

## SUPPLEMENTARY TABLES

**Supplementary Table 1. Partial correlations between metabolites, WMH volume, and cognitive function.**

	Executive function		Attention		Episodic memory	
	r	p	r	p	r	p
ACC(GABA+/Cr)	0.342	<b>0.001</b>	0.237	<b>0.030</b>	0.121	0.274
ACC(Glx/Cr)	-0.035	0.749	-0.112	0.310	-0.052	0.639
PCC(GABA+/Cr)	0.241	<b>0.027</b>	0.225	<b>0.040</b>	0.184	0.094
PCC(Glx/Cr)	0.029	0.790	0.034	0.761	0.295	<b>0.007</b>
WMH volume (cm <sup>3</sup> )	-0.397	<b>&lt;0.001</b>	-0.177	0.108	-0.005	0.967

Abbreviations: GABA+: GABA plus co-edited macromolecules and homocarnosine; Glx: glutamate-glutamine; ACC: anterior cortical cortex; PCC: posterior cortical cortex.

**Supplementary Table 2. Mediation effects of metabolites on the association between WMH volume and executive function.**

Metabolites	Total effect (c)			Direct effect (c')			a		b		Indirect effect (ab)		
	Effect	$\beta$	p	Effect	$\beta$	p	$\beta$	p	$\beta$	p	Effect	BootSE	95% CI
ACC(GABA+/Cr)				-0.090	-0.334	<b>0.002</b>	-0.267	<b>0.008</b>	0.273	<b>0.018</b>	-0.020	0.010	(-0.042, -0.004)
ACC(Glx/Cr)				-0.111	-0.416	<b>&lt;0.001</b>	-0.111	0.325	-0.080	0.439	0.002	0.004	(-0.003, 0.012)
PCC(GABA+/Cr)	-0.109	-0.407	<b>&lt;0.001</b>	-0.103	-0.386	<b>&lt;0.001</b>	-0.104	0.359	0.202	<b>0.045</b>	-0.006	0.007	(-0.022, 0.008)
PCC(Glx/Cr)				-0.110	-0.409	<b>&lt;0.001</b>	0.041	0.714	0.047	0.656	0.001	0.003	(-0.004, 0.009)

Abbreviations: GABA+: GABA plus co-edited macromolecules and homocarnosine; Glx: glutamate-glutamine; ACC: anterior cortical cortex; PCC: posterior cortical cortex.

**Supplementary Table 3. Mediation effects of metabolites on the association between WMH volume and attention.**

Metabolites	Total effect (c)			Direct effect (c')			a		b		Indirect effect (ab)		
	Effect	$\beta$	p	Effect	$\beta$	p	$\beta$	p	$\beta$	p	Effect	BootSE	95% CI
ACC(GABA+/Cr)				-0.033	-0.115	0.291	-0.267	<b>0.008</b>	0.210	0.074	-0.016	0.011	(-0.041, 0.002)
ACC(Glx/Cr)				-0.052	-0.185	0.083	-0.111	0.325	-0.126	0.226	0.004	0.005	(-0.002, 0.017)
PCC(GABA+/Cr)	-0.049	-0.171	0.108	-0.043	-0.151	0.151	-0.104	0.359	0.197	0.055	-0.006	0.008	(-0.024, 0.007)
PCC(Glx/Cr)				-0.049	-0.173	0.106	0.041	0.714	0.039	0.709	0.001	0.004	(-0.006, 0.012)

Abbreviations: GABA+: GABA plus co-edited macromolecules and homocarnosine; Glx: glutamate-glutamine; ACC: anterior cortical cortex; PCC: posterior cortical cortex.

**Supplementary Table 4. Mediation effects of metabolites on the association between WMH volume and episodic memory.**

Metabolites	Total effect (c)			Direct effect (c')			a		b		Indirect effect (ab)		
	Effect	$\beta$	p	Effect	$\beta$	p	$\beta$	p	$\beta$	p	Effect	BootSE	95% CI
ACC(GABA+/Cr)				0.009	0.033	0.777	-0.267	<b>0.008</b>	0.140	0.261	-0.010	0.010	(-0.033, 0.008)
ACC(Glx/Cr)	-0.001	-0.005	0.967	-0.003	-0.010	0.927	-0.111	0.325	-0.052	0.636	0.002	0.004	(-0.006, 0.011)
PCC(GABA+/Cr)				0.004	0.014	0.897	-0.104	0.359	0.181	0.095	-0.005	0.008	(-0.026, 0.006)
PCC(Glx/Cr)				-0.005	-0.017	0.877	0.041	0.714	0.294	0.007	0.003	0.009	(-0.015, 0.022)

Abbreviations: GABA+: GABA plus co-edited macromolecules and homocarnosine; Glx: glutamate-glutamine; ACC: anterior cortical cortex; PCC: posterior cortical cortex.