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The metabolic changes in the hippocampus of an atherosclerotic rat model and the regulation of exercise

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Objective atherosclerosis has been associated with the progression of cognitive impairment and dementia. Several features, such as high oxygen consumption, a large content of peroxidation-sensitive polyunsaturated fatty acids (PUFAs) and a strong dependency on the supply of glucose make the brain vulnerable to even small metabolic changes. The hippocampus is closely related to memory and learning function, and prone to ischemic injury. However, using metabolomics technology to explore metabolites of hippocampus from atherosclerosis animals is rarely reported. We aim to reveal the metabolic changes during atherosclerosis, and clarify the possible role of exercise in regulating hippocampus metabolism.
Methods we established a rat model of atherosclerosis(n=18) along with control group (n=10). The model group was assigned into the AS group (n=8) and the TAS group (n=8), which was intervened by running exercise for 4 weeks. A Y maze test was performed to evaluate initial memory. Metabolomics based on GC-MS was applied to detect small molecules metabolites in rat hippocampus.
Results we found that the AS and TAS group both showed elevation in HDL, meanwhile decrement in TC and LDL after 4 weeks' intervention. The behavioral test showed rats from AS group entered less frequently into and spent less time in the novel arm than rats from C group ($P<0.01$), while other indexes showed no difference. Compared to the C group, metabolites including xylulose 5-phosphate, threonine, succinate and nonanoic acid were markedly elevated, whereas methyl arachidonic acid and methyl stearate decreased in the AS group. Meanwhile, the levels of succinic acid, branched chain amino acids, nonanoic acid and desmosterol decreased, whereas methyl arachidonic acid, methyl stearate, and glyceraldehyde-3-phosphate elevated in the hippocampus of the TAS group in comparison with the AS group.
Conclusions A series of metabolic changes implicated in the hippocampus of atherosclerotic rats, including a decrease in anaerobic glycolysis and TCA cycle, an activation of pentose phosphate pathway, and a disturbance in fatty acid oxidation and cholesterol synthesis, which could lead to insufficient ATP in the hippocampus and related to the behavioral changes of atherosclerotic rats, while running exercise may take part in regulating metabolism to normal state in the hippocampus of atherosclerotic rats.