

Supplementary materials

Metabolic impact of methamphetamine on the systemic metabolism of rats and potential markers of methamphetamine abuse

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Table S1 The identified endogenous compounds in rat serum

Retention Time	m/z	Compound
4.605	152	3-Hydroxypyridine
4.705	174	Pyruvic Acid
4.935	190	Ethanedioic Acid
5.035	219	Lactate
5.135	131	2-Hydroxyisobutyric Acid
5.160	177	Glycolic Acid
5.530	116	Alanine
5.660	204	Glycine
5.715	174	Acetylglycine
6.095	233	3-Hydroxybutyric Acid
6.145	188	Heptanoic Acid
6.185	189	2-Oxoisocaproic Acid
6.250	130	Alpha-Aminoisobutyricacid
6.420	261	Urea
6.670	218	Valine
6.675	144	2-Keto-3-Methylvaleric Acid
6.750	191	Bis-Hydroxyacetic Acid
6.850	174	Silamine
7.085	299	Phosphate
7.145	158	Leucine
7.210	218	Glycerol
7.310	142	Proline
7.325	218	Isoleucine
7.335	247	Succinic Acid
7.525	256	Uracil
7.600	292	Glyceric Acid
7.630	245	Fumaric Acid
7.750	292	2,3-Dihydroxybutanoic Acid
7.835	218	Serine
8.060	291	Threonine
8.215	373	Decanedioic Acid
8.310	290	Beta.-Alanine
8.335	233	3,4-Dihydroxybutanoic Acid
8.400	243	Citrulline
8.545	320	Aminomalonic Acid
8.625	243	2,5-Diaminovalerolactam
8.685	233	Malic Acid
8.785	156	Pyroglutamic Acid
8.845	293	Methionine
8.895	232	1h-Indole-Acetic Acid
8.895	232	Aspartic Acid
8.980	230	Hydroxyproline
9.125	329	Creatinine
9.230	292	Threonic Acid
9.500	246	Glutamic Acid
9.500	142	Ornithine
9.530	218	Phenylalanine

9.635	257	Lauric Acid
9.770	231	Asparagine
9.795	326	Taurine
9.820	204	Gluconic Acid
10.335	156	Glutamine
10.350	357	Glycerol-3-Phosphate
10.655	157	2-Ketoglutaric Acid
10.690	273	Citric Acid
11.100	254	L-Histidine
11.165	307	Fructose
11.205	319	Glucose
11.265	319	Glucose
11.265	218	Lysine
11.365	319	Glucose
11.445	361	D-Galactono-1,4-Lactone
11.610	311	Cis-9-Hexadecenoic acid
11.720	313	Palmitic Acid
11.815	333	1h-Indole-3-Propanoic Acid
11.855	204	Beta-D-Methylglucopyranoside
11.945	305	Myo-Inositol
12.020	441	Uric Acid
12.055	298	Methyl Octadecanoate
12.180	327	Heptadecanoic Acid
12.260	305	Myo-Inositol
12.425	307	Kynurenine
12.475	337	Linoleic Acid
12.505	339	Oleic Acid
12.570	202	Tryptophan
12.625	341	Stearic Acid
12.950	218	Cystine
13.150	150	Arachidonic Acid
13.385	367	11-Eicosaenoic Acid
13.595	290	5-Hydroxytryptamine
13.670	387	Myo-Inositol-1-Phosphate
14.085	371	Monopalmitin
14.900	399	Monostearin
17.085	502	Alpha-Tocopherol
17.325	458	Cholesterol
18.245	472	Campesterol
18.990	516	Cholic Acid
19.160	486	Sitosterol

Table S2 The identified endogenous compounds in rat urine

Retention Time	m.z	Compound
4.705	174	Pyruvic Acid
5.035	191	Lactate
5.135	131	2-Hydroxyisobutyric Acid
5.16	205	Glycolic Acid
5.525	116	Alanine
5.655	202	N-Butylamine
5.66	204	Glycine
5.715	174	Acetylglycine
6.100	233	3-Hydroxybutyric Acid
6.135	241	Monomethylphosphate
6.14	188	Heptanoic Acid
6.63	189	Urea
6.745	191	Benzoic Acid
6.845	174	2-Aminoethanol
7.080	314	Phosphate
7.21	218	Glycerol
7.305	142	Proline
7.31	116	Silylamine
7.335	247	Succinic Acid
7.525	241	Uracil
7.600	292	Glyceric Acid
7.625	245	Fumaric Acid
7.745	292	2,3-Dihydroxybutanoic Acid
7.835	204	Serine
7.95	130	Methamphetamine*
8.000	259	Mesaconic Acid
8.06	291	Threonine
8.335	233	3,4-Dihydroxybutanoic Acid
8.565	274	Glycine
8.68	335	Butanedioic Acid
8.680	233	Malic Acid
8.785	156	Pyroglutamic Acid
8.890	217	Erythrose
8.96	217	Erythritol
9.115	288	2-Ketoglutaric Acid
9.145	292	Threonic Acid
9.185	307	Erythritol Per-Tms
9.31	296	Oxidized Dithioerythritol
9.45	329	Creatinine
9.495	246	Glutamic Acid
9.525	296	4-Hydroxyphenylacetic Acid
9.85	307	Lyxose

9.850	307	Ribose
9.965	277	5-Hydroxyindole
10.180	375	Aconitic Acid
10.22	307	Arabitol
10.220	319	Xylitol
10.255	218	Canavanine
10.300	217	Ribitol
10.305	277	Fucose
10.515	206	Hippuric Acid
10.590	292	2-Keto-L-Gluconic Acid
10.595	292	Ribonic Acid
10.685	465	Citric Acid
10.84	218	Cysteine
10.94	318	Scyllo-Inositol
10.965	274	Ascorbic Acid
11.025	431	Allantoin
11.36	319	D-Glucose
11.435	333	Glucuronic Acid
11.715	313	Palmitic Acid
11.87	333	Galactonic Acid
11.945	305	Myo-Inositol
12.015	456	Uric Acid
12.145	319	N-Acetyl Glucosamine
12.26	305	Inositol
12.365	319	Galactose
12.47	319	D-Glucitol
12.5	319	Mannitol
12.625	341	Stearic Acid
12.745	406	2-Quinolinecarboxylic Acid
13.145	357	Pseudo Uridine
13.33	217	Beta.-Dl-Arabinopyranose
13.655	217	Glucoheptulose
13.72	259	Ononitol
13.825	375	Beta.-D-Glucopyranosiduronic Acid
14.495	217	Allonic Acid
14.565	259	Xylobiose
14.61	361	Lactose
15.630	375	4-Hydroxyhippuric Acid

Table S3 Relative abundance of urine metabolites in rats exposed to METH (n=6)

Metabolic Pathways	Metabolites	Pre	D5	D5+2
Amino acids	Serine	8.58±1.65	36.34±24.35*	4.25±1.87
	Glutamate	15.24±6.24	61.95±3.40**	5.93±3.05
	Glycine	20.27±8.75	57.38±37.46	22.63±17.42
	Alanine	16.58±4.90	56.47±16.40*	11.04±5.75
FFAs and lipids	Glycerol	2.46±0.74	6.60±2.78*	1.83±0.75
	Palmitic acid	8.18±4.61	8.77±3.24	5.31±1.00
	Stearic acid	5.35±2.04	5.18±1.43	3.34±0.56
	3-Hydroxybutyrate	1.12±0.35	3.69±2.06*	0.56±0.28
Organic acid	Hippurate	57.91±13.24	31.65±10.48**	14.30±2.81**
	Lactate	5.22±1.08	13.05±1.79**	12.43±0.97**
	Galactonate	31.36±15.08	80.39±46.90*	13.90±11.23
	Pyruvate	2.02±0.32	4.33±2.08*	1.12±0.26
TCA intermediates	Fumarate	3.35±1.33	16.37±7.91*	1.64±0.64
Others	Succinate	7.95±2.85	38.16±12.78*	8.52±7.18
	Citrate	27.50±17.82	31.55±1.24	16.70±7.02
	Myo-Inositol	12.33±3.44	45.80±12.20**	5.80±4.11
Parent drug	5-hydroxyindoleacetic acid	59.03±18.30	21.87±9.56**	21.50±8.45
	METH	0.04±0.11	145.29±102.28**	0.16±0.13

Note: Peak areas of the metabolites were normalized against those of the internal standard, and the data are given as the mean ± SD. Pre, pre-administration of METH; D5, exposure to METH for 5 days; D5+2, withdrawal of METH for 2 days.

* P < 0.05, significantly different compared with control; ** P < 0.01, significantly different compared with control.

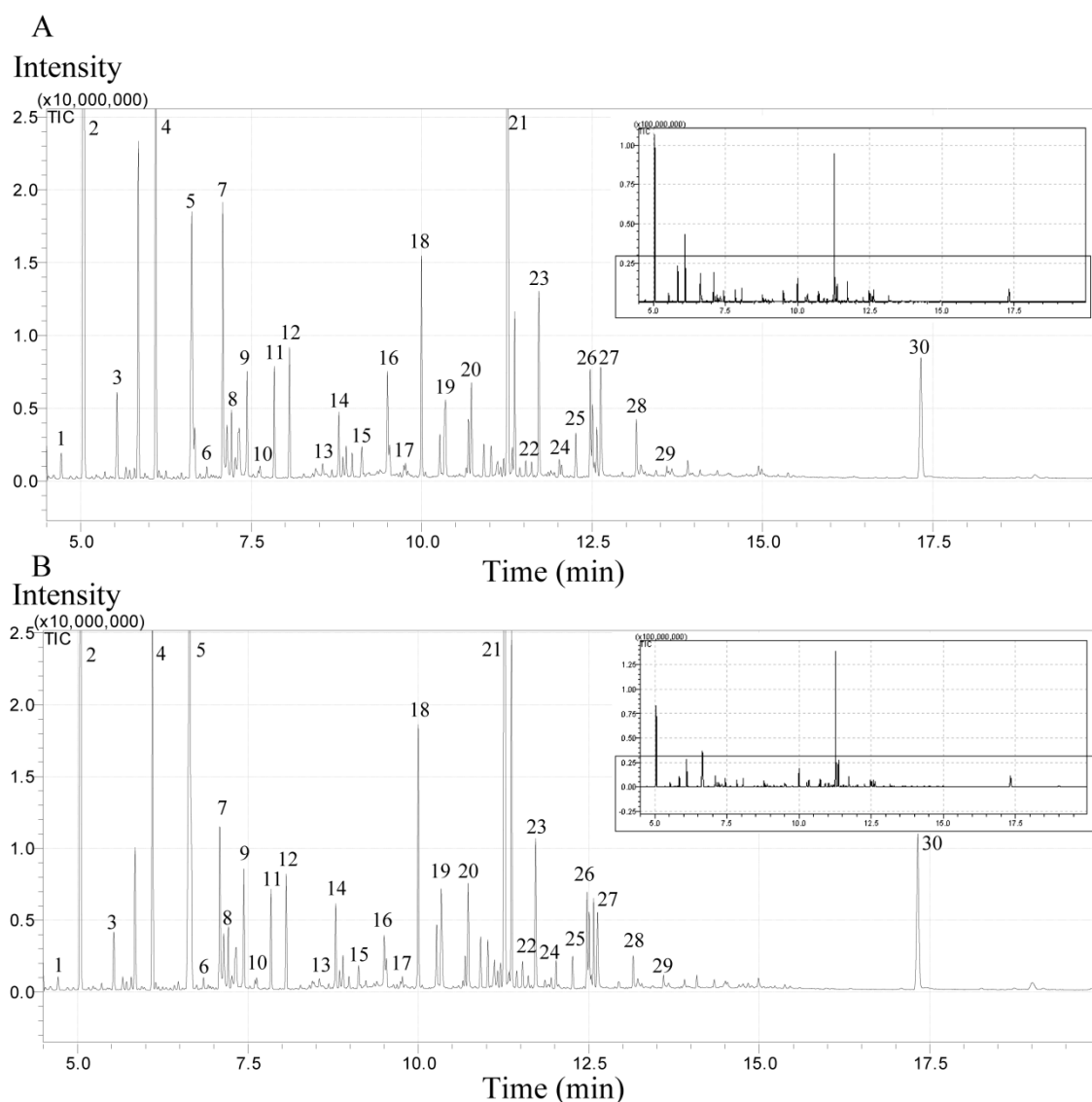


Figure S1 Typical GC/MS chromatograms of serum from the METH-treated rats and controls.

A. Pretreatment with METH; B. 5 days after treatment with METH. 1. Pyruvate; 2. Lactate; 3. Alanine; 4. 3-Hydroxybutyrate; 5. Urea; 6. Silanamine; 7. Phosphate; 8. Glycerol; 9. Glycine; 10. Fumarate; 11. Serine; 12. Threonine; 13. Aminomalonate; 14. Pyroglutamate; 15. Creatinine; 16. Glutamate; 17. Asparagine; 18. Methyl tetradecanate; 19. Glutamine; 20. Myristic Acid- C^{13} (IS); 21. Glucose; 22. Cis-9-Hexadecenoic acid; 23. Palmitic acid; 24. Urate; 25. Myo-Inositol; 26. Oleic acid; 27. Stearic acid; 28. Arachidonic acid; 29. 5-Hydroxytryptamine; 30. Cholesterol.

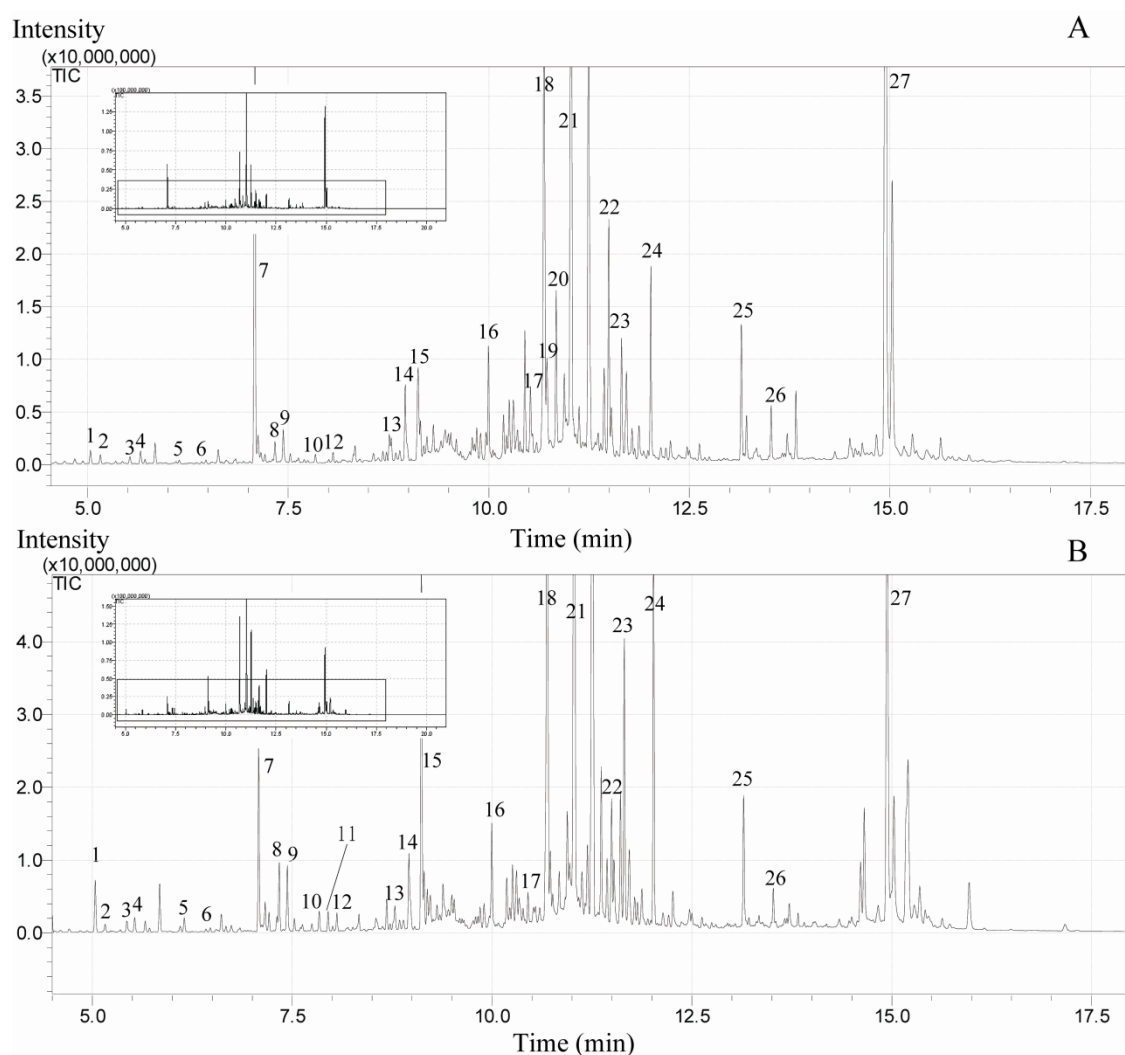


Figure S2 Typical GC/MS chromatograms of urine for the METH-administered rats and the control. A. Preadministration; B. 5 days after administration. 1. Lactate; 2. Hydroxyacetate (Glycolic Acid); 3. Alanine; 4. N-Butylamine; 5. 3-Hydroxybutyrate; 6. Urea; 7. Phosphate; 8. Succinate; 9. Glycine; 10. Serine; 11. METH; 12. Threonine; 13. Proline; 14. Hydroxyproline; 15. Creatinine; 16. Methyl-tetradecanate; 17. Hippurate; 18. Citrate; 19. Myristic Acid- C^{13} (IS); 20. Cysteine; 21. Allantoin; 22. Sorbitol; 23. Glucuronate; 24. Urate; 25. Pseudouridine; 26. Beta.-D-Glucopyranosiduronic Acid; 27. Lactose.

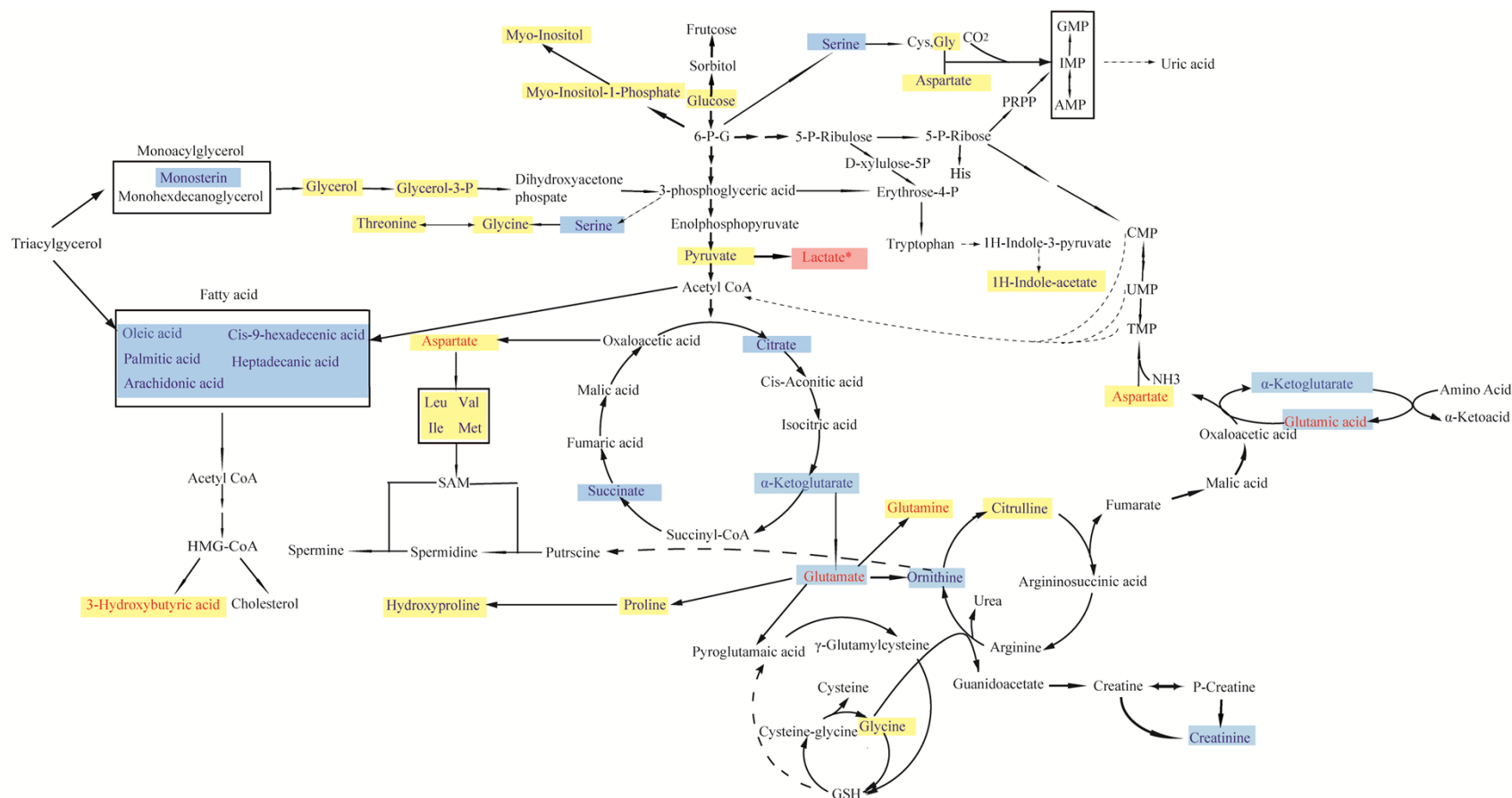


Figure S3 The effects of METH on endogenous metabolites and the involved metabolic pathways. METH perturbed metabolites primarily involved in glycolysis, lipid metabolism and amino acid turnover, while the withdrawal of METH restored most of the metabolites towards baseline levels. Compounds labeled in red and blue represent higher and lower levels (relative to the control), respectively, after treatment with METH; compounds with a yellow background indicate the metabolites restored to baseline level after withdrawal of METH; and compounds with a blue or pink background do not suggest a significant modulation of the metabolites, which were still lower or higher after the withdrawal

of METH. *, metabolites identified in urine.