Reproducibility of glutamate, GABA and glycine in human brain, as measured by optimized ^{1}H MRS at 7T

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PURPOSE: Precise and reliable detection of the primary excitatory neurotransmitter, glutamate (Glu), and inhibitory neurotransmitters, γ-aminobutyric acid (GABA) and glycine (Gly) in the human brain is important for research in neuro-psychiatric diseases [1, 2]. The proton signals of these metabolites are extensively overlapped and thus the spectral analysis is complicated. The purpose of this study is to demonstrate good separation of the signals and clinically acceptable reproducibility of the metabolite measurements by optimized ^{1}H MRS at 7T.

METHODS: 6 healthy volunteers (4 female; 2 male; age of 47 ± 11) were recruited in this study. In order to evaluate the reproducibility of brain metabolites, each subject underwent two examinations with intervals of 3 – 5 days using point-resolved spectroscopy (PRESS) with echo times (TE) of 92 ms [3] and 150 ms [4] in a 7T whole-body MR scanner (Philips Medical Systems). ^{1}H MRS data were obtained from the anterior cingulate cortex (ACC) and acquisition parameters included: voxel size = 30x20x15 mm^3, TR = 2.5 s, sweep width = 5 kHz, number of sampling points = 4096, and number of averages = 256. The RF carrier frequency was set to 2.5 ppm for PRESS TE = 92 ms and 3.55 ppm for PRESS TE = 150 ms respectively. High-resolution T_1w-MPRAGE was acquired and used for elimination of cerebrospinal fluids contamination within the voxels. Spectral fitting was performed with LCModel software [5], using basis spectra calculated incorporating the volume localizing RF and gradient pulses of PRESS with published chemical shift and J-coupling constants [6]. Metabolite levels were quantified using water signal as reference. Relaxation effects were corrected using published T_2 values [7, 8]. To evaluate reproducibility, Coefficient of Variance (CV) and Intraclass Correlation Coefficient (ICC) were calculated with two-way analysis of variance (ANOVA) [9, 10].

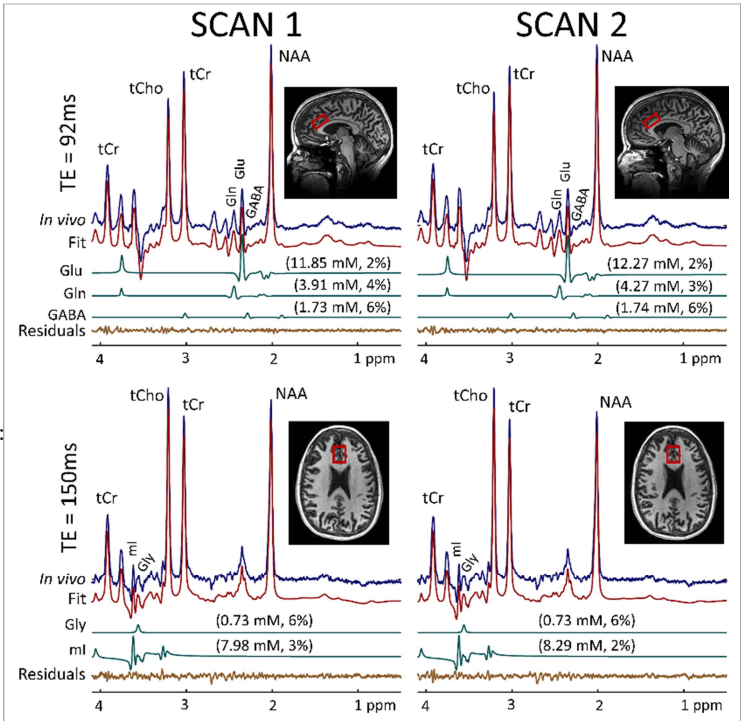

Fig.1: Representative *in vivo* test-retest spectra from the anterior cingulated cortex of a normal subject, obtained with PRESS TE= 92 ms and 150 ms at 7T, are shown together with LCModel fits, residuals and metabolites signals. The numbers in brackets are concentrations (mM) and CRLBs.

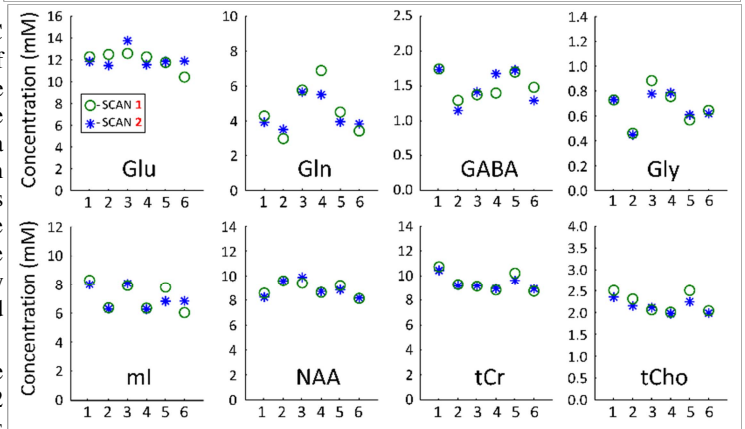

Fig.2 Metabolites estimates (mM) in six subjects from test-retest (SCAN 1 and 2) examination.

RESULTS: Representative i*n vivo* spectra of test-retest scans in ACC region of a subject are displayed in Figure 1. Complete separation of Glu, Gln and GABA was well reproduced at TE = 92 ms with ignorable residuals and CRLBs lower than 6%. Using PRESS TE =150 ms, the Gly peak at 3.55ppm fully separated from myo-inositol (mI), giving a Gly CRLB of 6%. Concentrations of eight metabolites estimated from test-retest scans in the 6 subjects are shown in Figure 2. The estimations were nearly identical between two scans. CV and ICC values are presented in Table 1. CVs were smaller than 0.03 for most of the metabolites, while being larger for Gln (0.096). ICCs of GABA and Gly were higher than 0.90 while Glu and Gln were slightly lower (0.81 and 0.88).

DISCUSSION AND CONCLUSION: The present study reports the reproducibility of Glu, Gln, and GABA estimates by PRESS TE = 92 ms and the reproducibility of Gly by PRESS TE = 150 ms. The low CVs (0.03) and high ICCs (0.90) together with low CRLBs (2-3% for Glu, 4% for Gln, 8% for GABA and 6% for Gly), indicated high reproducibility and high precision of the MRS measurements. In conclusion, the present study demonstrates reproducible and precise estimation of Glu, Gln, GABA and Gly in the human brain by optimized PRESS 92 ms and 150 ms at 7T.

Table 1. Reproducibility test results.

Metabolite	CV	ICC	Concentration(mM)	CRLB(%)
Glu	0.021	0.81	12.01 ± 0.79	1.9 ± 0.3
Gln	0.096	0.88	4.51 ± 1.18	3.3 ± 1.6
GABA	0.020	0.91	1.50 ± 0.21	7.5 ± 1.3
Gly	0.017	0.95	0.67 ± 0.13	5.7 ± 1.0
mI	0.002	0.92	7.08 ± 0.86	2.6 ± 0.7
NAA	0.004	0.93	8.91 ± 0.60	1.0 ± 0.0
tCr	0.002	0.96	9.44 ± 0.67	0.7 ± 0.5
tCho	0.060	0.87	2.19 ± 0.19	1.0 ± 0.0

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