Plasma metabolomics study on the anti-depression effect of different exercise modes on CUMS model rats

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Objective Objective: To study the anti-depression effect of different modes of exercise on CUMS rats and explore the mechanism by [1] H-NMR metabonomics methods.

Methods Methods: Healthy male SD rats were got on sugar consumption training within one week of adaptive feeding, rats with similar scores were then randomly divided into control group (group C), model group (group M), aerobic exercise group (group A), and resistance exercise group (group R) by open field test. Chronic unpredictable mild stress (CUMS) procedure was conducted for four weeks, assess the success or failure of the model through behavioral indicators (rat increased amount of body weight, sucrose preference, crossings and rearings in open field test). The rats that were successfully modeled continued to undergo CUMS procedure for four weeks, and the rats in group A and group R were given different exercise training at the same time. After the end of training, the rats were executed and the blood sample was taken from the abdominal aorta to determine plasma superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSH-PX) activity and malondialdehyde (MDA) content. In order to further explore the mechanism of action of different exercise modes, the plasma was analyzed by [1]H-HMR metabonomics technique and the metabolic pathways were analyzed by metaboAnalyst.

Results Results**:** 1) After 4 weeks of CUMS, the behavioral indicators of group M, group A and group R were significantly lower than those of group C ($p<0.05$，$p<0.01$，$p<0.001$), indicating that the rat model of CUMS was prepared successfully. 2) After 4 weeks of exercise intervention, the behavioral indicators, SOD, CAT and GSH-PX activities of rats in group C, group A and group R were significantly higher than those in group M($p<0.05$，$p<0.01$), MDA content is significantly lower than that in group M ($p<0.01$), there was no significant difference in behavioral and biochemical indicators between the group A and the group R. 3)A total of fifteen pathological markers were found in group M, such as isoleucine, valine, N-acetyl glycoprotein and so on ($P<0.05$ and $VIP>1$). Six metabolites among the fifteen pathological markers reverted significantly afteraerobic exercise training ($P<0.05$ or $P<0.001$), such as N-acetyl glycoprotein, leucine, lactic acid, LDL, glucose and acetoacetate, which mainly involved in 3 metabolic pathways including ketone bodies, butanoate metabolism, and biosynthesis of branched-chain amino acids. Another six metabolites reverted significantly after resistance exercise training ($P<0.01$ or $P<0.001$), such as lactic acid, glucose, creatine phosphate, acetoacetic acid, inositol and choline, which mainly involved in 3 metabolic pathways including ketone bodies, butanoate metabolism, and inositol phosphate metabolism. The above results suggest that both modes of exercise can improve the characteristics of plasma metabolites of depressed rats.

Conclusions Conclusion: Different modes of exercise can effectively improve depressive symptoms, reduce the oxidative stress and adjust the plasma biomarkers of depressed rats to varying degrees, which may be related to different metabolic pathways involved in exercise modes.