Correlation-based cross validation of PRESS, MEGA PRESS editing and 2D JPRESS at 3T

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Introduction

In vivo detection of neurotransmitters and antioxidants such as N-acetyl-aspartate (NAA), glutamate (Glu), glutamine (Gln), gamma-aminobutyric acid (GABA), and glutathion (GSH) is a key component for the investigation of the pathophysiological processes behind psychiatric disorders. Non-invasive quantification of these metabolites was reported to be possible at 3T by dedicated ^{1}H MRS methods such as 1D PRESS with short or optimized echo times, 2D J-solved PRESS (JPRESS) and MEGA-PRESS spectral editing (Fig 1). However, there is an ongoing debate about the potential of individual methods to detect Glu, Gln, GABA and GSH reliably at 3T. In this work, PRESS (TE = 23ms and 80ms), 2D JPRESS and MEGA PRESS are hence cross validated against each other using a correlation approach in order to reveal their potential for quantification of the above mentioned coupled spin systems at 3T.

Materials and Methods

Institutional Ethics Committee approval and informed written consent were obtained from all volunteers. Measurements were performed on a 3T whole body system (Philips Healthcare, Best, The Netherlands) using a transmit/receive head coil (20 µT). All four ^{1}H MRS methods were applied in centrum semiovale (CSO), visual cortex (VISC), cerebellum, and perigenual anterior cingulate cortex (pACC) of 10 healthy volunteers for each brain region, resulting in 40 volunteers in total. These brain regions show different concentrations for the metabolites of interest and were chosen to introduce sufficient concentration variance to make a correlation based cross-validation possible. Scan parameters are as follows: **1D PRESS**: TR/TE= 3000/23ms (PRESS_Sh) and 3000/80ms (PRESS_80), spectral averages (NSA)=128 with the exception of 512 NSA for pACC; **MEGA-PRESS** (MEGA): TR/TE=3000/68ms, NSA = 256 in 16 blocks; **2D JPRESS:** TR/TE=1500/26ms, NSA=8 and 100 TE increments with 2ms spacing were used. Second order FASTERMAP shimming was applied. VAPOR was used for water suppression and inner volume suppression (IVS) was achieved using 6 saturation bands. IVS localized voxel sizes were 33.3x13.9x15.3mm for CSO (7082 ml); 21.7x21.4x20.1mm for VISC (9334 ml); 22.5x20x20mm for cerebellum (9000 ml); and 20x18x25mm for pACC (9000 ml). Metabolite/creatine concentrations were compared between all methods since creatine concentrations are known to be almost constant over different brain regions. Spectra were corrected for DC offset, phase, and eddy currents for all methods. Basis spectra were simulated for all methods using GAMMA. 1D PRESS and MEGA-PRESS spectra were analyzed in LC-Model and 2D JPRESS spectra were analyzed using Prior knowledge Fitting (ProFit). Correlation analyses were performed in MATLAB and Pearson's correlation coefficient (r) and significance of the correlation coefficient (ρ) were calculated.

Results and Discussion

As expected highly significant correlations were observed for NAA between all four methods pairs (Tab 1), which demonstrates the feasibility of this cross-validation approach. Also Glu could be detected with all four methods and all correlations were significant (Fig 2, Tab 1), with the strongest correlation found between PRESS_sh and JPRESS. Both JPRESS and MEGA enable GABA quantification at 3T which resulted in a significant correlation of GABA / Cr ratios between these two methods, while MEGA suffered from MM co-editing. To our surprise highly significant correlations between PRESS_Sh and JPRESS were found for GABA, Gln and GSH, which indicates that an excellent B_0 shim quality of < 8Hz water FWHM enables detection of coupled spin systems with short TE PRESS at 3T. Gln however could be quantified with PRESS_Sh in only 17 out of 40 volunteers (CRLB < 100), whereas JPRESS enabled detection of Gln in all cases (CRLB < 20). CRLBs as estimated by LC-Model for GABA, Gln and GSH were not indicative for the high correspondence between PRESS_Sh and JPRESS, which questions CRLBs being good predictors for quantification precision.

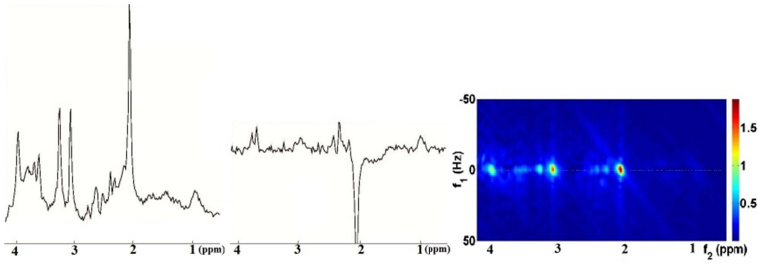

Figure 1: *Example spectra for PRESS with TE shortest (left), MEGA-PRESS GABA editing (middle), and 2D JPRESS (right).*

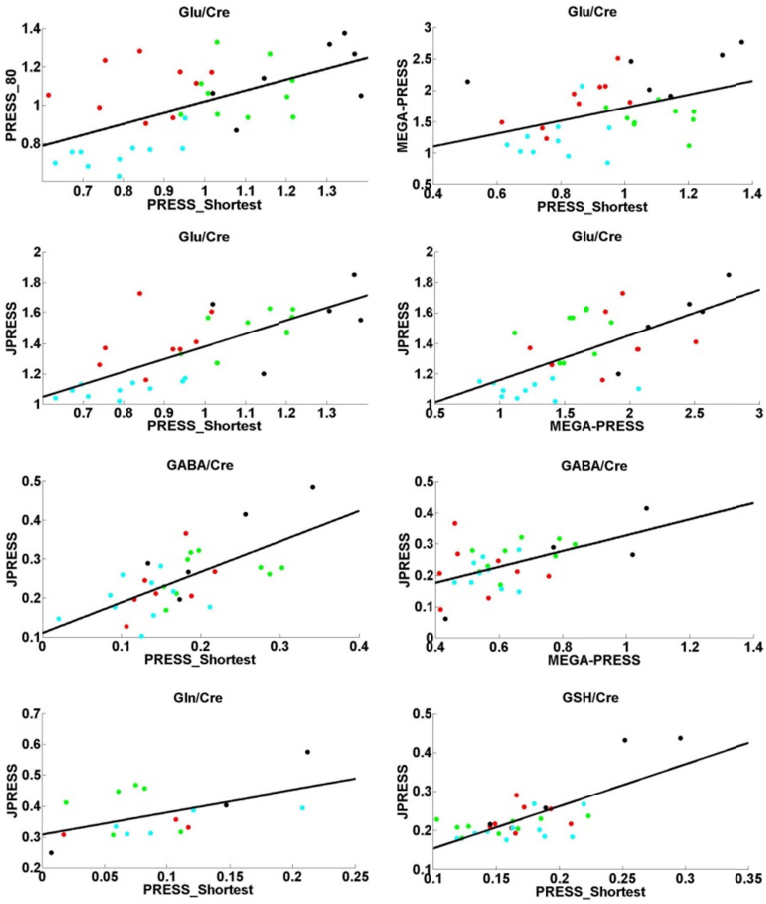

Figure 2: *Correlation Analyses between different methods for different metabolites using metabolite/creatine concentration ratios (CSO: red, VISC: green, cerebellum: magenta, pACC: black dots).*

	NAA	Glu	GABA	Gln	GSH
PRESS_Sh & JPRESS	r=0.925 ρ<0.001	r=0.726 ρ<0.001	r=0.657 ρ<0.001	r=0.525 ρ=0.031	r=0.721 ρ<0.001
MEGA & JPRESS	r=0.782 ρ<0.001	r=0.632 ρ<0.001	r=0.535 ρ=0.002	n.s.	n.s.
PRESS Sh & 80	r=0.944 ρ<0.001	r=0.588 ρ<0.001	n.s.	n.s.	n.s.
PRESS_Sh & MEGA	r=0.739 ρ<0.001	r=0.441 ρ=0.009	n.s.	n.s.	n.s.

Table 1: *Correlation Statistics*