Accuracy and reproducibility of short-TE MRS measurements of GABA at 3T as a function of linewidth and SNR

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Introduction. In-vivo magnetic resonance spectroscopy (MRS) detection of GABA is commonly performed using spectral editing techniques such as MEGA [1], or multiple quantum filtering [2]. Such editing techniques enable selective observation of GABA by removal of overlapping resonances, however, they are limited by low efficiency, macromolecule contamination, and low metabolite yield. It has been shown that unedited in-vivo detection of GABA (along with 17 other metabolites) is possible at 3 Tesla by combining a very short echo-time (TE) MRS acquisition [3] with an LCModel analysis approach [4]. While this technique may enable quantification of GABA under some circumstances, the efficacy of the technique is expected to depend strongly upon experimental conditions such as spectral linewidth (LW) and signal-to-noise ratio (SNR), which may vary across centres, scanners and even brain regions. Therefore, the purpose of this study is to investigate the accuracy and reproducibility of short-TE MRS measurements of GABA as a function of the LW and SNR of the acquisition.

Methods. This study was performed using a similar methodology to the one described recently by Hancu [5]. First, a complete metabolite basis set consisting of 20 individual metabolites was simulated using an in-house implementation of the density matrix formalism. A spin-echo sequence was simulated to approximate the SPECIAL technique [3] at 3 Tesla with TE = 8.5 ms, and metabolite chemical shifts and coupling constants were taken from [6]. Following the simulation of the individual metabolites, a simulated spectrum with a specific SNR and LW was generated by combining the metabolite basis spectra in approximate in-vivo concentrations. Lipid, macromolecule, and residual water signals were added to the spectrum, and noise was added such that the desired SNR (defined as the maximum metabolite peak height divided by the standard deviation of the added noise) was achieved. For a given SNR and LW, the above procedure was repeated 500 times with different noise seeds, and in each of the 500 repetitions, the concentration of each metabolite was allowed to vary slightly about its mean value to approximate normal subject-to-subject variation. Having now generated 500 simulated spectra with the same experimental conditions (LW and SNR), this entire procedure was repeated for different sets of experimental conditions. In total, every combination of eleven different LW values (ranging from 2-12 Hz) and ten different SNR values (ranging from 50 to 500) was tested, for a total of 110 experimental conditions, and 55,000 simulated spectra. All of the spectra were then processed using LCModel with the same basis set used to generate the simulated datasets. Finally, the LCModel estimates of GABA concentration were recorded for each run, and stored alongside the corresponding actual concentrations that were recorded previously. For each set of experimental conditions, reproducibility was assessed by computing the reproducibility error (%E_R): first, the estimated GABA concentrations were plotted versus the actual values, and a linear least squares fit was performed. The %E_R was then calculated as the average of the absolute values of the fit residuals, divided by the average of the fitted values. Accuracy, on the other hand, was assessed by computing the mean percent error (%E_E): the average of the percent difference between estimated and actual values.

Results and Discussion. Results. Figure 1 shows scatter plots of estimated versus actual GABA concentration values for two sets of experimental conditions. The first set has a LW of 9 Hz and an SNR of 150, which corresponds approximately to the average experimental conditions observed in SPECIAL MRS of the anterior cingulate cortex (ACC) (voxel = 2 x 2 x 2.5 cm, t_{acq} ~10 min). Under these conditions, the %E_R and %E_E were found to be 17% and 16% respectively. The second set has a LW of 6 Hz and an SNR of 200, which corresponds approximately to the average experimental conditions observed in SPECIAL MRS of the posterior cingulate cortex (PCC) (voxel = 2 x 2 x 2.5 cm, t_{acq} ~ 10 min). Under these conditions, the %E_R and %E_E were found to be 10% and 3% respectively. Figure 2 shows contour plots for %E_R (a) and %E_E (b) of GABA concentration estimates as a function of LW and SNR. The two experimental conditions corresponding to the ACC (red) and PCC (blue) are marked on these 2-D plots for reference. Discussion. These data clearly demonstrate that the accuracy and reproducibility of short-TE GABA measurements are strongly dependent on the experimental conditions (LW and SNR). As expected, the maximum accuracy and reproducibility are observed at high SNR and low LW. However, large %E_R and %E_E are observed as LW increases, even if SNR is high. Under experimental conditions corresponding to both ACC and PCC regions, a %E_R of less than 20% is observed, indicating that the short-TE approach is reproducible and able to detect changes in GABA concentration in the human brain. The contour plot of %E_E in Figure 2b demonstrates systematic errors in GABA concentration estimates under certain experimental conditions. It may be possible to use this information to retrospectively correct data that was acquired under experimental conditions where a known systematic error exists, as suggested by [5]. In conclusion, the accuracy and reproducibility of short-TE GABA measurements have been assessed as a function of LW and SNR, and it was found that short-TE MRS of GABA does produce accurate and reproducible estimates of GABA concentration under experimental conditions achievable in the human brain.

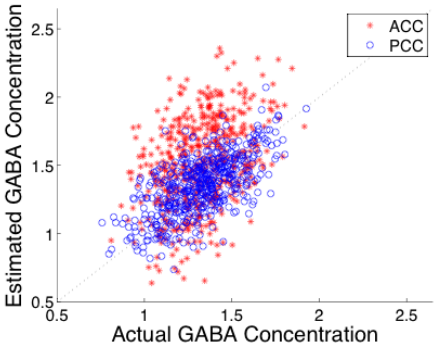

Figure 1. Scatter plots of estimated vs actual GABA concentrations in experimental conditions corresponding to ACC (LW=9, SNR=150, red), and PCC (LW=6, SNR=200, blue).

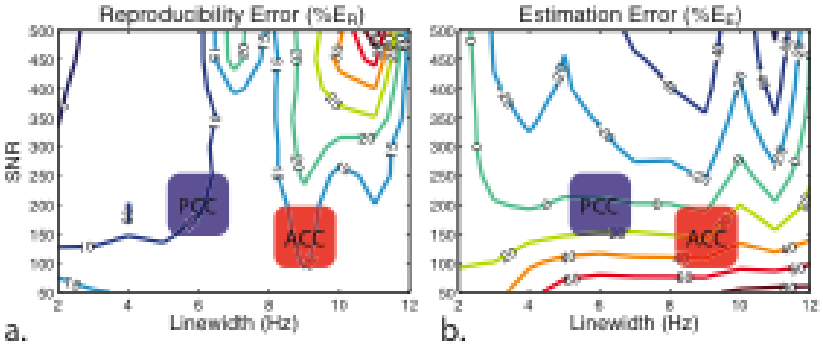

Figure 2: a) Reproducibility error and b) Estimation error as a function of SNR and LW. Experimental conditions corresponding to ACC and PCC are marked in red and blue, respectively.

References. [1] Mescher M et al. NMR Biomed (1998); 11. [2] Choi IY et al. Magn Reson Med (2004); 51. [3] Mekle R et al. Magn Reson Med (2009); 61. [4] Provencher S. Magn Reson Med (1993); 30. [5] Hancu I. NMR Biomed (2009); 22. [6] Govindaraju V et al. NMR Biomed (2000); 13.