Electronic supplementary information.

Figure legends

Supplementary table 1 LC elution gradient in both positive and negative ionization modes.

Supplementary table 2 Method validation results of stability and repeatability in this study.

Supplementary Fig. 1 PCA score plots of pair comparisons between different groups both in positive and negative ionization modes.

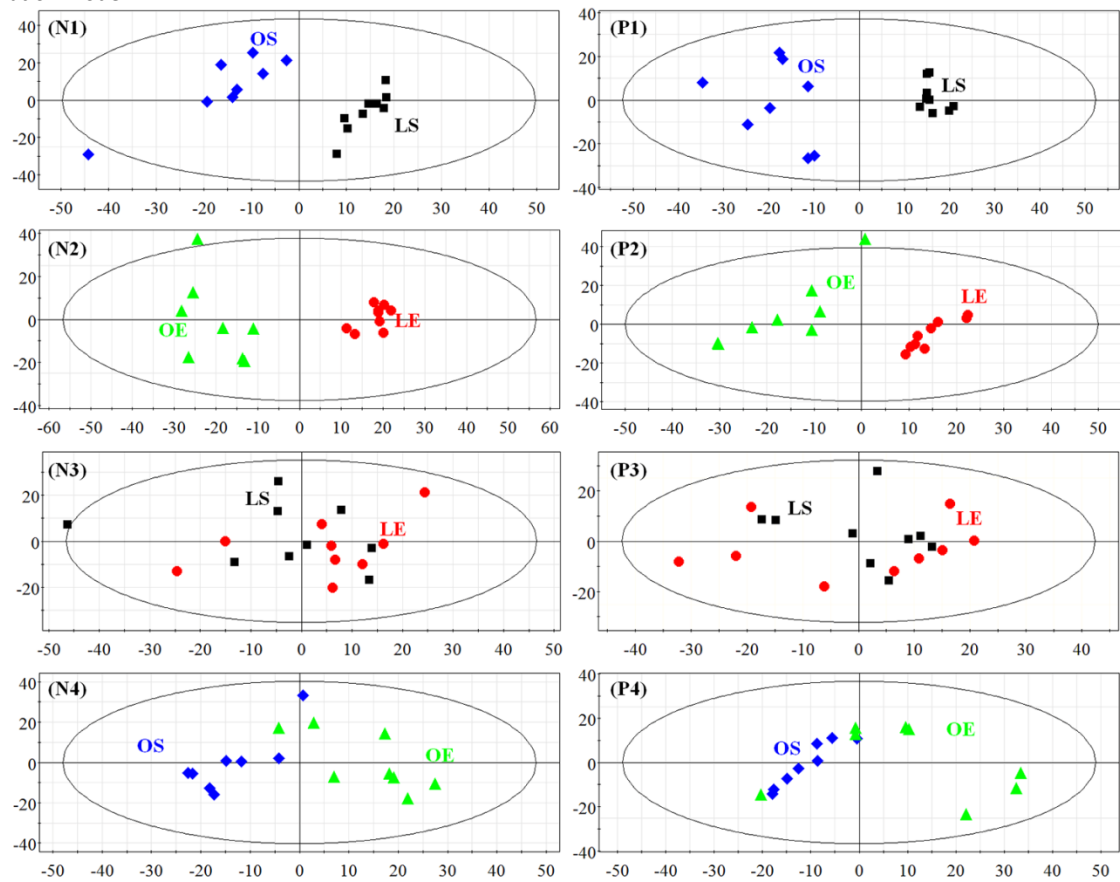Supplementary Fig. 2 PCA score plots of all four groups in positive and negative ionization modes.

Supplementary Table 1. LC elution gradient in positive and negative ion modes.

No.	Positive ion mode		Negative ion mode	
	Time (min)	B%	Time (min)	B%
1	0.0	2.0%	0.0	0.0%
2	2.0	2.0%	2.0	0.0%
3	14.0	55.0%	9.0	50.0%
4	20.0	98.0%	16.0	100.0%
5	24.0	98.0%	20.0	100.0%

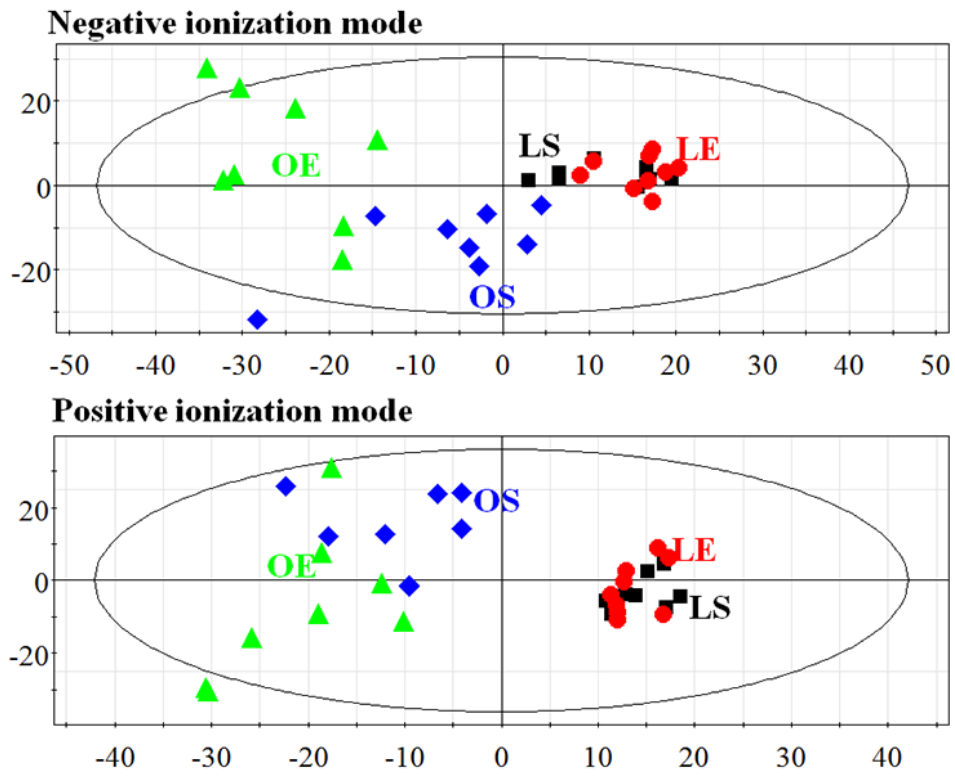Supplementary Table 2. Results of method validation of stability and repeatability.

Compounds	Stability		Repeatability	
	Area (RSD%)	R.T. (RSD%)	Area (RSD%)	R.T. (RSD%)
L-Lysine	1.58	1.28	6.14	1.36
Pantothenic acid	3.34	0.33	1.35	0.3
Palmitoylcarnitine	7.66	0.07	4.05	0.11
12-HETE	6.13	0.04	3.64	0.04
N-Acetylleucine	5.75	0.35	7.78	0.21

Supplementary Fig. 1. PCA score plots of pair comparisons between different groups both in positive and negative ionization mode.

Note: N1-4: PCA score plots in negative ionization mode. P1-4: PCA score plots in positive ionization mode. LS: *db/m+* mice treated with sedentary, black square; LE: *db/m+* mice treated with exercise training, red dot; OS: *db/db* mice treated with sedentary, blue diamond; OE: *db/db* mice treated with exercise training, green triangle.

Supplementary Fig. 2. PCA score plots of all four groups in positive and negative ionization mode.

Note: LS: *db/m+* mice treated with sedentary, black square; LE: *db/m+* mice treated with exercise training, red dot; OS: *db/db* mice treated with sedentary, blue diamond; OE: *db/db* mice treated with exercise training, green triangle.