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Effects of voluntary wheel running exercise on learning and memory function of young mice and related mechanisms.

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Abstract

Objective: This study is to investigate the effects of appropriate exercise on learning and memory function of mice, and the related mechanisms involving PAI-1 and miRNA (miR)-30b.

Methods: Mice were subjected to the voluntary wheel running exercise training for 8 m. Morris water maze test was performed to assess the animal learning and memory function. Quantitative real-time PCR was conducted to detect the mRNA expression levels, while Western blot analysis and ELISA were used to determine protein expression levels. Bioinformatics analysis and dual-luciferase reporter assay were used to predict and confirm the up-stream regulator of PAI-1.

Results: Morris water maze test showed that, compared with the control group, the escape latency was significantly declined in the exercise group. The swimming distance was significantly declined, while the platform crossing number was significantly increased, in the exercise group. Quantitative real-time PCR and Western blot analysis showed that, compared with the control group, the mRNA and protein expression levels of PAI-1 in both the hippocampus and plasma were significantly declined in the exercise group. According to the bioinformatics analysis, miR-30b might be the up-stream regulator of PAI-1, which was confirmed by the dual-luciferase reporter assay. In addition, compared with the control group, the expression levels of miR-30b in both the hippocampus and plasma samples were significantly elevated for the exercise group.

Conclusion: Appropriate amount of exercise might contribute to the improvement of the mouse learning and memory function, which might involve the up-regulated miR-30b expression and down-regulated PAI-1 expression in the hippocampus and plasma.

Keywords: Learning and memory function; voluntary wheel running exercise; plasminogen activator inhibitor-1 (PAI-1); miRNA (miR)-30b.

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Introduction

Human brain is a very complex organ, and the normal function of cerebral cortex provides the basis for cognition. Any factors associated with cerebral cortex functional and structural alterations could lead to learning and memory disorders. So far, investigation of learning and memory function has mainly focused on hippocampus, in which the neurons represent the research hotspots in recent years [1].

Studies have shown that children's learning and memory ability could greatly benefit from appropriate amount of exercise [2]. Moreover, it has been demonstrated that prolonged active exercise can elevate the expression of BDNF mRNA in rat hippocampus, and enhance the learning and memory ability [3]. Furthermore, it has been shown that, in rat models, active training could significantly improve their performance in the maze test, indicating significantly increased learning and memory function [4]. In addition, running exercise has also been shown to be able to promote the rat hippocampus neural activity and synaptic activity, thereby promoting the learning and memory function [5]. These findings suggest that appropriate amount of exercise training could improve the body's learning and memory function. However, the specific underlying mechanisms are still unclear. Learning and memory ability is related to the brain blood flow [6]. Brain tissue ischemia, hypoxia, and nerve cell necrosis induced by head trauma, cerebral vascular inflammation, cerebral vascular stenosis, and cerebral embolism have been recognized as physiologically inducing factors for the pathogenesis of cognitive disorders [7]. Therefore, brain vascular lesions have been intensively studies for its involvement in the process of cognitive impairment in recent years.

Abnormal hemorheology is one of the causes of brain vascular disorders. Plasminogen activator inhibitor-1 (PAI-1) is a serine protease inhibitor that inactivates plasminogen activator t-PA