

Decoupling of Brain Temperature and Glutamate in Recent-Onset of Schizophrenia: A 7 Tesla ¹H-Magnetic Resonance Spectroscopy Study

Supplemental Information

Table S1. Neuropsychological Tests Within Each Cognitive Domain

Cognitive Domain	Neuropsychological Tests and Measures Used
Processing Speed	Salthouse Perceptual Comparison Test (1) Grooved Pegboard Test (2)
Attention/Working Memory	Brief Test of Attention (3) Digit Span (Forward and Backward) (4)
Verbal Memory	Hopkins Verbal Learning Test (5)
Visual Memory	Brief Visuospatial Memory Test (6)
Ideational Fluency	CIFA Word Fluency (7) CIFA Design Fluency (7)
Executive Function	Modified Wisconsin Card Sorting Test (8)

Table S2. Comparison of MRS Outcome Variables Between Patients with Recent-Onset Schizophrenia (SZ) and Controls

Characteristics	SZ (N=20)	Control (N=20)	P value
Tissue Segmentation			
Gray Matter Fraction	0.60 ± 0.13	0.63 ± 0.13	0.471
White Matter Fraction	0.30 ± 0.14	0.29 ± 0.15	0.730
Cerebrospinal Fluid Fraction	0.10 ± 0.02	0.09 ± 0.03	0.077
Imaging Data Quality			
Glutamate CRLB (%)	1.85 ± 0.37	1.95 ± 0.22	0.305
NAA CRLB (%)	1.70 ± 0.47	1.60 ± 0.50	0.520
GABA CRLB (%)	5.20 ± 0.62	5.35 ± 0.67	0.466
Gln CRLB (%)	6.00 ± 1.30	6.15 ± 1.60	0.746
Glutathione CRLB (%)	3.70 ± 0.73	4.00 ± 1.03	0.295
Myo-inositol CRLB (%)	2.35 ± 0.49	2.40 ± 0.50	0.752
NAAG ^a CRLB (%)	11.75 ± 3.45	13.86 ± 2.91	0.170
GPC+PCh CRLB (%)	1.94 ± 0.87	1.90 ± 0.91	0.879
NAA+NAAG CRLB (%)	1.83 ± 0.38	1.75 ± 0.44	0.539
Glutamate+Gln CRLB (%)	1.89 ± 0.32	1.95 ± 0.22	0.508
Total creatine CRLB (%)	1.05 ± 0.22	1.15 ± 0.37	0.305

CRLB = Cramer-Rao Lower Bound; NAA = *N*-acetylaspartate; GABA = γ -amino-butyric acid; Gln = Glutamine; NAAG = *N*-acetylaspartylglutamate; GPC = Glycerophosphocholine; PCh = Phosphocholine.

^aSample size includes 8 SZ and 14 Control for NAAG.

Table S3. Core Body Temperature and Brain Temperature Values in Patients with Recent-Onset Schizophrenia (SZ) and Controls

Temperature	SZ (N=20)	Control (N=20)	<i>P</i> value^a
Core Body Temperature (°C, mean ± SD)	36.42 ± 0.375	36.40 ± 0.470	0.882
Brain Temperature (°C, mean ± SD)	37.25 ± 0.433	37.08 ± 0.634	0.314
<i>P</i> value ^b	< 0.001	< 0.001	-

^at-test between cohorts; ^bpaired t-test between measures within each cohort.

Table S4.**A. Correlation Between Temperature and Metabolite Levels in Patients with Recent-Onset of Schizophrenia (SZ) and Controls**

Group Temperature	SZ (N=20)		Control (N=20)	
	CBT	BT	CBT	BT
Metabolite				
Glutamate/tCr*	0.416 (0.068)	0.294 (0.209)	0.036 (0.880)	-0.527 (0.017)
NAA/tCr*	0.151 (0.524)	0.285 (0.223)	-0.076 (0.752)	-0.112 (0.638)
GABA/tCr	0.422 (0.064)	0.278 (0.235)	0.132 (0.580)	-0.303 (0.194)
Gln/tCr	-0.055 (0.818)	0.411 (0.072)	-0.273 (0.245)	-0.336 (0.148)
Glutathione/tCr	-0.173 (0.465)	-0.276 (0.238)	-0.270 (0.249)	-0.189 (0.425)
Myo-inositol/tCr	-0.269 (0.251)	0.069 (0.771)	-0.013 (0.955)	-0.136 (0.567)
NAAG/tCr ^a	-0.813 (0.014)	0.007 (0.987)	0.045 (0.878)	-0.135 (0.645)
GPC+PCh/tCr	-0.487 (0.029)	-0.063 (0.791)	-0.131 (0.582)	0.156 (0.510)
NAA+NAAG/tCr	-0.010 (0.968)	0.200 (0.339)	0.014 (0.955)	-0.207 (0.382)
Glutamate+Gln/tCr	0.279 (0.234)	0.362 (0.117)	-0.068 (0.775)	-0.568 (0.009)

Pearson's correlation coefficients are listed with *P* value indicated in parentheses. *Correlation of temperature measures with both Glutamate/tCr and NAA/tCr are reported as primary outcomes. Other metabolites reported using the LCModel are reported as exploratory outcomes. ^aSample size includes 8 SZ and 14 Control for NAAG/tCr.

CBT = Core Body Temperature; BT = Brain Temperature. tCr = Total Creatine; NAA = *N*-acetylasparatate; GABA = γ -amino-butyric acid; Gln = Glutamine; NAAG = *N*-acetylaspartylglutamate; GPC = Glycerophosphocholine; PCh = Phosphocholine.

Table S4 (continued).**B. Correlation Between Temperature and Clinical Characteristics in Patients with Recent-Onset of Schizophrenia (SZ) and Controls**

Group Temperature	SZ (N=20)		Control (N=20)	
	CBT	BT	CBT	BT
Neuropsychological Performance				
Composite ^a	0.021 (0.930)	-0.152 (0.521)	-0.047 (0.845)	0.132 (0.578)
Processing Speed ^a	-0.025 (0.917)	-0.349 (0.132)	-0.290 (0.214)	0.117 (0.624)
Attention/Working Memory ^a	0.108 (0.651)	0.147 (0.536)	-0.074 (0.764)	-0.021 (0.932)
Verbal Memory ^a	0.037 (0.877)	-0.128 (0.591)	-0.046 (0.846)	0.305 (0.191)
Visual Memory ^a	0.124 (0.603)	-0.199 (0.400)	0.136 (0.568)	0.286 (0.222)
Ideational Fluency ^a	0.162 (0.496)	0.243 (0.302)	-0.082 (0.732)	0.153 (0.519)
Executive Function ^a	-0.272 (0.245)	-0.280 (0.233)	0.244 (0.300)	-0.360 (0.119)
SAPS ^b	0.305 (0.190)	-0.043 (0.856)	-	-
SANS ^b	-0.184 (0.438)	-0.032 (0.892)	-	-
CP Equivalent Dose ^a	0.448 (0.048)	0.035 (0.883)	-	-

^aPearson's correlation coefficient. ^bSpearman's correlation coefficient. *P* value is indicated in parentheses.

CBT = Core Body Temperature; BT = Brain Temperature; SAPS =Scale for the Assessment of Positive Symptoms; SANS = Scale for the Assessment of Negative Symptoms; CP =Chlorpromazine.

Supplemental References

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