

Table S1 Baseline information of the subjects

Patients No.	Gender	Age (years)	Clinical characteristics	Coffee consumption
1	F	29	Healthy and undergo MRI	1–2 cups/day
2	M	50	Healthy and undergo MRI	3–4 cups/day
3	M	39	Healthy and undergo MRI	1–2 cups/day
4	F	24	Healthy and undergo MRI	1–2 cups/day
5	M	49	Healthy and undergo MRI	2–3 cups/day
6	F	38	Healthy and undergo MRI	3–4 cups/day
7	M	28	Healthy and undergo MRI	1–2 cups/day
8	M	53	Healthy and undergo MRI	1–2 cups/day
9	M	44	Healthy and undergo MRI	2–3 cups/day
10	F	22	Healthy and undergo MRI	<1 cup/day
11	F	20	Healthy and undergo MRI	<1 cup/day
12	F	19	Healthy and undergo MRI	<1 cup/day
13	M	20	Healthy and undergo MRI	<1 cup/day
14	M	19	Healthy and undergo MRI	<1 cup/day
15	F	22	Healthy and undergo MRI	<1 cup/day
16	F	21	Healthy and undergo MRI	<1 cup/day
17	M	20	Healthy and undergo MRI	<1 cup/day
18	M	22	Healthy and undergo MRI	<1 cup/day
19	F	20	Healthy and undergo MRI	<1 cup/day
20	M	22	Healthy and undergo MRI	<1 cup/day
21	F	20	Healthy and undergo MRI	<1 cup/day
22	F	19	Healthy and undergo MRI	<1 cup/day
23	F	19	Healthy and undergo MRI	<1 cup/day
24	M	18	Healthy and undergo MRI	<1 cup/day
25	M	21	Healthy and undergo MRI	No consumption
26	F	23	Healthy and undergo MRI	No consumption
27	F	32	Healthy and undergo MRI	No consumption
28	M	20	Healthy and undergo MRI	No consumption
29	M	21	Healthy and undergo MRI	No consumption
30	F	25	Healthy and undergo MRI	No consumption
31	F	24	Healthy and undergo MRI	No consumption
32	F	18	Healthy and undergo MRI	No consumption
33	F	24	Healthy and undergo MRI	No consumption
34	M	20	Healthy and undergo MRI	No consumption
35	F	19	Healthy and undergo MRI	No consumption
36	F	21	Healthy and undergo MRI	No consumption
37	M	27	Healthy and undergo MRI	No consumption
38	M	24	Healthy and undergo MRI	No consumption
39	F	23	Healthy and undergo MRI	No consumption
40	F	23	Healthy and undergo MRI	No consumption
41	M	30	Healthy and undergo MRI	No consumption
42	M	33	Healthy and undergo MRI	No consumption
43	M	20	Healthy and undergo MRI	No consumption
44	F	24	Healthy and undergo MRI	No consumption
45	F	26	Healthy and undergo MRI	No consumption

No., number; M, male; F, female; MRI, magnetic resonance imaging.

**Table S2** Cerebral metabolites in the thalamus voxel measured by MRS in healthy adult subjects pre-coffee, and 30 and 120 min post-coffee

Metabolite	Coffee consumption	Pre-coffee, mean ± SD	Post-coffee 30 min, mean ± SD	Post-coffee 120 min, mean ± SD	Interaction effect		Main effects	
					Time × group (P value)	Time (P value)	Group (P value)	
GABA <sup>+</sup>	–	3.75±0.42	3.48±0.34	4.09±1.27	–	0.011*	–	–
Glu	≥1 cup/day	8.07±0.66	8.61±0.76	8.00±1.59	0.007*	0.088	<0.0001*	
	<1 cup/day	8.87±0.85	9.24±0.98	8.94±0.54				
	NCD	9.50±1.20	9.12±0.80	9.74±0.56				
GPC/GPC + PCH	≥1 cup/day	2.38±0.19	2.35±0.14	2.43±0.08	0.001*	0.012*	0.001*	
	<1 cup/day	1.96±0.05	2.13±0.13	2.01±0.17				
	NCD	2.04±0.17	2.11±0.183	1.98±0.26				
Ins	≥1 cup/day	4.34±0.31	4.25±0.33	4.31±0.25	0.001*	0.009*	0.298	
	<1 cup/day	3.99±0.49	4.54±0.59	4.34±0.65				
	NCD	4.16±0.37	4.38±0.58	4.03±0.35				
Cr + PCr	≥1 cup/day	7.59±0.33	7.71±0.18	7.96±0.10	0.001*	0.060	0.003*	
	<1 cup/day	8.20±0.49	8.28±0.30	8.21±0.24				
	NCD	7.88±0.45	7.80±0.23	7.67±0.17				
Glx	≥1 cup/day	11.33±0.45	11.21±1.56	11.13±2.09	0.001*	0.002*	0.014*	
	<1 cup/day	11.82±1.36	12.79±1.37	11.92±1.24				
	NCD	12.68±1.72	12.17±1.65	12.63±0.54				

Two-way repeated-measures ANOVA was performed. \*, statistically significant results ( $P < 0.05$ ). MRS, magnetic resonance spectroscopy; SD, standard deviation; GABA<sup>+</sup>,  $\gamma$ -aminobutyric acid-positive macromolecule; Glu, glutamate; NCD, non-coffee drinkers; GPC, glycerylphosphocholine; PCH, phosphocholine; Ins, myo-inositol; Cr, creatine; PCr, phosphocreatine; Glx, glutamate and glutamine; ANOVA, analysis of variance.

**Table S3** Cerebral metabolites in the posterior cingulate cortex voxel measured by MRS in healthy adult subjects pre-coffee, and 30 and 120 min post-coffee

Metabolite	Coffee consumption	Pre-coffee, mean ± SD	Post-coffee 30 min, mean ± SD	Post-coffee 120 min, mean ± SD	Interaction effect	Main effects	
					Time × group (P value)	Time (P value)	Group (P value)
GABA <sup>+</sup>	≥1 cup/day	3.09±0.28	3.18±0.27	3.02±0.36	0.064	0.213	0.089
	<1 cup/day	3.21±0.24	3.06±0.61	3.25±0.26			
	NCD	3.02±0.52	3.12±0.21	3.38±0.32			
Glu	≥1 cup/day	10.26±0.18	9.93±1.08	10.39±1.44	<0.0001*	<0.0001*	0.028*
	<1 cup/day	10.72±0.31	10.11±0.59	10.62±0.72			
	NCD	10.60±0.71	10.14±0.85	10.34±0.61			
GPC/GPC + PCH	≥1 cup/day	1.32±0.13	1.43±0.24	1.42±0.24	0.016*	<0.0001*	0.026*
	<1 cup/day	1.10±0.12	1.09±0.09	1.09±0.07			
	NCD	1.19±0.12	1.19±0.12	1.20±0.10			
Ins	≥1 cup/day	4.95±0.04	4.88±0.21	5.05±0.40	0.528	0.107	0.009*
	<1 cup/day	5.16±0.23	4.97±0.50	5.14±0.53			
	NCD	5.53±0.50	5.08±0.43	5.34±0.46			
Cr + PCr	≥1 cup/day	7.66±0.35	7.41±0.22	7.78±0.37	0.354	0.131	0.035*
	<1 cup/day	7.31±0.36	7.38±0.35	7.40±0.36			
	NCD	7.23±0.32	7.14±0.48	7.16±0.31			
Glx	≥1 cup/day	14.07±0.37	13.59±0.83	14.65±1.96	<0.0001*	<0.0001*	0.239
	<1 cup/day	14.39±0.39	14.17±1.00	15.02±1.77			
	NCD	14.07±1.01	13.61±1.53	14.52±1.07			

Two-way repeated-measures ANOVA was performed. \*, statistically significant results (P<0.05). MRS, magnetic resonance spectroscopy; SD, standard deviation; GABA<sup>+</sup>,  $\gamma$ -aminobutyric acid-positive macromolecule; Glu, glutamate; NCD, non-coffee drinkers; GPC, glycerylphosphocholine; PCH, phosphocholine; Ins, myo-inositol; Cr, creatine; PCr, phosphocreatine; Glx, glutamate and glutamine; ANOVA, analysis of variance.