

Supplementary Online Content

Kraguljac NV, White DM, Reid MA, Lahti AC. Increased hippocampal glutamate and volumetric deficits in unmedicated patients with schizophrenia. *JAMA Psychiatry*. Published online October 9, 2013.
doi:10.1001/jamapsychiatry.2013.2437.

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1: Demographics and Clinical Measures^a

	SZ (n=27)	HC (n=27)	t/X ²	p value
Gender (% male)	74.10	74.10	0.000	1.0
Age	32.63 (9.28)	32.85 (9.39)	0.087	.93
Parental Occupation ^b	6.67 (5.37)	5.38 (3.89)	-0.917	.37
Smoking status (% smokers)	81.50	55.60	5.878	.02
Smoking (packs per day)	0.97 (0.54)	0.80 (0.46)	-0.912	.37
Diagnosis				
Schizophrenia	23			
Schizoaffective Disorder	4			
Illness Characteristics				
Illness Duration (years)	10.48 (8.65)			
First episode	5			
Prior antipsychotic treatment				
Antipsychotic naive	11			
Antipsychotic free interval (months)	24.74 (45.37)			
BPRS ^c				
Total	44.50 (11.59)			
Positive	8.42 (3.14)			
Negative	6.77 (2.69)			
RBANS ^d				
Total index	72.22 (13.94)	98.15 (14.19)	6.773	< .01
Immediate memory	78.63 (17.94)	99.44 (12.38)	4.962	< .01
Visuospatial	71.11 (15.43)	95.30 (16.58)	5.549	< .01
Language	83.22 (14.55)	96.89 (13.87)	3.663	< .01
Attention span	80.11 (18.01)	103.93 (16.97)	5.001	< .01
Delayed memory	76.85 (18.29)	97.59 (8.46)	5.348	< .01

SZ, schizophrenia; HC, healthy control

a Mean (SD) unless indicated otherwise

b Ranks determined from Diagnostic Interview for Genetic Studies (1 – 18 scale); higher rank (lower numerical value) corresponds to higher socioeconomic status

c Brief Psychiatric Rating Scale (1 – 7 scale); positive (conceptual disorganization, hallucinatory behavior, and unusual thought content); negative (emotional withdrawal, motor retardation, and blunted affect)

d Repeatable Battery for the Assessment of Neuropsychological Status

eTable 2: Hippocampal neurometabolites in subjects with CRLB< 20%

	HC (n=27) Mean (SD) [CRLB; SD]	SZ (n=26) Mean (SD) [CRLB; SD]	% difference SZ contrasted to HC	F (p value) ^a
Glx/Cr	0.60 (0.08) [0.09; 0.01]	0.66 (0.11) [0.11; 0.03]	+10	4.827 (.03)
NAA/Cr	1.28 (0.10) [0.04; 0.01]	1.23 (0.13) [0.04; 0.01]	-4	1.540 (.22)
Cho/Cr	0.91 (0.08) [0.03; 0.01]	0.88 (0.10) [0.03; 0.01]	-3	1.853 (.18)
Glx/Cr:NAA/Cr	0.479 (0.06)	0.543 (0.11)	+12	7.443 (< .01)

SZ, schizophrenia; HC, healthy control; CRLB, Cramer-Rao Lower Bounds; NAA, *N*-acetyl-aspartate; Glx, glutamate and glutamine; Cho, choline; Cr, creatine;

^aMultivariate Analysis of covariance (MANCOVA), within-group factor metabolite level, between group-factor disease state (HC/ SZ), age, smoking (packs per day), voxel grey matter and white matter content as covariates.

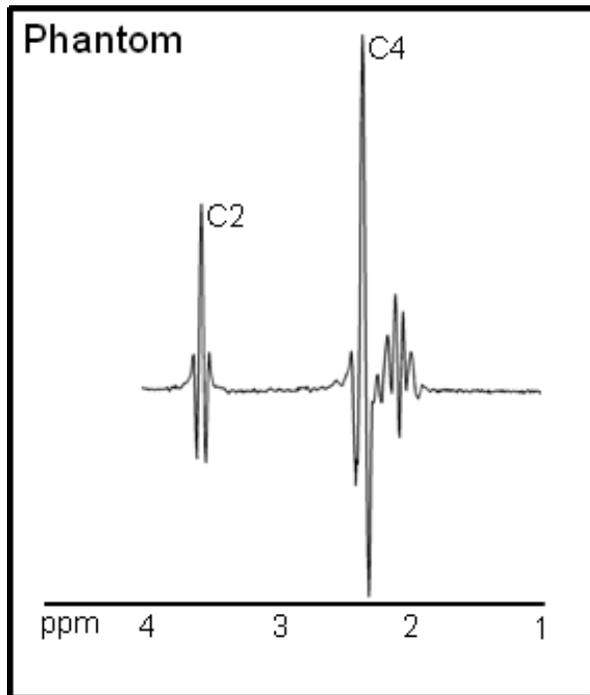
eTable 3: Hippocampal neurometabolites in chronic schizophrenia, medication naïve patients and first episode patients

	SZ chronic (n= 16) Mean (SD) [CRLB; SD]	SZ med naïve (n= 11) Mean (SD) [CRLB; SD]	SZ first episode (n= 5) ^a Mean (SD) [CRLB; SD]	F (p value) ^b
Glx/Cr	0.67 (0.12) [0.11; 0.04]	0.64 (0.09) [0.12; 0.04]	0.64 (0.11) [0.10; 0.02]	0.704 (.41)
NAA/Cr	1.21 (0.14) [0.04; 0.01]	1.27 (0.11) [0.04; 0.01]	1.22 (0.05) [0.04; 0.01]	0.732 (.40)
Cho/Cr	0.89 (0.13) [0.03; 0.01]	0.86 (0.08) [0.03; 0.01]	0.85 (0.02) [0.03; 0.01]	0.286 (.60)
Glx/Cr:NAA/Cr	0.56 (0.14)	0.51 (0.01)	0.52 (0.07)	1.361 (.26)

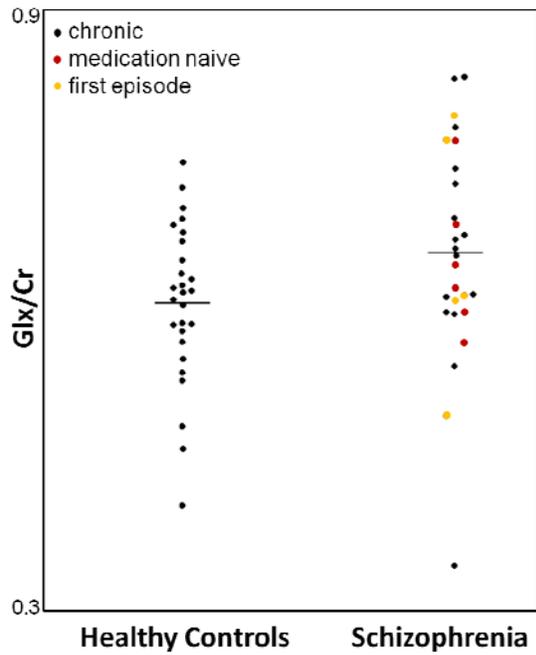
SZ, schizophrenia; HC, healthy control; CRLB, Cramer-Rao Lower Bounds; NAA, *N*-acetyl-aspartate; Glx, glutamate and glutamine; Cho, choline; Cr, creatine;

^aall first episode patients are medication naïve, this column represents a subset of prior column: SZ med naïve (n=11)

^bgroups are SZ chronic and SZ med naïve, Multivariate Analysis of covariance (MANCOVA), within-group factor metabolite level, between group-factor prior exposure to medication (SZ chronic/ SZ med naïve), age, smoking (packs per day), voxel grey matter and white matter content as covariates



eFigure1: Glutamate phantom spectrum. Phantom solution of 20mM glutamate in buffer (30mM NaHCO₃ and 30mM NA₂CO₃, ph 7.1). The C2 resonance is located at 3.75ppm (not included in prior knowledge) and the C4 resonance is located at 2.35ppm. Both resonances have a large center peak with two dephased outer components, therefore glutamate was modeled as triplet.



eFigure2: Glx/Cr ratios showing individual measurements and means (horizontal lines) in the hippocampus in patients with schizophrenia and healthy controls. Red dots correspond to Glx/Cr ratios in medication naïve patients and yellow dots correspond to first episode psychosis patients (all first episode psychosis patients are also medication naïve)