Reproducibility of glutamate and glutamine quantification in the cingulate cortex using proton echo planar spectroscopic imaging

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Introduction

The cingulate cortex (CC) in the medial wall of the brain is involved in a wide range of pathological conditions including psychiatric disorders and chronic pain [1,2,3]. As the major excitatory neurotransmitter of the brain, glutamate (Glu) plays an important role not only in the pathology of these conditions but also as a mechanism for drug intervention. Glutamine (Gln) is the precursor of both Glu and Gamma-Amino Butyric acid (GABA), the major inhibitory neurotransmitter of the brain. Quantification of the Glu and Gln metabolism in CC may therefore provide important information about pathological mechanisms and drug dynamics. Proton Echo Planar Spectroscopy Imaging (PEPSI) is a fast Magnetic Resonance Spectroscopic imaging (MRSI) method that can be used to assess the distribution of brain metabolites [4]. In this study, we propose a 2-diemensional MRSI protocol based on the PEPSI sequence to detect Glu and Gln in CC in less than 10 minutes. To further improve the detection of Glu alone, which is in almost the same spectral range as Gln using ^{1}H MRS, a spectral editing method based on TE averaging (TEavg) were used to reduce the contribution of Gln and in turn enhance Glu in the spectra [5]. Using this protocol, the reproducibility of the metabolite concentrations of Glu, Gln and the combination of Glu and Gln (Glx) was evaluated with short-TE PEPSI and TEavg PEPSI.

Methods

Sixteen healthy subjects (7 males/ 9 females; mean±SD: 29.9±8.2; range: 21 to 49 years;) were scanned on a 3T MR system (Trio, SIEMENS Medical Solutions, Erlangen, Germany) with a 32-channel head coil array. The reproducibility of MRSI was evaluated by 2 PEPSI protocols: (1) constant short TE (TE30) and (2) TE average (TEavg). All subjects were scanned twice on the same day (without leaving the scanner) for the assessment of within-day reproducibility. Eight subjects returned for the same experiment around 2 weeks later for the assessment of between-week reproducibility. Initially, a high-solution 3D T1 image was obtained for localization of the medial wall and CC in the right hemisphere. The following parameters were used: sagital PEPSI acquisition; 14mm slice thickness; 8 x 8 mm^2 in-plane resolution; FOV=256 x 256 mm^2; and TR=1500 ms. Up to 8 slices of outer volume lipid suppression were applied along the perimeter of the brain. TE30 parameters were TE = 30 ms and NEX = 8 and for TEavg, eight TEs were used from 35 ms to 185 ms with 20 ms increments. An additional non-water suppression (NWS) PEPSI scan was acquired using single average for automatic phase correction and calibration of metabolic concentrations.

Standard post processing was performed for the PEPSI data as described previously [4]. After reconstruction, spectra were quantified with LCModel [6]. Metabolite concentrations of N-Acetyl Aspartate (NAA), total Creatine (tCr), Choline (Cho), myo-Inositol (mI), Glu, Gln and Glx were quantified using the water-scaling method. ROIs of the entire medial wall and CC were manually selected on the individual anatomical images (Figure 1). The concentrations and Cramer-Rao Lower Bound (CRLB) of all metabolites were calculated for each ROI. The within-day and between-week reproducibility of TE30 and TEavg protocols were assessed by the coefficient of variance (COV).

Results and Discussion

Representative maps of metabolite concentrations and CRLB from one subject are shown in Figure 2. The mean metabolite concentrations were similar for the two protocols except for Gln, Glx and mI (Table 1). The CRLB for NAA, tCr, and Cho were less than 8% for both protocols (Table 1). As expected, smaller CRLB for Glu and higher CRLB for Gln were found with TEavg indicating successful spectral editing/ suppression of Gln. Overall, COV for TE30 were less than 5% for the medial wall and 8% for CC (Table 2). For TEavg, COVs were less than 6% for the medial wall and 10% for CC except for Gln (~20%), which is in accordance with the CRLB results. It is noteworthy that although a better fit was obtained for Glu with TEavg there was no obvious difference in Glu COV between the two protocols. In conclusion, the small COVs make PEPSI suitable for assessment of short-term and long-term changes in brain metabolites of the medial wall. Compared to the TEavg protocol, the TE30 protocol had similar performance on Glu but provides more accurate quantification of Gln and other metabolites.

Reference

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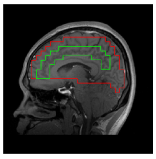

Figure1 The ROIs of medial wall (red) and CC (green) of one subject

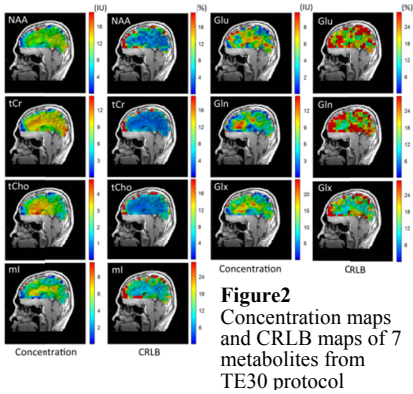

Figure2 Concentration maps and CRLB maps of 7 metabolites from TE30 protocol

	CONC.(I.U.)		CRLB(%)	
TE30	Medial Wall	CC	Medial Wall	CC
NAA	11.22±0.95	11.64±0.96	5.38±0.46	4.87±0.60
tCr	9.43±0.72	9.95±0.71	4.57±0.26	3.88±0.31
tCho	2.55±0.32	2.63±0.35	5.72±0.49	4.81±0.48
mI	5.08±0.52	5.32±0.62	12.61±0.85	10.94±1.01
Glu	6.06±0.39	5.80±0.38	22.25±1.62	22.54±2.28
Gln	8.58±0.66	9.03±1.00	18.93±2.17	17.30±2.72
Glx	13.02±0.83	14.03±1.24	15.37±1.56	13.53±1.96
TEavg	Medial Wall	CC	Medial Wall	CC
NAA	12.47±1.16	12.33±1.21	7.34±0.66	6.36±1.01
tCr	6.96±0.50	7.37±0.48	4.83±0.43	3.93±0.39
tCho	2.03±0.24	2.11±0.25	5.96±0.46	4.92±0.47
mI	7.27±0.49	7.36±0.45	19.05±1.34	17.20±1.90
Glu	7.17±0.40	7.38±0.53	19.22±1.81	16.96±2.10
Gln	5.73±1.68	4.67±0.98	29.06±3.21	29.21±5.34
Glx	8.72±0.51	9.04±0.73	18.76±1.71	16.37±2.11

Table 1 The average and standard deviation of concentration and CRLB for all 16 subjects.

COV(%)	Within-day		Between-week	
	Medial		Medial	
TE30	Wall	CC	Wall	CC
NAA	1.22%	1.43%	1.67%	2.86%
tCr	1.52%	1.97%	2.31%	2.59%
tCho	2.52%	2.49%	2.13%	3.64%
mI	2.52%	4.00%	2.60%	4.87%
Glu	5.13%	7.26%	3.77%	7.71%
Gln	3.50%	5.10%	3.24%	6.85%
Glx	2.46%	4.38%	3.52%	3.67%
	Medial		Medial	
TEavg	Wall	CC	Wall	CC
NAA	2.63%	4.09%	2.86%	3.95%
tCr	1.81%	2.23%	2.11%	3.03%
tCho	2.25%	2.35%	4.20%	5.11%
mI	5.14%	9.68%	5.31%	8.74%
Glu	5.25%	7.31%	5.40%	6.09%
Gln	13.72%	19.10%	19.22%	22.04%
Glx	5.80%	8.29%	4.64%	5.93%

Table 2 Within-day and between-week COV of both protocols.