Multi-vendor GABA-edited MRS

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Target audience: Researchers interested in MRS of GABA, and those applying MRS in multi-site studies.

Purpose: GABA-edited MRS shows great promise for studying the role of inhibitory neurotransmission in normal brain function and disease. Although MRS is a quantitative technique, GABA measurements are currently presented as integral ratios to Creatine (Cr), or in institutional units, making comparing data between studies difficult-to-impossible. The purpose of this study is to characterize GABA-edited MRS acquisitions on GE, Philips and Siemens systems through phantom measurements and to normalize in vivo measurements across vendors.

Background: Several experimental factors differ between different implementations of the MEGA-PRESS[1] sequence for the measurement of GABA, including the shape and timing of slice-selective and editing pulses. These can have a complex impact on the shape of the edited GABA signal[2], but their impact on quantification can be summarized by two numbers – the editing efficiency κ of the sequence for GABA and the relative co-editing efficiency ratio μ of macromolecular (MM) signals. We define editing efficiency as the ratio of the edited signal in the difference spectrum to the perfectly refocused ON signal acquired at the same echo time (with κ=1 indicating perfect editing). This definition highlights the fact that editing efficiency losses can occur both from imperfect refocusing of coupling in ON spectra and from imperfect coupling evolution in OFF spectra. Co-editing of MM signal occurs because editing pulses placed at 1.9 ppm partially invert the MM signal at 1.7 ppm (0.2 ppm off-resonance); μ=1 indicates equal editing efficiency of MM and GABA.

Methods *Phantom (20 mM GABA and 20 mM glycine (Gly)):* A saturation-recovery series (0.5<TR<20 s) was acquired to determine T_1 of the 3 ppm GABA and the 3.55 ppm Gly signals. An editing-on echo-time (TE) series (68<TE<350 ms) was also acquired to determine their T_2s. On 3T GE HDx, Philips Achieva and Siemens Tim Trio scanners, edited spectra were acquired with: TE 68 ms; 14 ms editing pulses applied at 1.9 ppm (ON) and 7.5 ppm (OFF) interleaved; TR 2s; voxel size (3 cm)^3. κ for GABA was calculated as the ratio of the integral of the 3 ppm GABA signal in the difference spectrum to the relaxation-adjusted (using measured T_1 and T_2 of Gly and GABA) integral of the Gly signal in the OFF spectrum (assumed equal to the perfectly refocused GABA signal). The relative co-editing efficiency ratio μ of MM is assumed to be equal to the ratio of GABA editing efficiency with pulses at 1.9 ppm to that with editing pulses offset by 0.2 ppm, determined from a further series with offsets of 0-0.6 ppm.

In vivo: Informed consent was obtained under local IRB approval. GABA-edited MR spectra were acquired from a (3cm)^3 sensorimotor voxel in 5 healthy volunteers on all three MR scanners. Additional parameters included: TE/TR 68/2000 ms; 14 ms editing pulses applied at 1.9 ppm (ON) and 7.5 ppm (OFF) interleaved. GABA concentration was initially calculated as a integral ratio to GABA in the Gannet analysis program[3], then corrected according to:

$$c_{\mathrm{GABA/Cr,\,corr}} = \frac{I_{\mathrm{GABA}}\mu_{\mathrm{Philips}}}{I_{\mathrm{Cr}}(\mu_{\mathrm{Philips}}+\mu_{\mathrm{Vendor}})\kappa_{\mathrm{Vendor}}}$$

with the additional assumption that the MM signal fraction acquired with the Philips acquisition is 50% (based on prior data not presented here).

Results: [T_1, T_2] of GABA and Gly in phantom were measured as [1840, 248] ms and [2640, 446] ms, respectively (Figure 1a and b). $\kappa_{\mathrm{Philips}}$, κ_{GE} and $\kappa_{\mathrm{Siemens}}$ were measured as 0.39, 0.44 and 0.37, and μ_{Philips}, μ_{GE} and μ_{Siemens} were measured as 0.75, 0.83 and 0.575, respectively (Figure 1c). Mean uncorrected *in vivo* GABA+/Cr integral ratios were 0.139±0.017, 0.156±0.020 and 0.115±0.006 for Philips, GE and Siemens. Corrected ratios were 0.176 ±0.022, 0.169±0.022 and 0.172±0.009, respectively, as shown in Figure 2. A multifactorial ANOVA shows that there is a significant interaction between vendor and the correction ($p<0.01$), with post-hoc univariate tests showing a significant difference between vendors for uncorrected ($p<0.006$) but not for corrected measurements ($p=0.73$).

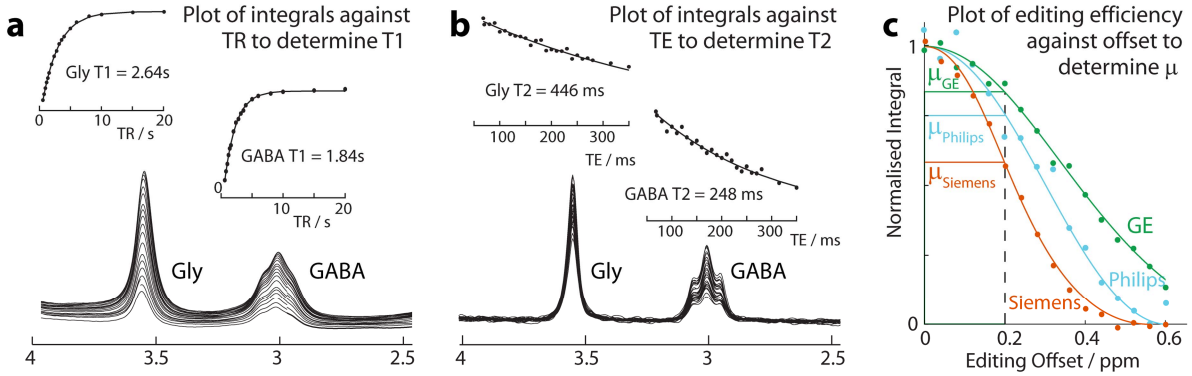

Figure 1: Phantom measurements to calculate a) T1, and b) T2, of GABA and Gly, and c) μ for each sequence.

Discussion: GABA-edited acquisitions are generally implemented by adding additional editing pulses to the vendor-supplied PRESS sequence; differences between vendors are found in the timing and amplitudes of RF pulses, which are known to impact editing efficiency and MM contamination. This abstract shows that correcting for these sequence-specific differences in GABA editing efficiency and MM co-editing ratio significantly improves the quantitative agreement between GABA/Cr ratios from different scanners. These κ and μ parameters can be determined for any implementation of the GABA-edited MRS to enable universal comparisons between sequences.

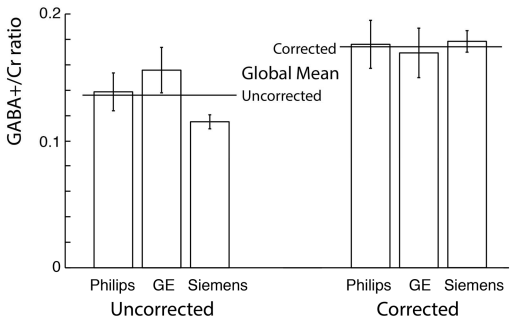

Figure 2: Uncorrected *in vivo* GABA+/Cr ratios (left) are significantly different between vendors. κ– and μ–correction removes this difference (right).

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References: 1. Mescher et al. NMR BioMed 1998. 2. Near et al. MRM 2013. 3. Edden et al. JMRI *in press*.