Investigating the reproducibility on the quantification of £^-aminobutyric acid (GABA) in visual cortex

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Introduction

γ-Aminobutyric acid (GABA) is major inhibitory neurotransmitter in human brain. Recently, GABA has been found to have high relationship with various neuron degenerative disorders. To measure GABA in brain, a spectral editing MRS technique called MEGA-PRESS sequence has been widely used[2]. However, performance on the quantification of GABA, which may be related to spectral editing efficiency and can be sensitive to noise due to its low concentration, needs to be carefully investigated. In this study, the inter-subject and intra-subject reproducibility of GABA quantification were evaluated using three quantification methods including integration, fitting using two Gaussian shape and LCModel.

Methods

In this study, sixteen healthy subjects (10 male, 6 female, age = 21.9±1.4) were included and scanned on 3T MR system (Skyra, Siemens Medical Solutions, Erlangen, Germany). MRS voxels were positioned to cover both left and right visual cortex. Water suppressed spectra were acquired using MEGA-PRESS sequence with editing pulse (20 ms Gaussian) alternated between 1.9 ppm and 7.5 ppm. The scanning parameters are: voxel size = 30x25x25mm³, TR/TE=2000/70ms and measurements = 260. Interleaved editing-on and editing-off spectra were acquired in the scan. A non-water suppressed MRS was acquired using PRESS sequence with the same experiment parameters. For each subject, GABA scans were repeated twice after adjusting shimming and frequency to access reproducibility of this method.

The post-processing of MRS data was done by a self-developed program in MATLAB. Spectra with resonance frequency shifted more than 13 Hz were excluded to ensure the acceptable spectral editing efficiency. Frequency shift information was acquired base on the NAA location in editing-off spectra. Frequency shift correction was carried out by aligning the NAA peak on editing-off spectra and same alignment was applied on editing-on spectra. Editing-on and editing-off spectra were averaged respectively. Spectral-editing spectrum was obtained by the subtraction of editing-on and editing-off spectra. Quantification of GABA signal was done by LCModel, direct integration and fitting using two Gaussian functions after linear baseline correction. Quantified GABA signals were normalized to water signal acquired from NWS scan and creatine (Cr) signal quantified on the editing-off spectra. Inter-subject and intra-subject coefficient of variance (CV) were calculated for these three quantification methods.

Results

Inter-subject and intra-subject CVs of quantified GABA were summarized in Table1. In general, integration and fitting shows similar GABA+/H_2O and GABA+/Cr level. Three quantification methods exhibit similar intra-subject CV ranging from 11.1% to 15.3%. Inter-subject CVs ranges from 19.7% to 26.2%. Among all quantification methods, intra-subject CV of GABA+ quantified by fitting were around 3% higher than those quantified by LCModel and integration. Lowest inter-subject CV were found in the of GABA+ quantified by integration. GABA+ normalized to water gives slightly lower intra-subject CV than those to creatine.

Discussion and Conclusions

In this study, reproducibility accessed by inter-subject CV on the quantification of GABA signal was investigated using three quantification strategies and two normalized referenced. The higher intra-subject CV found in GABA+ quantified by fitting can be attributed to unstable fitting of GABA from baseline and line shape distortion in some subjects. The CVs can be improved when a more complex fitting algorithms is applied as results in LCModel. However, according to the consistency of averaged GABA+ level quantified in fitting and integration, we think the quantification of GABA+ on GABA spectra using simple fitting or integration algorithm can be sufficient compared to LCModel. Improved intra-subject CV in GABA+/H_2O than GABA+/Cr may be attributed to higher signal to noise ratio of water than creatine. However, the difference between normalized references is less than 1%. For the comparison of our results to previous reports in visual cortex[2], the intra-subject CVs are in agreement to previous results but quantified GABA+ level are lower. A possible reasons is that partial volume correction especially correction for cerebral spinal fluid is not performed in this study, which lead to underestimation of quantified GABA+ level. There are other reports showing even lower intra-subject CV[1,3] but in those studies more averages or larger voxel size were adopted. Therefore, same improvement in reproducibility can be expected when we apply larger voxel and more averages. Inter-subject CVs in this study are higher than previous reports in visual cortex[2] and other regions[1,3]. We believed the extra variability comes from the tissue heterogeneity between subjects especially cerebral spinal fluid. Partial volume correction is therefore necessary to be included in the post processing in the future. In conclusion, our results showed that GABA+ quantified by direct integration is relatively stable among three quantification methods, which implies simple quantification strategy is sufficient for GABA spectra. Water and creatine can serve as stable reference standard for signal normalization.

Table 1 Inter- and intra-subjects results of three methods

		Inter-subject		Intra-subject	
Method		Mean ± SD	CV	Mean ± SD	CV
LCModel	GABA/ H_2O	2.04±0.480	23.4%	2.06±0.247	12.0%
	GABA /Cr	0.17±0.044	25.0%	0.18±0.023	12.8%
Integration	GABA/ H_2O	0.12±0.027	21.7%	0.12 ±0.014	11.1%
	GABA /Cr	0.22 ±0.042	19.7%	0.22±0.026	12.0%
Fitting	GABA/ H_2O	0.13±0.034	26.2%	0.13 ±0.019	14.6%

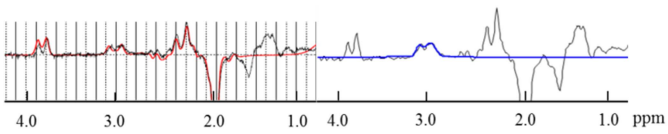

Figure1: GABA spectra from one subject and fitted using (left) LCModel and (right) two Gaussian peaks

Reference

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