Comparison of the Repeatability of GABA-Edited Magnetic Resonance Spectroscopy with and without Macromolecule Suppression

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TARGET AUDIENCE: Imaging scientists interested in GABA-edited MRS acquisition and correcting for macromolecular contamination.

PURPOSE: The quantification of the inhibitory neurotransmitter γ-aminobutyric acid (GABA) in vivo using ^{1}H magnetic resonance spectroscopy (MRS) has provided insights into pathology and healthy behaviour. Nonetheless, a problem with the quantification of GABA using J-difference edited MRS is that co-edited macromolecules (MM) contaminate the GABA signal. The GABA resonance at 3.0 ppm is detected by applying frequency-selective editing pulses to the coupled GABA resonance at 1.9 ppm. However, these editing pulses partially affect an MM resonance at 1.7 ppm, which is coupled to an MM resonance also at 3.0 ppm. Thus, when GABA is quantified from the 3.0 ppm peak, it contains an MM contribution[1]. Using a symmetric editing-based suppression technique, it is possible to suppress the MM signal[2]. The aim of this study was to evaluate and compare the repeatability of GABA-edited MRS with and without macromolecule suppression.

Fig. 1. Representative placement of MRS voxels in the (a) occipital lobe and (b) anterior cingulate of one participant.

METHODS: GABA concentration was measured in 15 healthy participants (8 females; mean age = 26.1 ± 5.1 years) using a 3T GE Signa HDx MRI scanner with an eight-channel receive-only head coil. In two separate sessions, spectra were acquired in a 30 x 30 x 30 mm^3 voxel in the occipital lobe (OCC; Fig. 1a) and in a 20 x 30 x 40 mm^3 voxel in the anterior cingulate (AC; Fig. 1b). Four 10-min MEGA-PRESS[3] acquisitions were taken in each brain region. Two of the four scans used a standard MEGA-PRESS sequence (TE = 68 ms; TR = 1800 ms; 332 averages; 4096 data points; 5 kHz spectral width) with 16-ms editing pulses placed at 1.9 ppm (ON scan) and 7.5 ppm (OFF scan), which includes MM contamination. The remaining two scans (TE = 80 ms; TR = 1800 ms; 332 averages; 4096 data points; 5 kHz spectral width) used symmetric MM suppression[2] where editing pulses (20-ms duration) were placed symmetrically about the MM resonance at 1.7 ppm (at 1.9 ppm [ON] and 1.5 ppm [OFF]). The MM resonance peak was thus excited equally, suppressing the signal in the difference spectrum (ON – OFF). MM-unsuppressed and MM-suppressed scans were interleaved and counterbalanced across participants. Raw spectra were processed and analysed in the GABA Analysis Toolkit (Gannet). Concentrations were referenced to internal tissue water, with corrections applied for relaxation times of water and GABA, editing efficiency and MR-visible water concentration. The quantified GABA measure that included an MM contribution is denoted as GABA+, whilst the GABA concentration corrected for MM contamination is labelled GABA$_{corr}$.

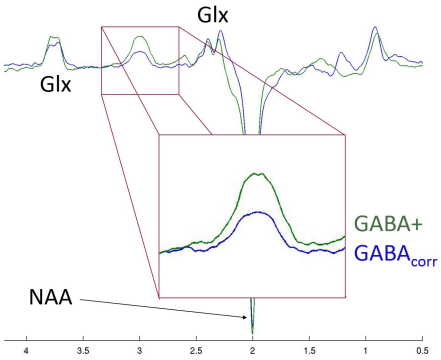

Fig. 2. Representative difference spectra acquired using standard editing (green) and symmetric MM suppression (blue), with respective GABA+ and GABA$_{corr}$ peaks indicated (inset).

RESULTS: Fig. 2 shows a clear difference in the GABA peak at 3.0 ppm in spectra acquired using the two methods. In the OCC, mean (± SD) GABA+ was 1.13 ± 0.07 institutional units (i.u.) and mean GABA$_{corr}$ was 0.54 ± 0.08 i.u. In the AC, mean GABA+ was 0.99 ± 0.15 i.u. and mean GABA$_{corr}$ was 0.43 ± 0.06 i.u. Thus, the fraction of the total signal "retained" following MM suppression (GABA$_{corr}$ / GABA+) was 0.48 in the OCC voxel and 0.43 in the AC voxel. Within-subjects coefficients of variation (CV$_{ws}$; CV = SD / mean * 100) and between-subjects coefficients of variation (CV$_{bs}$) are shown in Table 1. There was no statistical difference between CV$_{ws}$ for the two methods in either brain region (OCC: p = .07; AC: p = .57). Intraclass correlation coefficients (ICCs) were also calculated using a two-way mixed model with measures of absolute agreement.

DISCUSSION: The ratios between MM-suppressed and MM-unsuppressed GABA concentration fit well with previous findings that show an approximately 50% signal contribution from the MM resonance[4,5]. Based on the CV$_{ws}$ values for both regions, the MM-suppression technique is shown to be comparable in repeatability to standard GABA-editing. The suppression method produced higher ICC values than the standard method in both regions, suggesting that it is perhaps more sensitive to individual variability of MRS-measured GABA. This is in spite of a higher CV$_{ws}$ in the AC. ICC values were poorer for AC acquisitions than OCC ones, but this is likely due to inherently noisier spectra acquired in more frontal regions.

Table 1. Measures of repeatability and reliability for each acquisition method

	OCC		AC	
	GABA+	GABA$_{corr}$	GABA+	GABA$_{corr}$
CV$_{ws}$ [IQR]	4.0% [3.4–4.6%]	8.6% [6.9–9.6%]	14.8% [12.6–17.0%]	12.6% [11.4–14.6%]
CV$_{bs}$	6.1%	15.0%	14.7%	13.6%
ICC	0.64	0.73	0.17	0.40

CONCLUSION: The investigation of (potentially weak) correlational links between GABA concentration and healthy behaviour requires accurate and reliable quantification of GABA. MM-suppressed GABA measurement offers increased measurement specificity and potentially an increased ability to discriminate between participants.

REFERENCES: [1]Rothman et al., Proc Natl Acad Sci USA 1993;90:5662-5666. [2]Henry et al., Magn Reson Med 2001;45:517-520. [3]Mescher et al., NMR Biomed 1998;11:266-272. [4]Kegeles et al., Proc Intl Soc Magn Reson Med 2007;1391. [5]Aufhaus et al., Magn Reson Med 2013;69:317-320.