Impact of spectra quality on GABA quantitation with $^1$H-MEGA-PRESS sequence

Marianne Cleve¹, Alexander Guess¹, Patrick Hieber¹, Reinhard Rzanny¹, and Jürgen R. Reichenbach¹

¹Medical Physics Group, Institute of Diagnostic and Interventional Radiology I, Jena University Hospital - Friedrich Schiller University Jena, Jena, Germany

Target audience: Researchers and members of the Psychiatric MR Spectroscopy Study Group and of the Magnetic Resonance Spectroscopy Community.

Purpose: Proton magnetic resonance spectroscopy ($^1$H-MRS) offers the opportunity to quantify non-invasively neurotransmitters in the human brain and to obtain information about neurotransmitter turnover in physiological and pathological conditions [1]. However, since the spectroscopic quantitation of GABA is typically complicated by signal overlapping of other brain metabolites and its low concentration ($c_{\text{GABA}} = 1-2$ nM [2]), the exploration of inhibitory neurochemical mechanisms requires sophisticated techniques, such as $^1$H-MEGA-PRESS method. This spectral editing technique acquires a non-edited and an edited spectrum within one examination. The subtraction spectrum provides the elimination of disturbing resonances and thus facilitates the quantitation of GABA. In the present study the accuracy and reproducibility of GABA detection with $^1$H-MEGA-PRESS was evaluated in vitro and in vivo measurements. Simulations were performed with respect to SNR$_{\text{GABA}}$ and linewidth, while taking into account the limited acquisition time (TA) of in vivo studies.

Methods: All $^1$H-MEGA-PRESS measurements were performed using a 3 T whole-body MR scanner (Magnetom Trio TIM, Siemens, Germany) and a twelve channel phased array receive-only head matrix coil. In vitro spectra ($V = 25 \times 25 \times 25$ mm$^3$, TE/TR = 68/10000 ms, NAS = 64, repetition = 29) were acquired using a phantom containing GABA, Glu, Gln, Cr, NAA and ml in aqueous solution ($c_{\text{GABA}} = 10$ nM), mimicking the relative concentration ratios in the brain. The single spectra were adapted to in vivo conditions by successive line broadening (FWHM = 0.02-0.08 ppm) and adding extra noise (SNR$_{\text{GABA}} = 1-17$). The in vivo measurement was performed in the insular cortex of a healthy volunteer ($V = 30 \times 15 \times 15$ mm$^3$, TR = 4000 ms, NAS = 256). The in vivo data were used to generate nine spectra groups (by using a bootstrapping approach with 64 spectra) with varying SNR$_{\text{GABA}}$, which was adjusted by different numbers of averaged single spectra (NAS = 64, 80, 96, 128, 144, 160, 176, 192). The GABA multiplet at 3 ppm was quantified as a linear combination of three constrained singlets by using AMARES (jMRUI package [3]). Absolute GABA concentrations were estimated by normalising the intensity of the GABA multiplet with the internal reference (NAA). The accuracy and reproducibility of GABA quantitation were evaluated with respect to the impact of SNR$_{\text{GABA}}$ and linewidth on the mean concentrations and variation coefficients (CV).

Results: An original in vitro and a simulated line broadened $^1$H-MEGA-PRESS difference spectrum with additional noise are shown in Figure 1, which demonstrates the hampered quantitation of GABA (3 ppm) in vivo. Within the simulation range neither the SNR$_{\text{GABA}}$ nor the linewidth contribute substantially to the accuracy of GABA detection in vitro, since the calculated mean GABA concentrations reproduce very well the nominally adjusted concentration in the phantom ($10 \pm 0.5$ mM). Contrary to the mean values, the CV of the calculated concentrations reveals substantial variations with respect to the SNR$_{\text{GABA}}$ and linewidth (see Fig. 2). However, for a SNR$_{\text{GABA}} > 2$ the FWHM yields only a small impact on CV and for SNR$_{\text{GABA}} > 6$ CV remains nearly unaffected by FWHM. As expected, for high SNR$_{\text{GABA}}$ and narrow linewidths a high precision can be obtained (CV up to 2%). The calculated variations in vivo indicate a similar dependence on SNR$_{\text{GABA}}$ as discussed for the in vitro results, illustrated by the distribution of c$_{\text{GABA}}$ values in the boxplots of Figure 3.

Discussion: In the in vitro study the calculated GABA concentrations correspond very well to the nominally adjusted concentration in the phantom. For sufficiently small CVs (< 7 %) a SNR$_{\text{GABA}}$ of at least 2 is required, whereas for SNR$_{\text{GABA}} > 6$ the calculated CVs remain nearly independent of FWHM. Moreover, the results of the in vitro simulations conform to the in vivo measurements concerning the impact of SNR$_{\text{GABA}}$ on reproducibility. For brain investigations of pathological or physiological changes in GABA concentrations a high precision in metabolite quantitation is required. Thus, for in vivo measurements particularly SNR$_{\text{GABA}}$ has to be improved. While this is feasible by increasing NAS, the extension of TA of the measurement is limited. Another opportunity for SNR$_{\text{GABA}}$ optimization is the investigation of enlarged volumes, lacking in loss of localization, or the usage of apodization functions, accepting a tolerable line broadening.


Fig. 1 Difference spectra of the $^1$H-MEGA-PRESS sequence for a) in vitro conditions b) simulated in vivo conditions (FWHM = 0.03 ppm, SNR$_{\text{GABA}} = 4$).

Fig. 2 Changes in variation coefficient with respect to FWHM and SNR$_{\text{GABA}}$ in vitro.

Fig. 3 Distributions of in vivo c$_{\text{GABA}}$ values determined with varying SNR$_{\text{GABA}}$ in the insular cortex.