Supplementary Information

Non-targeted Metabolomics Approach Revealed Significant Changes in Metabolic Pathways in Patients with Chronic Traumatic Encephalopathy

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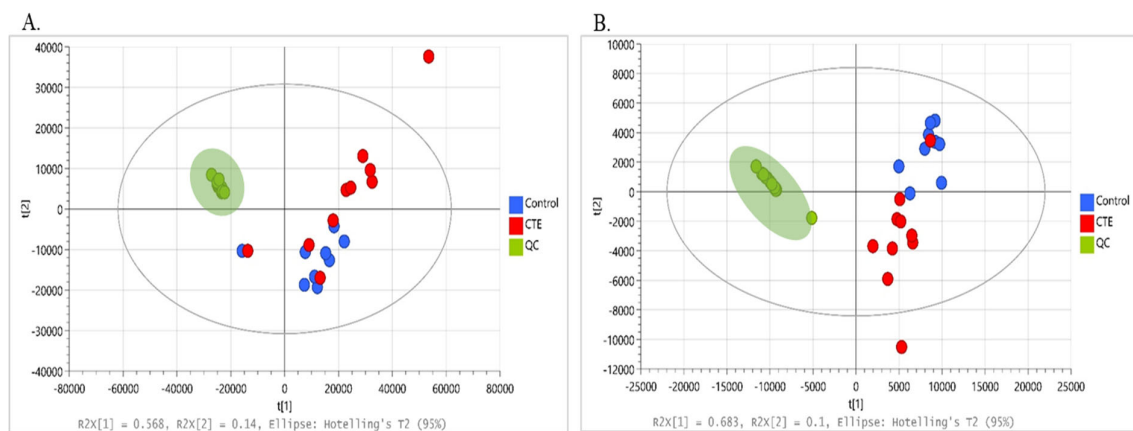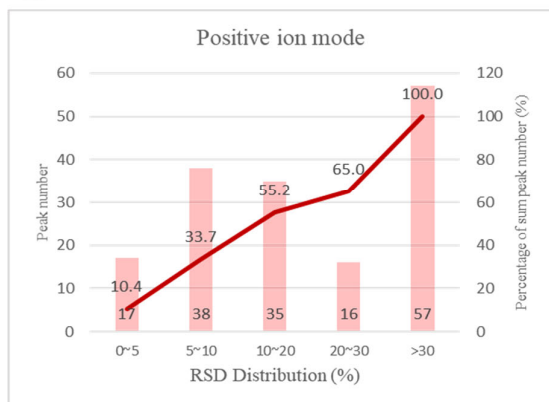
Figure S1. Principal component analysis (PCA) score plot of quality control (QC) samples.
(**A**) In positive ion mode. (**B**) In negative ion mode. Clustering of QC samples (green) indicate that the raw data was acquired with a good repeatability.
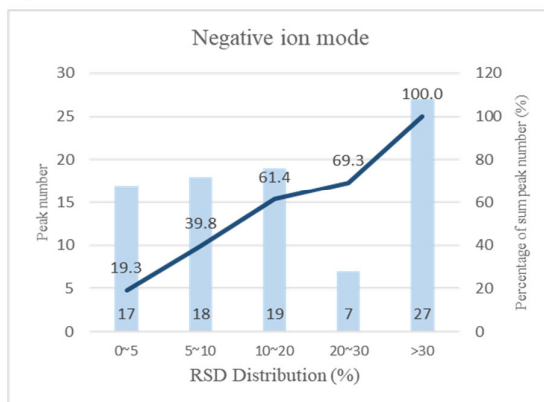
A.

Positive ion mode

B.

Negative ion mode

Figure S2. The relative standard deviation (RSD) of peaks in QC samples. (**A**) In positive ion mode. (**B**) In negative ion mode.
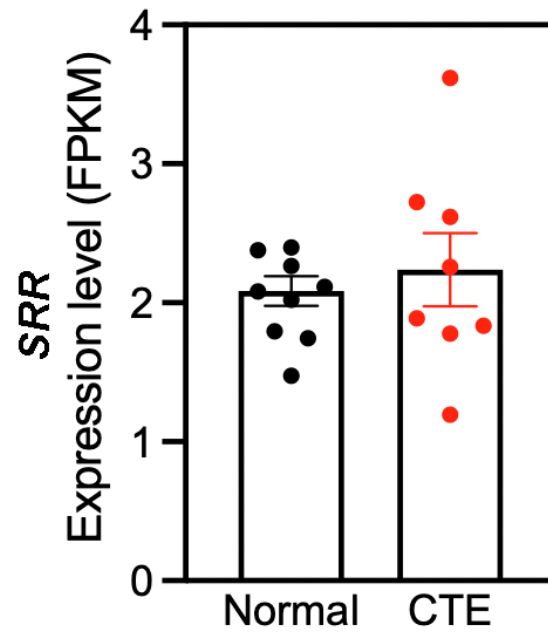
Figure S3. *Serine racemase* (*SRR*) **gene expression is slightly increased in CTE patients (***N* = 8) **compared to normal subjects (***N* = 8).** *P* value is 0.136

Table S1. Information on the postmortem brain tissues (superior temporal cortex) from control subjects and CTE patients. CTE stages [from stages I (mild) to IV (severe)] were determined according to Dr. McKee criteria based on the density and regional deposition of hyperphosphorylated tau (p-tau) pathology. The criteria for pathological diagnosis of CTE were adopted and refined by the National Institute of Neurological Disorders and Stroke (NINDS)/National Institute of Biomedical Imaging and Bioengineering (NIBIB).

Number	Case	Sex	Age	CTE Stage
1	Control	Female	101	N/A
2	Control	Female	87	N/A
3	Control	Male	74	N/A
4	Control	Male	86	N/A
5	Control	Female	87	N/A
6	Control	Male	89	N/A
7	Control	Male	67	N/A
8	Control	Male	82	N/A
9	Control	Male	61	N/A
1	CTE	Male	82	IV
2	CTE	Male	66	IV
3	CTE	Male	58	III
4	CTE	Male	79	IV
5	CTE	Male	52	III
6	CTE	Male	69	III
7	CTE	Male	70	IV
8	CTE	Male	82	IV
9	CTE	Male	66	IV
10	CTE	Male	53	III

Table S2. Reversed-phase LTQ-Orbitrap-MS gradient elution program for ESI+ and ESI− modes.

Time (min)	Mobile phase A (%)	Mobile phase B (%)
0	100	0
3	100	0
10	50	50
12	10	90
12.5	100	0
14	100	0

Table S3. The detailed results of metabolic pathway analysis.

Pathway Name	Total	Hits	Raw p	−log(10)p	FDR	Impact
Tyrosine metabolism	42	4	0.0001	4.15	0.0014	0.2460
Arginine and proline metabolism	38	4	0.0017	2.76	0.0110	0.1169
Glycine, serine and threonine metabolism	33	4	0.0104	1.98	0.0237	0.2267
Aminoacyl-tRNA biosynthesis	48	4	0.0127	1.90	0.0237	0.1667
Phenylalanine, tyrosine and tryptophan biosynthesis	4	2	0.0151	1.82	0.0237	1.0000
Phenylalanine metabolism	10	2	0.0151	1.82	0.0237	0.3571
Nicotinate and nicotinamide metabolism	15	1	0.0162	1.79	0.0237	0.1943
Retinol metabolism	17	1	0.0321	1.49	0.0359	0.2165