The CVS procedures as follows: (1) immobilization for 5h, (2) swimming in 15 °C water for 5min, (3) food withholding for 48h, (4) thermal stimulus in 45 °C water for 5min, (5) water intake forbidden for 48h, (6) electric shock to pelma (electric current for 1mA, 2s per shock, 2 shocks per minute), (7) noise stimulus at 110dB, and (8) stroboflash—2 flashs per second for 4h. These stimuli were presented in an unpredictable manner with one or two of these on each rat each day. Each stimulus was performed at least 3 times in 28 days.

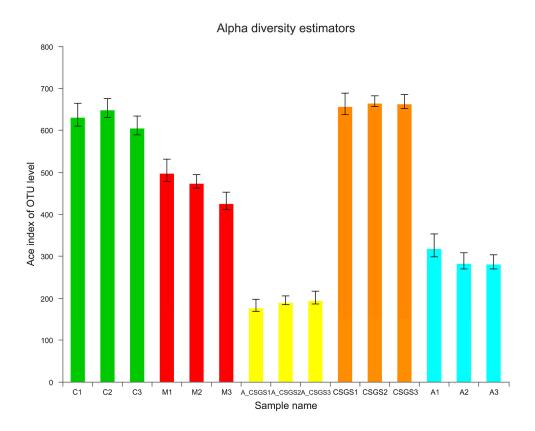


Figure S1. Alpha diversity plot of OTUs feces microbiota community in different treatment groups of rats.

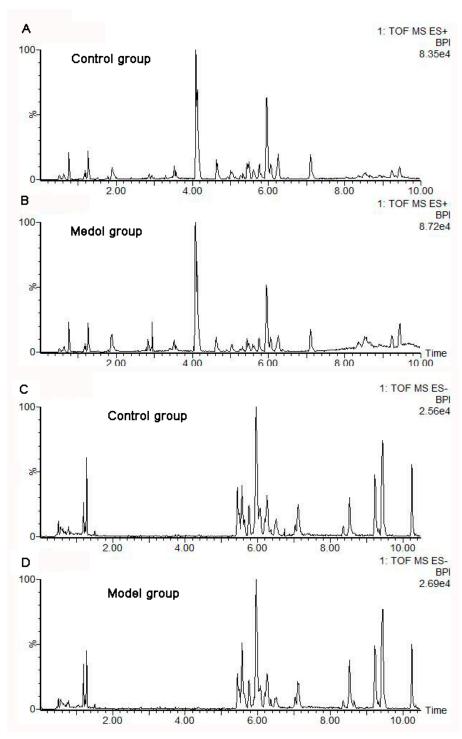


Figure S2. Typical UPLC-Q-TOF/MS base peak intensity (BPI) chromatograms of hippocampus samples from the control group and model group in positive ion mode (A and B) and in negative ion mode (C and D).

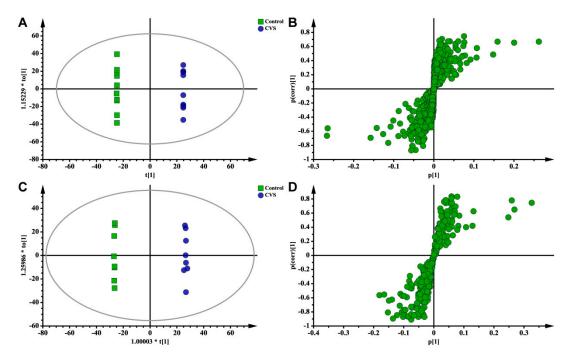


Figure S3. OPLS-DA and S-Plot score plot of hippocampus samples collected from different treatment groups of rats in (A and B, *R2X*=0.468, *R2Y*=1, *Q2* (*cum*)=0.743) positive and (C and D, R2X=0.57, R2Y=0.999, Q2 (cum)=0.859) negative ion mode.

Table S1 the sequencing number of each experimental group samples

Seq_number
52986
57182
30872
29550
32606
30656
43242
125702
48738
23504
33888
64957
26502
33920
27807