Cross-validation of PRESS, MEGA-PRESS editing and 2D JPRESS for neurotransmitter and antioxidant detection at 3T using the ERETIC reference standard

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Introduction

In vivo ^{1}H MR spectroscopy can provide insight into metabolic and physiological processes in the human brain. Increasing evidence underscores the role of N-acetyl-aspartate (NAA), gamma-amino-butyric acid (GABA), glutamate (Glu), glutamine (Gln) and glutathion (GSH) in various neurological and psychiatric disorders [1]. Hence, different ^{1}H-MRS methods can be useful diagnostic tools to investigate patho-physiological changes in metabolite concentrations. However, generally metabolite ratios e.g. to creatine are reported instead of concentrations, while a fundamental requirement for using spectroscopy as a clinical diagnostic tool is the ability to reliably detect concentration changes of individual metabolite signals from the measured spectrum. This is usually done by using internal or external reference signals of known concentrations. Because of structural tissue abnormalities in various diseases, the water reference standard is not reliable enough for spectral quantification, whereas external reference signals may provide more reliable results [2]. **In this work,** various ^{1}H 1D MRS protocols (PRESS, MEGA-PRESS GABA-editing) and localized 2D J-Resolved spectroscopy (JPRESS) are compared to investigate their ability of quantifying GABA, Glu, Gln and GSH accurately. ERETIC (Electric REference To access In vivo Concentration) has been applied as a reliable reference by injecting an artificial signal of known amplitude, phase and duration into the measured spectrum [2]. Next to this, a water reference scan was acquired for all sequences to calculate all metabolite ratios with the internal water reference method,which is the current gold-standard method for quantification of ^{1}H spectra in healthy tissue.

Materials and Methods

All measurements were performed on a 3T whole body system (Philips Healthcare, Best, The Netherlands) using a standard 3T transmit receive birdcage coil. MEGAPRESS [3] and JPRESS[4] combined with ERETIC are implemented at the 3T scanner. Eight healthy volunteers have been scanned using PRESS (TE=23ms, TE=80ms), MEGA-PRESS and JPRESS in a voxel (25x18x20mm) located in the occipital lobe ***(Fig 1)***. The following parameters were used for 1D PRESS TR/TE=3.0s/23&80ms, 128 averages and for MEGA-PRESS: TR/TE=3.0s/68ms, 256 averages. The parameters used for 2D JPRESS were as follows: TR/TE=1.5s/24ms, 8 averages per $\Delta t1$ and 100 $\Delta t1$ increments. Excellent water suppression was achieved using a VAPOR [5] pre-saturation sequence. The transmission coil for the ERETIC signal was mounted on top of the birdcage coil as close as possible to the receiver coil to avoid any signal variations due to patient loading. The broad-band tune channel of the scanner was used for the reference signal's transmission. This setup allowed free control of ERETIC signal frequency. To avoid the influence of any sources of parasitic coupling the ERETIC signal was sent over an optical transmission line. The offset frequency of the ERETIC signal was set to -600Hz which corresponds to the position of 0ppm. Inner volume saturation (IVS)[4] was applied to to avoid signal cancellation (1D sequences) or the appearance of J-refocused peaks (2D JPRESS). A basis set containing 18 metabolites was simulated for PRESS and JPRESS using GAMMA [6] for a field strength of 3T. The 1D PRESS spectra were processed using LC-Model, MEGA-PRESS spectra by using AMARES (JMRUI 3.0) and the 2D JPRESS data using prior knowledge fitting (ProFit)[7]. A selected group of metabolites was investigated: creatine (Cr), N-acetylaspartate (NAA), phosphorylcholine (PCh)+glycerylphosphocholine (GPC), γ-aminobutyric acid (GABA), glutamine (Gln), glutamate (Glu), glutathione (GSH) and myo-inositol (mI). The accuracy of the quantitation results normalized to ERETIC and internal water was characterized comparing standard deviation (SD%) of fitting results among all eight volunteers for all metabolites of interest.

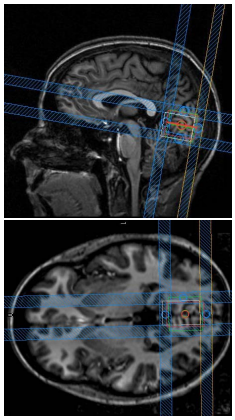
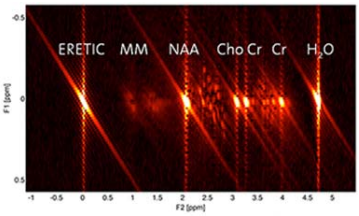


Figure 1: Localization of the voxel.



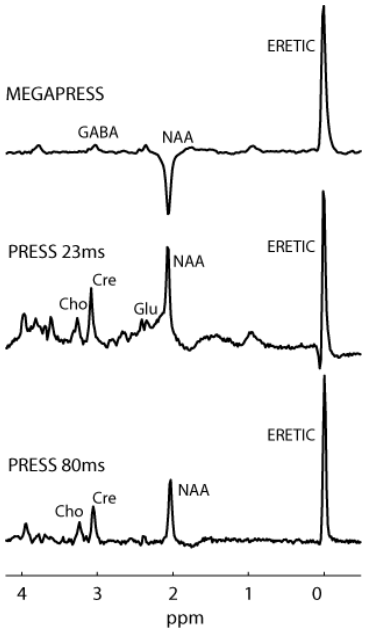


Figure 2: JPRESS, MEGA-PRESS, PRESS (23ms) and PRESS (80ms) spectra of a healthy volunteer with the ERETIC reference signal at 0 ppm.

Results and Discussion

Quantification results for the selected group of metabolites could be derived from all sequences, except for MEGA-PRESS with which we only quantified GABA. Next to this, in all the sequences the ERETIC signal was observed at exactly 0 ppm ***(Fig 2)***. In ***Table 1***, the standard deviation of the average normalized amplitudes of each metabolite (expressed as ratio to ERETIC, as well as to internal water) is presented. A comparison of the SD% values of each metabolite with 1D PRESS at both echo times shows a general reduction by using 2D JPRESS,especially when the ERETIC ratio is taken into account. For the detection of GABA the result of JPRESS is comparable to MEGA-PRESS. Hence, JPRESS shows to be the best method for simultaneous quantification of GABA, Glu, Gln, GSH and the conventional singlets, while MEGA-PRESS GABA-editing proofs to be a faster and reliable method for studies that target mainly GABA. The metabolite/ERETIC ratio shows to be a more stable and hence reliable quantification method compared to the metabolite/water reference ratio for all tested sequences. A detailed analysis of relative metabolite concentrations, fit covariance and between-sequence metabolite correlations is currently performed.

	PRESS(23MS)		PRESS(80MS)		JPRESS(24MS)		MEGA-PRESS	
	ERETIC Ratio (%SD)	Water Ratio (%SD)	ERETIC Ratio (%SD)	Water Ratio (%SD)	ERETIC Ratio (%SD)	Water Ratio (%SD)	ERETIC Ratio (%SD)	Water Ratio (%SD)
NAA	5%	8%	2%	3%	2%	5%		
PCh+GPC	14%	30%	10%	23%	14%	35%		
Cre	10%	21%	14%	25%	7%	21%		
mI	31%	59%	22%	55%	20%	63%		
Gln	25%	36%	47%	55%	21%	42%		
GSH	32%	51%	55%	58%	12%	35%		
GABA	44%	92%	50%	86%	28%	90%	25%	28%
Glu	13%	25%	15%	33%	6%	24%		

Table 1: Summary of metabolite/ERETIC and metabolite/internal water ratios calculated for conventional 1D SV MRS (PRESS & MEGA-PRESS) and 2D SV JPRESS.

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