Supplementary data

Potential of serum metabolites for diagnosing post-stroke cognitive impairment

Min Liu^{†,∥}, Kaige Zhou^{‡,∥}, Hailong Li[‡], Xin Dong[§], Guangguo Tan[⊥], Yifeng Chai[§],, Weizhong Wang ^{*,†}, Xiaoying Bi ^{1,‡}

[†]Departments of Physiology, College of basic medicine, Second Military Medical University, Shanghai 200433, China

[‡]Department of Neurology, Changhai Hospital, Second Military Medical University,

Shanghai 200433, China

§School of Pharmacy, Second Military Medical University, Shanghai 200433, China

[⊥]Department of Pharmaceutical Analysis, School of Pharmacy, Fourth Military Medical University, Xi'an 710032, China

Authors with equal contribution to the research.

¹ Corresponding Author: E-mail:bixy616@163.com; Tel.: +86-21-31161940; Fax: +86-21-31161940; (Bi X). E-mail: wangwz68@hotmail.com (Wang W); Tel.: +86-21-81870982.

Supplementary data

Table S1. Demographic and clinical details of recruited subjects;

Figure S1. Quality control (QC) plots of eleven randomly repeated runs of UHPLC–MS analysis using an artificial sample generated by principle component analysis using component 1 and 2. Peak area deviation could be evaluated by distribution of the runs. X-axis: run order; Y-axis: standard deviation. (A) QC plot for the first component from UHPLC–MS data; (B) QC plot for the second component from UHPLC–MS data;

Figure S2. Typical TICs obtained from plasma sample in different group in ESI positive mode based on UHPLC-Q-TOFMS. PSNIC group: post-stroke non-cognitive impairment group; PSCI-P: post-stroke cognitive impairment group.

Figure S3. Scores plots of OPLS-DA of PSNCI or PSCI patients vs healthy subjects, and permutation tests of their corresponding PLS-DA models. (A).
scores plot of OPLS-DA of PSNCI patients (●) versus healthy subjects (▲), (B). permutation test of PSNCI patients versus healthy subjects, (C). scores plot of OPLS-DA of PSCI patients (◆) versus healthy subjects (▲), (D). permutation test of PSCI patients versus healthy subjects.

Figure S4. Schematic overview of the disturbed metabolic pathways associated with stroke. Column value in histograms is expressed as mean±S.D.. Metabolites in red and blue represent progressive increase or decrease trend from healthy subjects to PSNCI patients to PSCI patients, respectively. PRPP, phosphoribosyl pyrophosphate.

Parameters	Training set				Test set	
	PSCI	PSNCI	Healthy	p value ^a	PSCI	PSNCI
Sample size	20	20	20	-	10	10
Gender (male/female)	10/10	10/10	10/10	-	5/5	5/5
Age(year)	66.10±6.50	67.50±8.64	67.30±6.81	0.811 ^{<i>b</i>}	67.40±6.85	66.80±7.54
Education(year)	10.02±3.33	10.51±3.39	11.11±3.89	0.243 ^b	10.34±4.27	10.29±4.47
MOCA	14.47±2.89	26.64±2.16	26.22±2.12	0.000 ^b	15.16±2.74	26.43±2.21
Cerebrovascular Risk						
Hypertention	10	14	-	0.197°	5	7
Hyperlipidemia	5	6	-	0.723°	3	3
Drinking	3	4	-	1.000°	2	3
Diabetes	4	10	-	0.057°	2	5
Smoking	4	7	-	0.288 ^c	2	4

Table 1. Demographic and clinical details of recruited subjects

^a The p value marked with "b" was calculated from One-way analysis of variance among PSCI, PSNCI and healthy group, and the p value marked with "c" was calculated from nonparametric test Mann–Whitney U test between PSCI group and PSNCI group.



Figure S1. Quality control (QC) plots of eleven randomly repeated runs of UHPLC–MS analysis using an artificial sample generated by principle component analysis using component 1 and 2. Peak area deviation could be evaluated by distribution of the runs. X-axis: run order; Y-axis: standard deviation. (A) QC plot for the first component from UHPLC–MS data; (B) QC plot for the second component from UHPLC–MS data



Figure S2. Typical TICs obtained from plasma sample in different group in ESI positive mode based on UHPLC-Q-TOFMS. PSNIC group: post-stroke non-cognitive impairment group; PSCI-P: post-stroke cognitive impairment group.



Figure S3. Scores plots of OPLS-DA of PSNCI or PSCI patients vs healthy subjects, and permutation tests of their corresponding PLS-DA models. (A). scores plot of OPLS-DA of PSNCI patients (●) versus healthy subjects (▲), (B). permutation test of PSNCI patients versus healthy subjects, (C). scores plot of OPLS-DA of PSCI patients (◆) versus healthy subjects (▲), (D). permutation test of PSCI patients versus healthy subjects.



Figure S4. Schematic overview of the disturbed metabolic pathways associated with stroke. Column value in histograms is expressed as mean±S.D.. Metabolites in red and blue represent progressive increase or decrease trend from healthy subjects to PSNCI patients to PSCI patients, respectively. PRPP, phosphoribosyl pyrophosphate.