

Supplementary Table S1. Calibration standards.

ANALYTE	Dynamic range of the curve (ng/ml)
Acetylcholine	3,12-400
Alanine	173,4-88800
Arginine	679,7-87000
Asparagine	62,5-20000
Aspartate	259,37-66400
Asymmetric dimethylarginine (ADMA)	7,81-500
Citrulline	234,37-60000
Creatine	62,5-8000
Gamma-aminobutyric acid (GABA)	3,12-200
Glutamate	286,7-146800
Glutamine	15625-250000
Glycine	292,2-74800
Histidine	292,96-154800
Isoleucine	514-131600
Kynurenic acid	187,5-6000
Kynurenine	9,76-5000
Leucine	515,6-132000
Lysine	285,15-146000
Methionine	3,66-30000
Phenylalanine	1287,5-82400
Proline	224,2-114800
D-Serine	117,18-1875
L-Serine	117,18-1875
Serotonin	4,68-600
Threonine	232-118800
Tryptophan	5625-180000
Tyrosine	706,25-90400
Valine	457,8-117200

Supplementary Table S2. Multiple reaction monitoring conditions for the metabolites.

	COMPOUND NAME	TRANSITION (M/Z)	FRAGMENTOR (V)	COLLISION ENERGY (V)	RETENTION TIME (MIN)
1	Acetylcholine	146-87	120	15	2.15
	D4-Acetylcholine	150-91	120	15	2.15
2	Alanine	194-105	120	20	10.08
	13C6Bz-Alanine	200-111	120	20	10.08
3	Arginine	279-105	135	30	7.68
	13C6Bz-Arginine	285-111	135	30	7.68
4	Asparagine	237-105	120	20	7.46
	13C6Bz-Asparagine	243-111	120	20	7.46
5	Aspartate	238-105	120	10	8.46
	13C6Bz-Aspartate	244-111	120	10	8.46
6	Asymmetric dimethylarginine (ADMA)	307.2-105	70	20	8.04
	13C6Bz- Asymmetric dimethylarginine (ADMA)	313-111	70	20	8.04
7	Citrulline	280-105	120	20	8.28
	13C6Bz-Citrulline	286-111	120	20	8.28
8	Creatine	132.1-90.2	90	9	2
9	Gamma-aminobutyric acid (GABA)	208-105	120	10	10.36
	13C6Bz-Gamma-aminobutyric acid (GABA)	214-111	120	10	10.36
10	Glutamate	252-105	120	20	9.08
	13C6Bz-Glutamate	258-111	120	20	9.08
11	Glutamine	251-105	120	20	8.17
	13C6Bz-Glutamine	257-111	120	20	8.17
12	Glycine	180-105	120	10	8.79
	13C6Bz-Glycine	186-111	120	10	8.79
13	Histidine	260-110	130	20	6.9
	13C6Bz-Histidine	266-110	130	20	6.9
14	Isoleucine	236-105	120	30	15.9
	13C6Bz-Isoleucine	242-111	120	30	15.9
15	Kynurenic acid	294-105	120	30	18.5
	13C6Bz-Kynurenic acid	300-111	120	30	18.5
16	Kynurenine	417-122	120	10	19.02
	13C6Bz-Kynurenine	429-128	120	10	19.02
17	Leucine	236-105	120	30	16.31
	13C6Bz-Leucine	242-111	120	30	16.31
18	Lysine	355-188	120	20	14.7
	13C6Bz-Lysine	367-194	120	20	14.7
19	Methionine	254-105	120	15	13.69
	13C6Bz-Methionine	260-111	120	15	13.69
20	Phenylalanine	270-120	120	10	16.48
	13C6Bz-Phenylalanine	276-120	120	10	16.48
21	Proline	220-105	120	20	11.03
	13C6Bz-Proline	226-111	120	20	11.03
22	D-Serine	210-105	120	20	7.70
	13C6Bz-D-Serine	216-111	120	20	7.70
23	L-Serine	210-105	120	20	7.99
	13C6Bz-L-Serine	216-111	120	20	7.99
24	Serotonine	385-264	140	20	20.6
	13C6Bz-Serotonine	397-270	140	20	20.6
25	Threonine	224-105	140	20	16.5
	13C6Bz-Threonine	230-111	140	20	16.5
26	Tryptophan	309-159	120	10	16.54
	13C6Bz-Tryptophan	315-159	120	10	16.54
27	Tyrosine	390-105	120	30	19.67
	13C6Bz-Tyrosine	402-111	120	30	19.67
28	Valine	222-105	120	30	13.61
	13C6Bz-Valine	228-111	120	30	13.61

Supplementary Table S3. Multivariate regression parameters for the effect of renal status

(control, chronic kidney disease or end-stage kidney disease) on the metabolites' plasma

levels. Models were adjusted for age, sex, body-mass index, hypertension, smoking status and diabetes.

	B	95%CI	SE	Beta	p-value
Alanine	-190.15	(-212.95 - -167.28)	11.63	-0.547	<0.0001
Arginine	-27.45	(-31.72 - -23.18)	2.18	-0.451	<0.0001
Asparagine	-9.9	(-11.46 - -8.35)	0.79	-0.434	<0.0001
Aspartate	-13.84	(-16.63 - -11.08)	1.42	-0.358	<0.0001
Citrulline	13.41	(9.4 - 17.42)	2.04	0.242	<0.0001
Glycine	22.12	(15.85 - 28.39)	3.19	0.267	<0.0001
Glutamate	-57.84	(-65.62 - -50.06)	3.96	-0.509	<0.0001
Glutamine	30.11	(-1.12 - 61.35)	15.91	0.073	0.059
Histidine	-17.38	(-22.02 - -12.73)	2.37	-0.283	<0.0001
Isoleucine	-31.76	(-39.12 - -24.41)	3.75	-0.353	<0.0001
Leucine	-301.77	(-356.75 - -246.79)	28.01	-0.387	<0.0001
Lysine	-47.26	(-56.45 - -38.07)	4.68	-0.369	<0.0001
Methionine	-3.97	(-5.11 - -2.83)	0.58	-0.267	<0.0001
Phenylalanine	-118.01	(-185.38 - -50.64)	34.32	-0.137	0.001
Proline	-58.57	(-79.01 - -38.12)	10.42	-0.221	<0.0001
D-Serine	0.07	(0.03 - 0.1)	0.02	0.152	<0.0001
L-Serine	-24.6	(-28.09 - -21.11)	1.78	-0.461	<0.0001
Tyrosine	-215.74	(-255.46 - -176.02)	20.23	-0.381	<0.0001
Threonine	-87.45	(-100.22 - -74.69)	6.5	-0.458	<0.0001
Tryptophan	-49.48	(-53.56 - -45.42)	2.07	-0.689	<0.0001
Valine	-175.51	(-202.94 - -148.09)	13.97	-0.454	<0.0001
Acetylcholine	0.16	(0.12 - 1)	0.02	0.271	<0.0001
Kynurenic acid	-0.49	(-0.56 - -0.42)	0.04	-0.498	<0.0001
ADMA	-0.29	(-0.32 - -0.27)	0.01	-0.693	<0.0001
Creatine	-5.9	(-6.83 - -4.96)	0.48	-0.435	<0.0001
GABA	-0.08	(-0.09 - -0.08)	0.004	-0.617	<0.0001
Kynurenine	-0.02	(-0.13 - 0.1)	0.06	-0.012	0.755
Serotonin	-0.22	(-0.24 - -0.2)	0.01	-0.663	<0.0001

B, regression coefficient; 95%CI, 95% confidence intervals; SE, standard error; Beta, standardized coefficient