

Table S1. Clinical characteristics of each patient included in this study

Patient	Sex	Age	Diagnosis
TBI-1	Male	23	CML
TBI-2	Male	21	ALL
TBI-5	Female	42	ALL
TBI-6	Male	29	NHL
TBI-7	Male	28	ALL
TBI-8	Male	21	AML
TBI-9	Male	22	ALL
TBI-10	Male	36	ALL
TBI-11	Female	22	ALL
TBI-12	Male	34	ALL
TBI-13	Male	40	NHL
TBI-14	Male	17	ALL
TBI-15	Female	28	NHL
TBI-16	Female	31	AML
TBI-17	Male	49	NHL
TBI-18	Female	32	ALL
TBI-19	Female	17	AML
TBI-20	Male	47	AML
TBI-21	Male	27	AML
TBI-22	Male	46	NHL
TBI-23	Male	20	NHL
TBI-24	Male	33	NHL
TBI-25	Male	51	ALL
TBI-26	Male	14	ALL
TBI-27	Male	39	NHL
TBI-28	Female	34	AML
TBI-29	Male	33	CML
TBI-30	Male	13	ALL
TBI-31	Male	32	ALL
TBI-32	Male	37	ALL
TBI-33	Female	33	AML
TBI-34	Male	40	NHL
TBI-35	Male	35	AML
TBI-36	Male	21	ALL
TBI-37	Male	10	AML
TBI-38	Male	15	ALL

Table S2. The statistical information of significantly differential metabolites based on pseudotargeted GC–MS method

Metabolites	Rt (min)	Peak Ion (m/z)	Pre-TBI	After-TBI	p value	FDR	Female		Male	
							p value	Fold Change	p value	Fold change
Lactate ^a	7.85	219	753.92±272.92	525.32±252.22	0.000137	0.00038	0.10938	0.7	0.001555	0.7
Glycolate ^a	8.32	66	0.19±0.07	0.14±0.03	0.000172	0.000427	0.3125	0.9	0.000342	0.8
Valine ^a	8.66	72	23.16±12.71	39.89±30.12	0.00051	0.000976	0.38281	1.1	0.000473	1.7
Acetoacetate ^a	9.45	89	0.54±0.60	1.62±3.33	0.016004	0.017006	0.64063	1.1	0.015633	2.4
3-hydroxybutyric acid (Hyb)	10.72	147	32.56±27.26	91.77±195.47	0.016753	0.017006	0.94531	1.4	0.011024	2
3-Methyl-2-Oxovaleric acid (OMV)	11.23	89	1.53±0.65	1.25±0.52	0.009959	0.011706	0.14844	0.7	0.042608	0.8
3-Hydroxyisovaleric acid (HMB)	12.07	131	0.70±0.49	1.28±0.81	1.15E-06	9.66E-06	0.007813	1.8	1.77E-05	1.8
Urea	13.23	189	780.33±338.31	1,227.54±642.70	0.000148	0.00038	0.14844	1.3	0.000381	1.5
Ethanolamine (ETA)	13.67	174	5.23±2.14	3.81±1.09	0.000148	0.00038	0.64063	0.9	0.000153	0.7
Leucine	14.34	158	43.59±12.73	77.49±67.44	0.002339	0.003483	0.015625	1.5	0.024749	1.4
Glycerol	13.97	205	33.38±35.55	50.23±42.64	0.016753	0.017006	0.3125	1.6	0.031709	1.6
Succinate	15.08	147	1.14±0.44	0.79±0.23	9.96E-05	0.000303	0.14844	0.8	0.000342	0.7
Threonine	16.95	218	18.19±11.42	27.04±14.98	0.016004	0.017006	0.25	1.6	0.029833	1.4
Malate	19.61	233	0.18±0.16	0.11±0.06	0.000186	0.000429	0.38281	0.9	0.000244	0.6
4-Hydroxy-L-proline (Hyp)	20.49	230	4.77±3.32	2.19±1.13	7.11E-07	9.53E-06	0.64063	0.9	1.04E-07	0.4
Benzoate	13.17	179	0.04±0.03	0.03±0.01	0.000991	0.001747	0.039063	0.8	0.012704	0.8
Hypotaurine	22.16	188	0.79±0.57	0.49±0.24	6.09E-05	0.000204	0.25	0.8	7.20E-05	0.7
Glutamate	22.78	246	30.04±20.95	20.21±9.34	0.009481	0.011343	0.3125	0.9	0.017887	0.7
Phenylalanine	22.81	218	44.85±19.81	32.92±12.40	0.000386	0.000783	0.078125	0.8	0.002234	0.7
Hypoxanthine	26.79	265	3.41±4.15	1.91±3.46	0.000186	0.000429	0.039063	0.5	0.002662	0.5
Citrate	27.13	273	3.84±1.91	2.62±1.22	0.00051	0.000976	0.10938	0.8	0.002902	0.7
1,5-Anhydroglucitol (AG)	27.76	217	31.63±17.41	18.46±12.95	2.21E-07	4.93E-06	0.015625	0.4	1.77E-05	0.6
D-Galactose (GAL)	28.47	319	18.61±13.69	23.80±8.69	0.002339	0.003483	0.94531	1	0.000875	1.5

Metabolites	Rt (min)	Peak Ion (m/z)	Pre-TBI	After-TBI	p value	FDR	Female		Male	
							p value	Fold Change	p value	Fold change
Lysine	29.23	174	54.66±19.23	86.19±45.85	1.76E-05	9.09E-05	0.3125	1.5	3.66E-05	1.5
Mannitol	29.30	319	2.20±5.68	5.35±9.81	0.000117	0.00034	0.38281	1.8	0.000106	2.4
gluconate	30.67	333	1.75±6.64	4.37±4.88	5.42E-06	3.63E-05	1	1.1	1.51E-05	9.2
Indole-3-propionic acid (IPA)	32.22	202	0.34±1.30	0.22±1.05	1.02E-06	9.66E-06	0.007813	0.4	0.000106	0.4
Myoinositol	32.37	305	11.56±6.24	7.32±3.46	1.33E-05	7.41E-05	0.054688	0.6	0.000244	0.7
Urate	32.65	441	28.63±21.61	8.48±9.99	3.77E-07	6.31E-06	0.007813	0.3	4.77E-06	0.2
Indolelactate	33.87	202	0.37±0.35	0.28±0.21	0.007009	0.008697	0.078125	0.7	0.040214	0.8

Note: For pseudotargeted GC-MS metabolic profiling, data was acquired with selected ion monitoring (SIM) mode.

Table S3 The statistical information of significantly differential metabolites based on pseudotargeted LC–MS method

Metabolites	Ion adducts	Rt (min)	Precursor Ion (m/z)	Product Ion(m/z)	CE (eV)	Pre-TBI	After-TBI	p value	FDR	Female		Male	
										p value	Fold Change	p value	Fold change
FFA(18:2)	[M-H] ⁻	14.82	279.2	279.2	22	8.89±6.41	15.05±14.28	0.01152	0.013082	0.38281	1.3	0.019113	1.6
FFA(18:1)	[M-H] ⁻	15.91	281.2	281.2	22	0.63±0.46	1.06±1.01	0.01152	0.013082	0.38281	1.3	0.019113	1.6
FFA18:3	[M-H] ⁻	13.74	277.2	277.2	22	1.77±1.66	5.49±11.71	0.001199	0.002061	0.007813	4.8	0.045118	1.7
Deoxycholic acid (DCA)	[M-H] ⁻	14.44	391.3	343.3	37	0.02±0.03	0.01±0.00	0.004598	0.006161	0.054688	0.6	0.042608	0.8
Glycodeoxycholic acid (GDCA)	[M-H] ⁻	12.79	448.3	74.1	38	0.014±0.02	0.007±0.01	0.006321	0.008145	0.10938	0.4	0.035754	0.5
Tryptophan	[M-H] ⁻	4.51	202.9	116.1	21	0.11±0.04	0.15±0.08	0.006658	0.008416	0.46094	1	0.006549	1.4
Glycochenodeoxycholate-3-sulfate (GCDCS)	[M-H] ⁻	12.60	528.2	448.2	38	0.14±0.18	0.05±0.04	0.000359	0.000753	0.078125	0.4	0.002662	0.4
Aspartate	[M+H] ⁺	9.16	134.2	74.1	13	0.02±0.01	0.01±0.01	0.005399	0.007093	0.3125	0.6	0.013624	0.8
Acetylcholine	[M+H] ⁺	8.73	146.1	87.1	13	0.48±0.20	0.64±0.31	0.004123	0.005638	0.10938	1.6	0.02805	1.2
Glutamine	[M+H] ⁺	0.81	147.1	84.1	16	0.39±0.12	0.57±0.24	0.000233	0.000519	0.039063	1.4	0.003161	1.4
Carnitine C3(AC3)	[M+H] ⁺	1.16	218.2	85.1	20	54.50±34.70	98.84±79.05	0.013288	0.014595	0.3125	2	0.026357	1.5
Creatinine	[M+H] ⁺	0.80	114.1	44.0	17	0.83±0.22	1.08±0.40	2.79E-05	9.83E-05	0.10938	1.1	0.000172	1.3
Ornithine	[M+H] ⁺	1.14	133.1	70.0	12	0.10±0.03	0.07±0.02	6.66E-06	4.05E-05	0.007813	0.5	0.000716	0.7
Daidzein	[M+H] ⁺	4.41	255.2	199.1	24	0.02±0.01	0.03±0.01	2.79E-05	9.83E-05	0.039063	1.5	0.000473	1.5
Carnitine C4(AC4)	[M+H] ⁺	2.02	232.1	85.0	19	48.42±30.44	155.61±150.29	1.94E-05	9.27E-05	0.015625	4.1	0.000425	2.1
Carnitine C18:1(AC18:1)	[M+H] ⁺	17.10	426.2	85.0	29	162.13±73.41	116.61±52.11	0.009023	0.010992	0.38281	1.1	0.000792	0.6
LPE16:0	[M+H] ⁺	9.90	454.3	313.2	22	6.99±3.89	12.72±7.78	2.33E-05	9.74E-05	0.039063	2	0.000583	1.7
LPE18:0	[M+H] ⁺	11.20	482.3	341.2	22	7.50±4.44	14.18±9.27	2.86E-06	2.13E-05	0.007813	1.9	0.000153	1.8
LPC16:0	[M+H] ⁺	9.80	496.3	184.1	27	1.54±0.28	1.72±0.35	0.003692	0.005378	0.38281	1.1	0.007629	1.1
LPC18:1	[M+H] ⁺	10.21	522.3	184.1	23	0.77±0.18	0.91±0.26	0.003902	0.005563	0.46094	1.1	0.006549	1.2
LPE22:6	[M+H] ⁺	9.62	526.3	385.3	18	1.59±1.08	2.77±1.79	0.000764	0.001383	0.007813	2.5	0.026357	1.7

Arginine	[M+H] ⁺	0.68	175.1	70.0	21	1.48±0.47	2.26±1.41	0.002206	0.003437	0.039063	1.5	0.017887	1.3
PC32:0	[M+H] ⁺	16.66	734.6	184.1	30	0.80±0.14	0.76±0.11	0.016753	0.017006	0.14844	0.9	0.06624	1
PC34:2	[M+H] ⁺	16.65	785.6	184.1	22	8.98±1.66	7.77±1.34	7.81E-05	0.000249	0.023438	0.9	0.001065	0.9
PC34:1	[M+H] ⁺	16.81	760.6	184.1	22	7.30±0.33	7.61±0.57	0.001538	0.002576	0.54688	1	0.001867	1
PC(O-36:2)	[M+H] ⁺	16.86	772.6	184.1	30	0.37±0.15	0.31±0.10	0.001959	0.003202	0.015625	0.8	0.026357	0.9
PC36:4	[M+H] ⁺	16.75	782.6	184.1	30	8.41±1.60	6.65±1.43	2.12E-05	9.48E-05	0.015625	0.7	0.001172	0.8
PC36:2	[M+H] ⁺	16.91	786.6	184.1	30	11.22±2.76	9.87±2.01	0.004123	0.005638	0.039063	0.9	0.031709	0.9
Carnitine C2(AC2)	[M+H] ⁺	0.87	204.1	85.0	15	583.49±354.45	820.19±397.52	0.012085	0.013495	0.007813	2.7	0.14377	1.2
PC(O-38:5)	[M+H] ⁺	16.68	794.6	184.1	42	0.07±0.02	0.04±0.01	3.11E-08	1.04E-06	0.007813	0.5	6.74E-06	0.6
PC38:6	[M+H] ⁺	16.35	806.5	184.1	30	0.11±0.03	0.07±0.02	3.20E-09	2.15E-07	0.007813	0.5	5.22E-07	0.6
PC38:4	[M+H] ⁺	16.45	810.5	184.1	30	0.22±0.07	0.16±0.06	0.000764	0.001383	0.10938	0.6	0.004778	0.7
PC40:6	[M+H] ⁺	17.07	834.6	184.1	45	0.24±0.07	0.16±0.06	1.02E-06	9.66E-06	0.078125	0.6	4.77E-06	0.6
PE38:4	[M+H] ⁺	16.40	768.6	627.5	22	0.69±0.63	1.82±2.17	0.000335	0.000723	0.3125	2	0.000526	2.7
PE40:6	[M+H] ⁺	17.02	792.6	186.5	22	3.22±2.77	5.70±4.29	0.002206	0.003437	0.25	1.6	0.008225	1.7
Hippurate	[M-H] ⁻	5.51	178.1	134.1	18	9.71±1.79	12.29±2.38	2.79E-05	9.83E-05	0.10938	1.1	0.000153	1.3

Note: ① For pseudotargeted LC-MS metabolic profiling, data was acquired with selected reaction monitoring (SRM) mode; ② PC , PC-O, LPC, PE , LPE and FFA represent phosphatidylcholines, alkyl and ether-linked substituent PCs, lyso-phosphatidylcholines, phosphatidylethanolamines , lyso-phosphatidylethanolamines and free fatty acids; ③ For paired analysis, FCs are calculated by computing the ratio between paired samples, (i.e. one FC per pair), and then compute their means (i.e. pair means).

Table S4 Statistical results of the linear stepwise regression method

Feature variable	Coefficient	Significance	VIF
(Constant)	2.296	.000	-
PC(O-38:5)	-3.781	.002	1.830
Urate	-.004	.003	1.596
Ornithine	-5.178	.000	1.298
Hippurate	.082	.000	2.094
Aspartate	-18.049	.000	1.117
AG	-.009	.000	1.688
GCDCS	-.818	.000	1.372
PC40:6	-1.554	.000	1.784
Hypoxanthine	.024	.001	1.530
Acetylcholine	-.298	.008	1.821

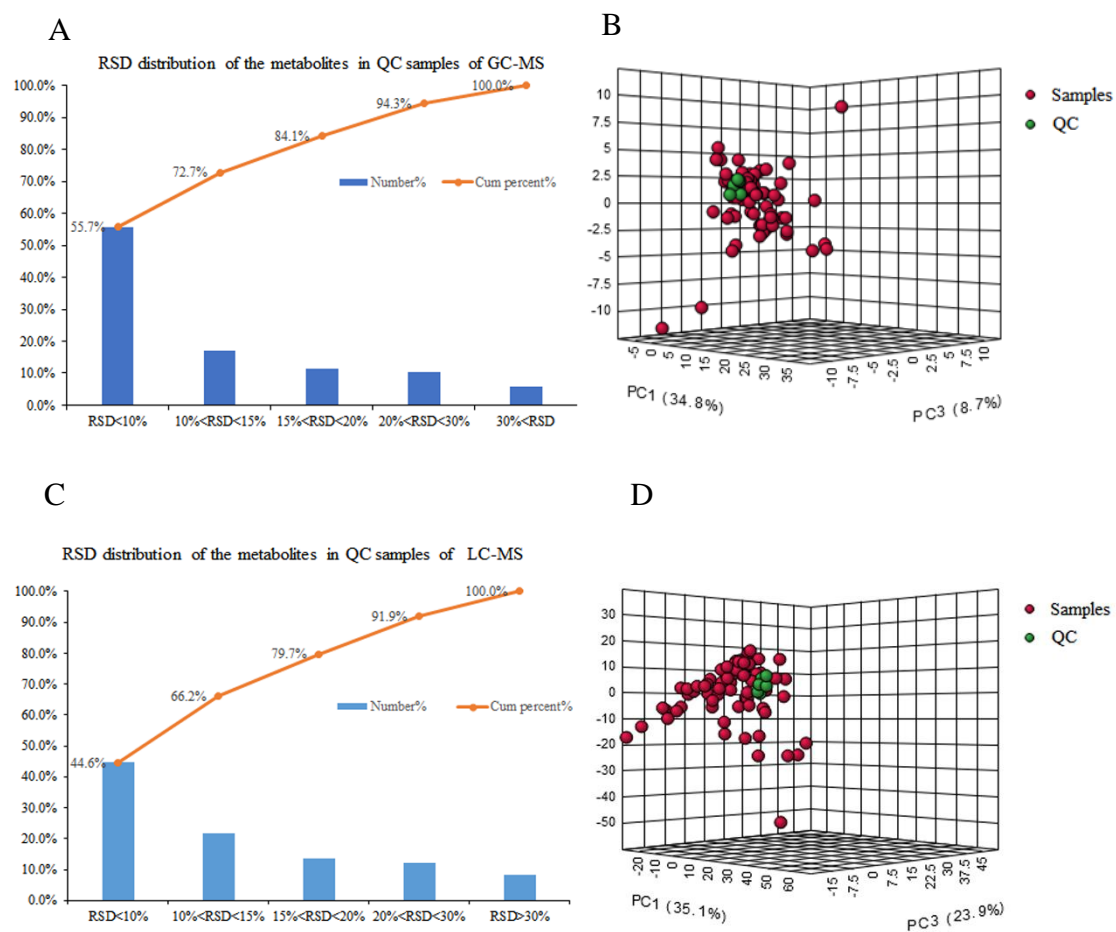


Fig.S1 RSD distributions of the metabolites in QC samples (A, C) and PCA score plots (B, D) of the sample distributions in GC-MS and LC-MS

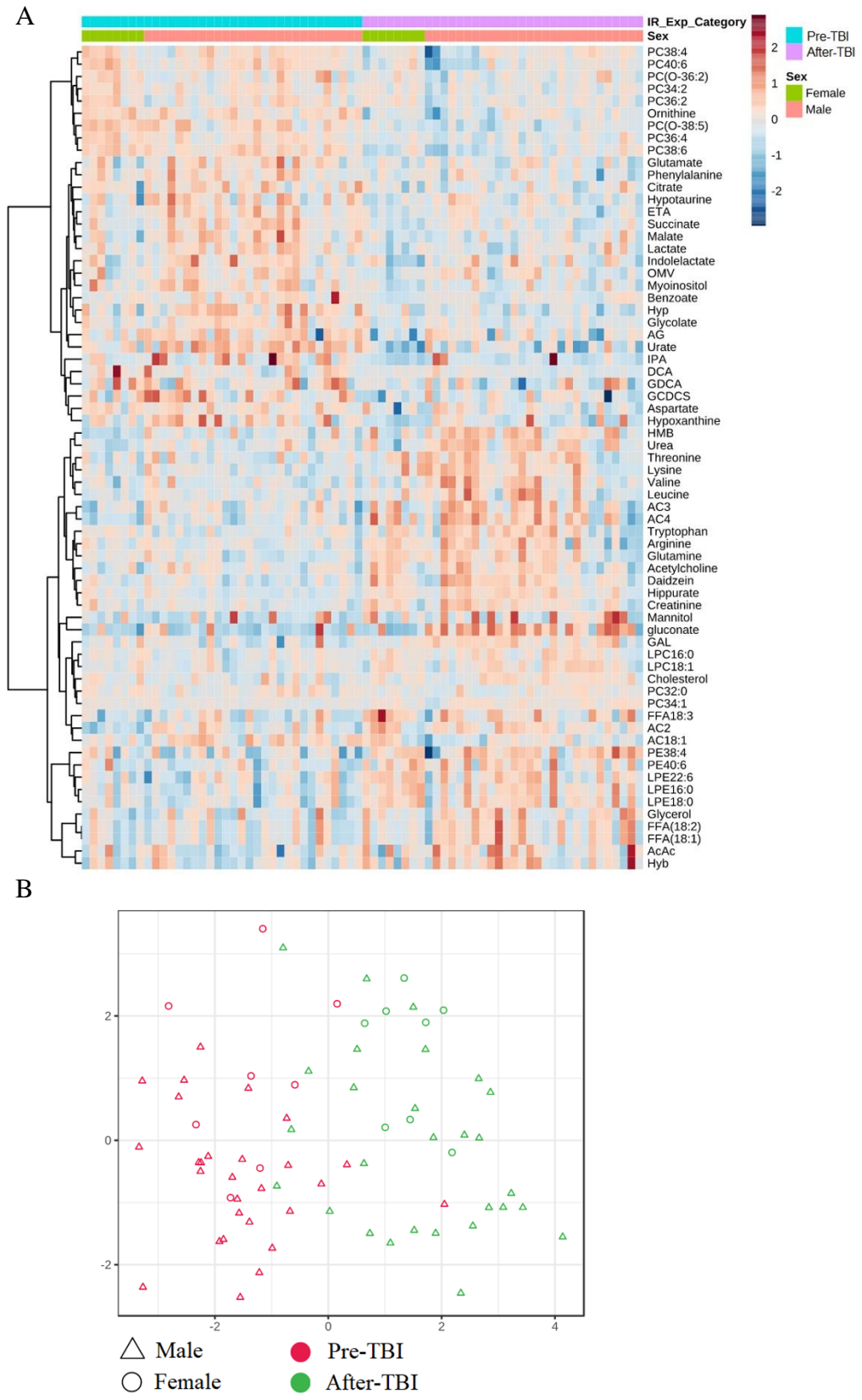


Fig.S2 Sex-dependent plasma metabolic pattern changes between Pre-TBI and After-TBI groups based on a heatmap (A) and a PCA plot (B).

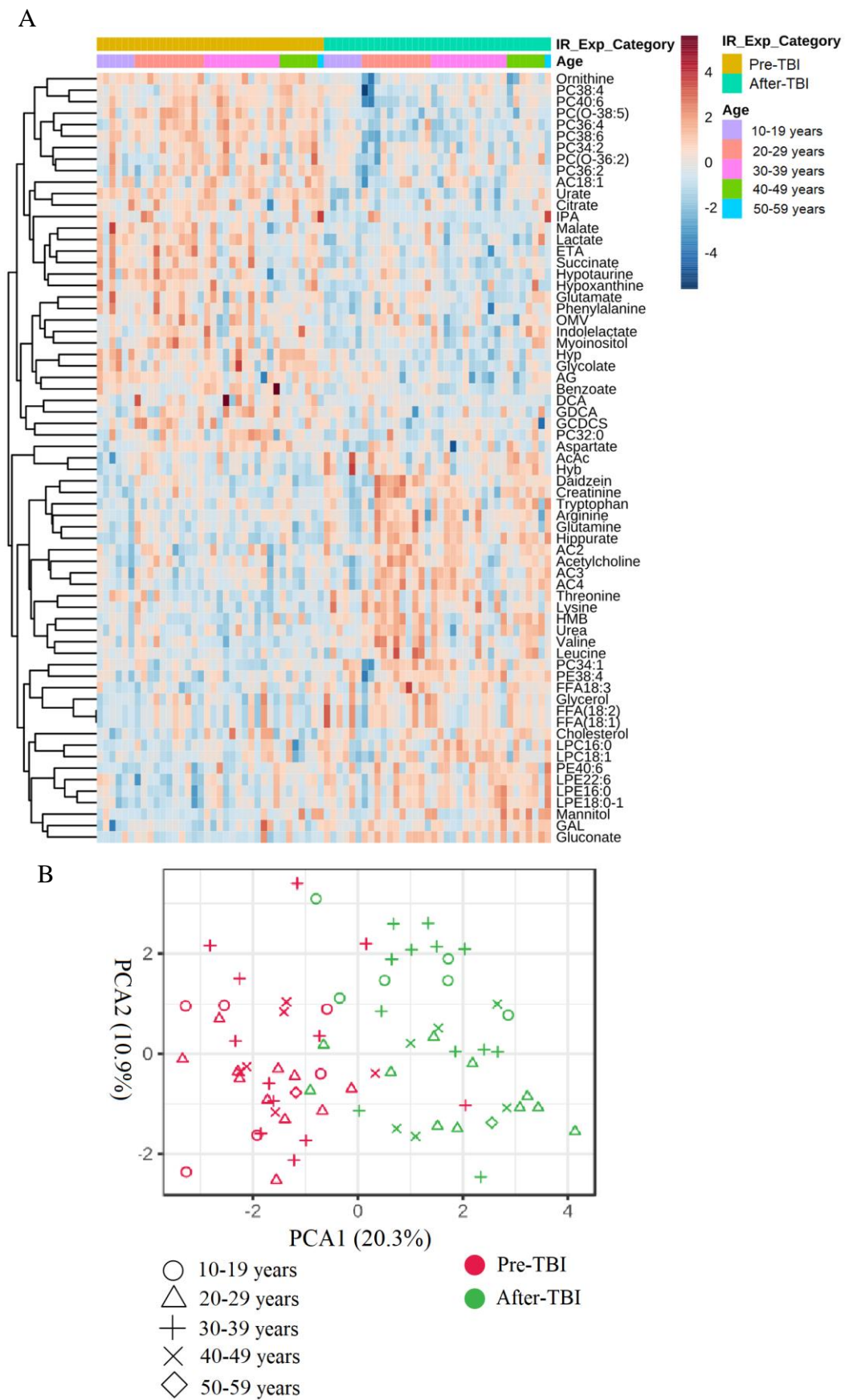


Fig.S3 Effect of age on plasma metabolic pattern changes in Pre-TBI and After-TBI groups based on a heatmap (A) and a PCA plot (B)

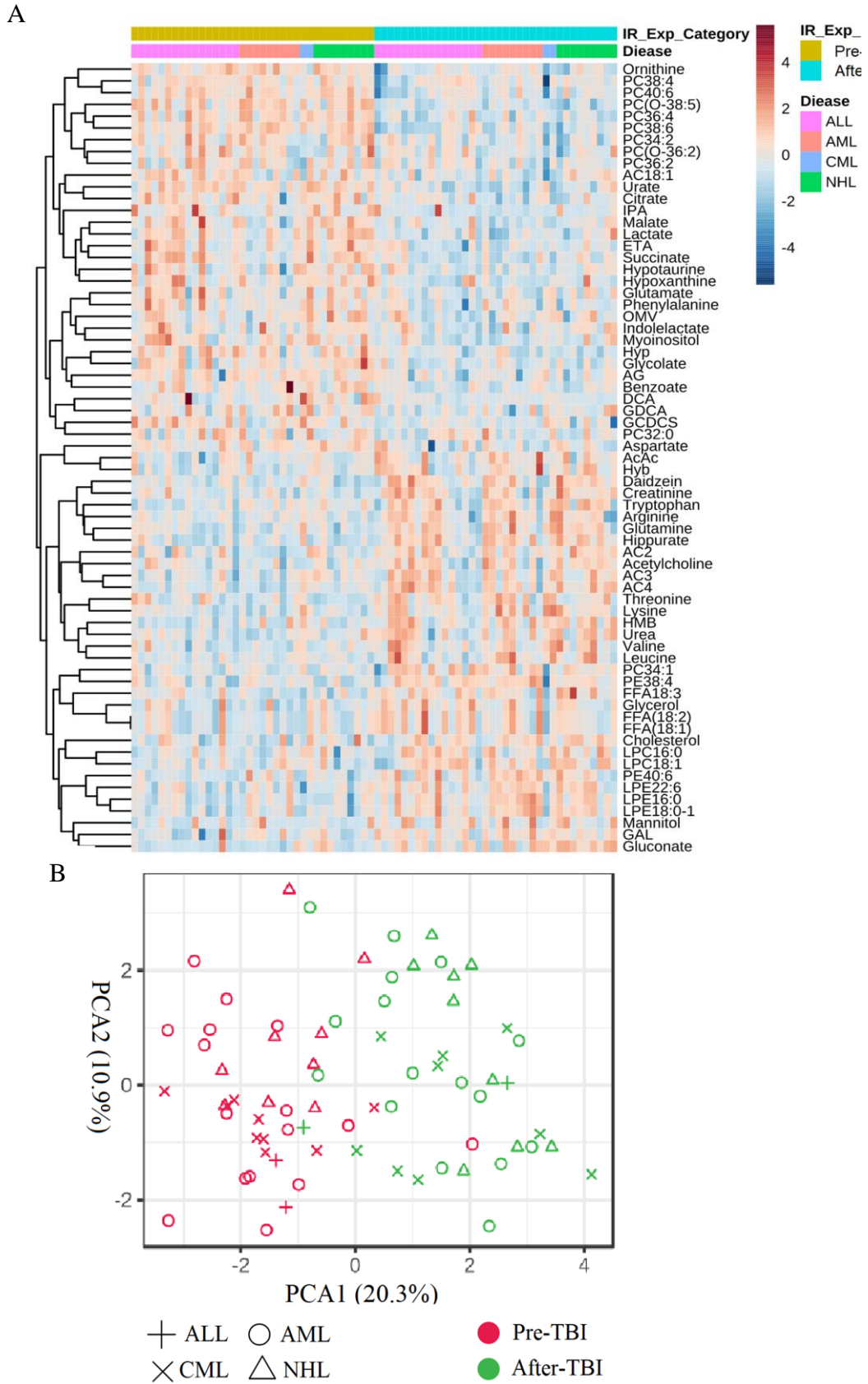


Fig.S4 Effect of disease type on plasma metabolic pattern changes in Pre-TBI and After-TBI groups based on a heatmap (A) and a PCA plot (B)

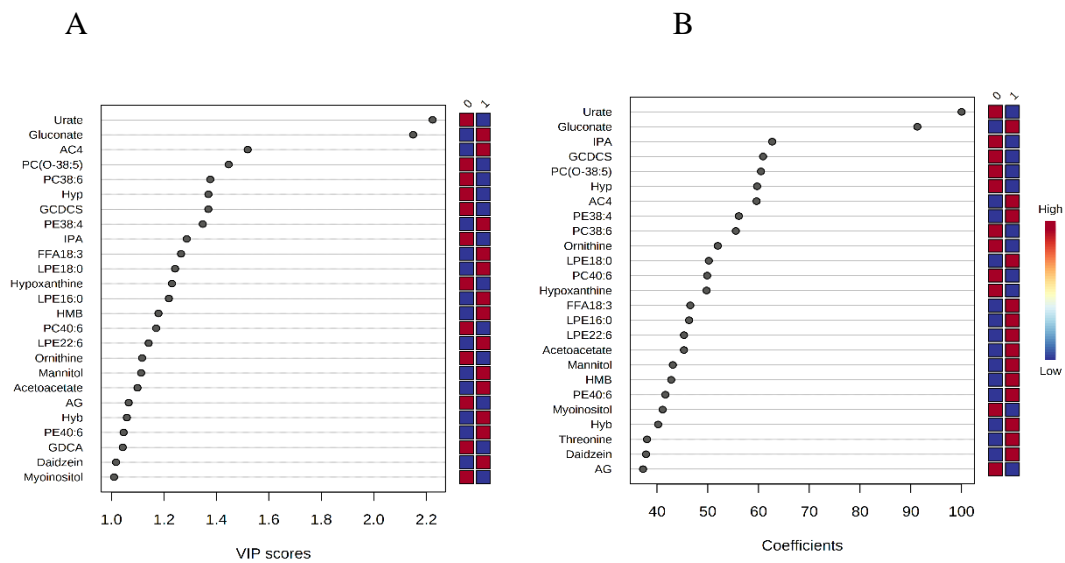


Fig.S5 The heatmap of VIP scores(A) and coefficients(B) from metabolites responsible for the separation observed in the PLS-DA model.