Voluntary wheel training attenuate brain aging in SAMP8 mice

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Objective Alzheimer’s disease (AD), is a progressive neurodegenerative disease. The pathological hallmarks including the deposition of senile plaque and neurofibrillary tangles (NFTs) in AD. The underlying molecular mechanisms for AD are not fully understood. Studies have shown that exercise as an economical and popular fitness method, long-term exercise can reduce the risk of AD, delay the occurrence of AD or delay the progression of AD. This study was to investigate the protective effect of the Voluntary wheel on cerebral cortex senescence in SAMP8 mice.

Methods Fifteen SPF-class 7-month-old SAMP8 mice were randomly divided into control group (CON), voluntary wheel group (V) and voluntary wheel with chloroquine group (VQ), with 5 mice in each group. Each group was under adaptive feeding for one week. After 3 days of adaptive voluntary wheel training for V and VQ groups, the experiment officially started. The V and VQ groups performed an 8-week voluntary wheel training and the VQ group received a daily intraperitoneal injection of chloroquine (40 mg/kg). After 8 weeks intervention, the Morris water maze test was used to determine the changes in spatial learning and memory ability of each group. After 24 hours of the end of this experiment, the mice were killed by breaking neck. The degree of hippocampal cell injury was detected by Nissl staining; the expression of apoptosis and senescence-associated protein in the cerebral cortex was detected by Western blot.

Results Compared with the CON group, the escape latency of the V group mice in the Morris water maze test was significantly shorter (P<0.01), the number of crossing target quadrants was significantly increased (P<0.05), however, the VQ group exacerbate above response compared with CON group. Nissl staining showed that the cells of cerebral cortex in the CON group had obvious damage, while the V group showed significant improvement. The VQ group had a significant damage compared with the V group; Western blot results showed that the expression of AD-like pathological changes such as BACE1 protein in the cortex of group V was significantly decreased, and the expression of P-GSK-3β protein was increased (P<0.01) compared with CON group. On the contrary, compared with V group, VQ alleviated the improvement effect of voluntary running, (P<0.05), the expression of apoptosis-related protein increased, and the decreased in CON group, while voluntary running intervention down-regulated BAX, Cleaved-caspase3, increased the Bcl-2 protein level compared with the CON group (P<0.05). Furthermore, compared with the CON group, the expression level of aging-related protein AC-P53 was decreased in the V group, and the expression level of Sirt1 was increased.

Conclusions The 8-week voluntary wheel training can significantly improve the learning and memory ability of SAMP8. Mechanismly, voluntary wheel training can improve the senescence of cerebral cortex by inhibiting cell apoptosis, the expression of AD-like pathological protein and increasing Sirt1 protein level.