Correction for tissue fractions in GABA-edited MRS

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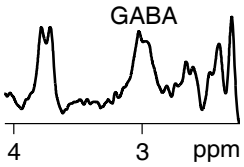
Purpose: To examine how GABA-edited MRS measures should be corrected for voxel gray/white matter composition.

Background: It is generally agreed that MRS measures of concentration should be corrected for voxel content (proportions of gray matter, GM, white matter, WM, and CSF within the voxel). However, there is little agreement of how this correction should be performed, particularly for metabolites like GABA that has different concentration in GM and WM.

Theory and Methods: Measured GABA can be correct according to $c_{\text{corr}} = \frac{c_{\text{voxel}}}{f_{GM}+\alpha f_{WM}}$, where c_{voxel} is the water referenced GABA measurement, f_{GM} and f_{WM} are the voxel fractions of GM and WM, respectively, and α is the ratio of WM to GM GABA concentration. Setting α=1 corrects for total tissue (CSF-correction), where as setting α=0 corrects based on the GM fraction. The impact of α (Fig 1) was examined by simulating uncorrected GABA measurements for a voxel of 8% CSF, varying WM and GM fraction and assuming c_{GM}=1, c_{WM}=0.5, and c_{CSF}=0. Corrected concentrations were calculated using α values of 1 (CSF correction), 0 (GM correction), 0.5 (the simulated correct value), 0.7 and 0.3 (incorrect estimates of α). The above correction normalizes c_{corr} to represent the measured concentration if the voxel was only GM. This is undesirable as no voxel will be purely GM. Therefore, we suggest: $c_{GMWM} = c_{\text{voxel}} \frac{\mu_{GM}+\alpha\mu_{WM}}{(f_{GM}+\alpha f_{WM})(\mu_{GM}+\mu_{WM})}$, where μ_{GM} and μ_{WM} are group-average GM and WM fractions of the voxel.



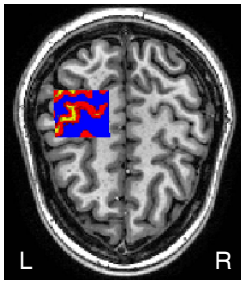


Fig 1. Example GABA spectra and segmented voxel, blue = WM, red = GM and yellow = CSF.

These corrections were compared using an *in vivo* dataset that included 5 regional GABA measurements in 16 healthy volunteers. Scanning was performed at 3T ('Achieva', Philips). T1-weighted whole brain images (MPRage, TR/TE = 8 ms/3.7 ms, 1 mm^3 isotropic voxels) were acquired and segmented with SPM8. GABA-edited spectra were acquired using editing pulses applied at 1.9 ppm and 7.46 ppm, interleaving every two transients across a 16-step phase cycle, TR/TE = 2s/68 ms; 320 transients, 2048 data points at a spectra width of 2 kHz and VAPOR water suppression. The 5 voxel locations were: visual cortex (OCC), auditory cortex (AUD), sensorimotor cortex (SM), frontal eye fields (FEF) and dorsolateral prefrontal cortex (DLPFC). All voxels were $(3cm)^3$, except for the AUD which was 4×3×2 cm^3.

Results: Example spectra and voxel segmentation are shown in Fig 1. The impact of α across a range of tissue fractions is shown in Fig 2. This correction normalizes towards an all GM voxel. Using the correct value of α, here simulated as 0.5 (cWM/cGM = 0.5, see methods) results in a corrected GABA measurement that is not affected by tissue fraction, as desire. For *in vivo* data, the CSF correction and the proposed GMWM correction increase the estimated GABA concentration (Fig 3) but to differing degrees, depending on the voxel. Variance is not significantly changed by the corrections (F test; p>0.3).

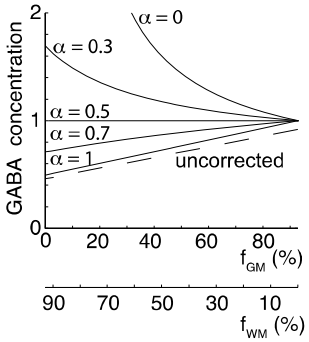


Fig 2. Impact of α simulations. Uncorrected GABA can be corrected for tissue content assuming different values for α. When the correct value of α is used (here, 0.5), the GABA concentration is unaffected by voxel tissue fraction. When α is increased, GABA is underestimated however, when α is too small, GABA is overestimated.

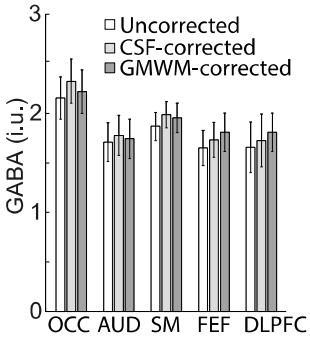


Fig 3. Comparison of GABA estimates with no correction, CSF-correction and the proposed GMWM-correction. Correcting for voxel composition does not significantly reduce variance.

Discussion: GABA quantification is impacted by voxel composition and tissue characteristics. Correcting for differences in tissue fraction attempts to remove inter-subject differences in voxel GM, WM and CSF fractions from the GABA measurement. For metabolites like GABA, that have different concentrations in GM and WM, a key factor is the relative GABA signal from WM and GM, here defined by α. CSF correction (α = 1) makes no attempt to address concentration differences driven by GM/WM make-up. Correcting by the GM fraction only (α = 0) overcorrects (and blows up for f_{GM} below 40%); thus is unstable and not recommended (Fig 2). Literature values for α are diverse but average to 0.41±0.23 [1-5]. As shown in Fig 1, it is better to overestimate than underestimate α - a value of 0.5 is used here. The aim for voxel tissue correction is to remove variance that is purely associated with tissue fractions from concentration measurements. We propose a correction that does this, while accommodating different concentrations for GM and WM. For homogeneous young cohorts, correcting for voxel composition does not substantially impact the variance of results.

References: [1] Zhu et al. Magn Reson Med 2011; 65(3): 603
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