Comparison of MEGA-PRESS and A-PRESS for the measurements for GABA concentration in the brain of healthy volunteers

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Target Audience: Neuroscientists and radiologists.

Introduction γ-Aminobutyric acid (GABA), the major inhibitory neurotransmitter in brain, is present at low millimolar concentrations and is difficult to resolve at 3T due to resonance couplings and overlap. Several different methods have been proposed, the most commonly used of which involves use of selective editing (MEGA) along with PRESS, SPECIAL or Semi-LASER[1]. Recently, a single-shot method optimized for GABA using an asymmetric PRESS variant (TE1 = 30 ms; TE2 = 75 ms) has been described[2]. Here, we tested this method alongside standard MEGA-PRESS acquisitions.

Methods ^{1}H MRS MEGA-PRESS (TR = 2000 ms, TE = 68 ms, bandwidth = 2000 Hz, 256 averages, scan duration 8 min 48 s) and A-PRESS (TR = 2000 ms, TE1 = 30 ms; TE2 = 75 ms, bandwidth = 2000 Hz, 128 averages, scan duration 4 min 52 s) were acquired at Philips 3T (Achieva TX, Best, the Netherlands) in 10 volunteers (8 M, 2 F, 23.7 ± 3.7 y) from a 3 x 3 x 3 cm^3 VOI located in the parietal lobe using an 8-channel phased-array head coil following acquisition of a T1-weighted (3D) turbo field echo (TFE) for localization. The MEGA-PRESS data were processed using GANNET v2.0 and AMARES (jMRUI v 3.0) algorithms while the A-PRESS data were analysed using QUEST (jMRUI, v4, bld 162). Statistical analysis used GraphPad Prism.

Results GABA and Creatine estimates, and their SD% and fit errors MEGA and A-PRESS data are shown in **Table 1**. There was a significant positive correlation between measurement of Cre (**Fig. 1A, B**) obtained using MEGA-PRESS (GANNET and jMRUI) and A-PRESS ($r^2 = 0.86$, $P < 0.0001$ and $r^2 = 0.89$, $P < 0.0001$, respectively) and between the two creatine estimates using MEGA-PRESS ($r^2 = 0.93$; $P < 0.0001$; **Fig. 1C**) but a much weaker relationship between the various GABA measurements made using MEGA-PRESS (**Fig. 1D**). Also, there was a positive correlation between measures of GABA obtained using MEGA (GANNET and jMRUI) and A-PRESS ($r^2 = 0.24$, $P < 0.0001$ and $r^2 = 0.65$, $P < 0.0001$, respectively). There was a strong linear relationship between the GABA and Cre fit errors using APRESS ($r^2 = 0.8$; $P = 0.004$) but a weaker one in the case of MEGA-PRESS GANNET fit errors ($r^2 = 0.46$; $P = 0.03$). There was no relationship between GABA/Cre ratios measured using A-PRESS and either of the two MEGA-PRESS measures ($r^2 = 0.0002$, GANNET and $r^2 = 0.094$, jMRUI) or between the two methods of fitting the MEGA-PRESS spectra ($r^2 = 0.19$). Finally, the size of the fit errors was not associated with shim quality (width at half height of the water peak) or with spectral noise measures.

Table 1 GABA/Cre measured with MEGA and A-PRESS

	MEGA-PRESS (GANNET)	MEGA-PRESS (jMRUI)	A-PRESS (jMRUI)
GABA/Cre	0.10 ± 0.01	0.117± 0.006	0.205±0.030
SD (%)	11	5	15
Fit-Error (GABA)	5.8 ± 1.1%	18 ± 4 %	38 ± 12 %
Fit-Error (Cre)	10.1 ± 0.9%	5 ± 1 %	4.6 ± 1.1 %

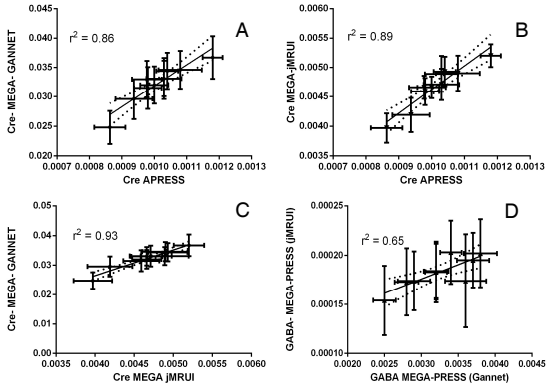

Fig. 1 Correlations between Cre measured by A. MEGA-GANNET and A-PRESS B. MEGA-jMRUI and A-PRESS, C. MEGA-GANNET and MEGA-jMRUI, and GABA measured by D. MEGA-jMRUI and GANNET.

Discussion Direct comparison of these two methods using comparable metrics is not possible. Errors in fit determined using jMRUI reflect a statistical model that fits all metabolites simultaneously, while the errors generated from fit by GANNET do not consider errors propagated in preprocessing (frequency alignment, subtraction etc.). Further, there are time and signal to noise penalties that are not considered. Instead, we have looked for consistency in the data generated by the acquisition methods and by the two fitting approaches. While there is generally good to excellent consistency between Creatine measures and estimates, the GABA measurements are highly variable. It is difficult to quantify GABA using A-PRESS even at 7T[4] due to low contrast between GABA and neighbouring NAA acetyl singlet peak (Fig. 2). The GABA correlations reported here are similar to those reported recently by authors[3] comparing MEGA-SPECIAL with short TE SPECIAL for GABA measurements ($r = 0.58$ (r^2 ~0.39) $P < 0.05$). Our findings suggest that, despite obtaining consistent fit errors in model estimates, there is considerable uncertainty in GABA measurements made using the different techniques, especially when compared to the certainty for measuring "easy" metabolites such as creatine. This variability may go some way to explaining inconsistent findings in the GABA literature (e.g. [5,6]).

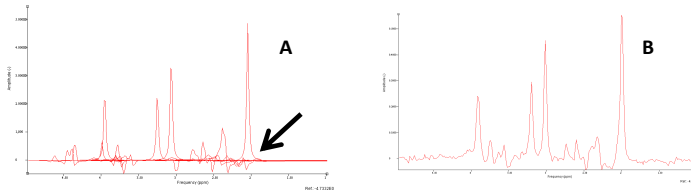

Fig.2 Simulated (A) and acquired (B) A-PRESS spectra.

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