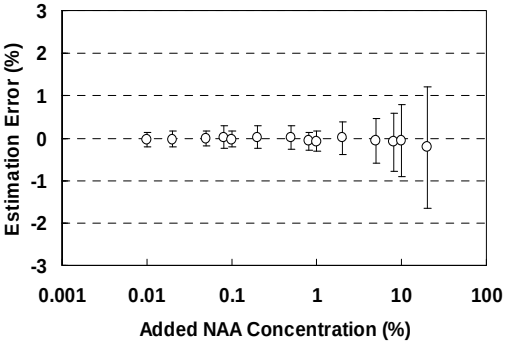

Figure 2. The percentage estimation errors of NAA concentrations analyzed using LCModel for ten spectra plotted as the manually added NAA concentration, showing good accuracy with average errors within ±0.2%.

Discussion and Conclusion

Our results from virtual titration suggest that alterations in NAA concentration can be detected reliably using quantitative analysis tools such as the LCModel. In addition, changes of NAA concentrations by 0.8% or more are expected to be detected and distinguished from fitting uncertainty with a 95% confidence interval. Although the imprecision of estimation error tends to increase at large values (> 1.8%) of added NAA concentrations, this does not cause severe detection problems because of the intrinsically large changes in NAA. Therefore, the 2.7% increase of NAA concentration in our fMRS data could be considered credible, and it might suggest that the concentration of NAA would change during visual stimulation.

We conclude that quantitative analysis of fMRS data seems to allow detection of 0.8% changes ultimately in NAA concentration at 3.0 Tesla, and visual stimulation has the potential to affect the metabolism of NAA.

References

[1] Mangia S et al. *Magnetic Resonance Imaging 24:343-348 (2006)*
[2] Zhu XH and Chen W. *Magnetic Resonance in Medicine 46:841–847 (2001)*
[3] Baslow MH et al. *J Mol Neurosci 32:235–245 (2007)*
[4] Shih YY et al. *Journal of Magnetic Resonance Imaging 28:351–358 (2008)*
[5] Provencher SW. *Magnetic Resonance in Medicine 30:672–679 (1993)*