Letter to editor

Effect of exercise on the improvement of age-induced cognitive impairment: With emphasis on cross talk between the brain and skeletal muscles

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Dear Editor-in-Chief

The brain weighs about 1.36 kg and is mainly composed of blood. Although the brain includes only 2% of the body's weight, it receives 25% of the whole body oxygen consumption, 15% of the cardiac output volume and 2000 L of blood flow per day (Hartmann et al., 1994; Ohta et al., 1992; Xing et al., 2017). The brain has largest and most complex structure of the central nervous system. This organ regulates the functions of human body and stands for the basis of higher neural activities such as consciousness, alertness, learning, memory, intelligence, spirit and language learning. Cognitive function in a person means the brain ability to process, store, and extract information. In addition, this ability is a kind of advanced psychological function such as thinking, memory, and attention. Cognitive function plays an irreplaceable role in our daily life and study. Based on Cognitive psychology, the brain can modify its structure and function according to environmental changes and the experience of different types of exercising, especially exercise training, plays a crucial role in the evolution of the brain (Barnes. 2015; Raichlen et al., 2017). For example, exercise can positively affect synaptic plasticity and synaptic function to promote cerebral cortex, neural network and hippocampus function (an important structure in the memory information processing) (Ding et al., 2006; Li et al., 2019; Loprinzi et al., 2017). Exercise also has a significant effect on brain metabolism. Exercise not only promotes physical health of people, but also prevents mental illness and delays cognitive aging (Robinson et al., 2018).

Brain function depends on nerve fibers, number of neurons and synapses. The cognitive performance is also closely related to the number of nerve fibers and synaptic connections, which can be reduced by diseases and aging process. The neurotrophics factors, such as neurotrophic factor (NGF) and brain-derived neurotrophic factor (BDNF) are required to provide nutrients to maintain the structure and function of nerve fibers and synaptic connections (Ivanov, 2014). However, with aging, sharp decrease of dendritic branches, degeneration of glial cells, the reduction of neuron number and contraction of nerves may impede the transmission of electrical signals in the nervous system, leading to the shrinkage of gray matter in the brain and cognitive impairment (Reisberg et al., 2008; Thorin-Trescases et al., 2018).

Several studies have shown that an active lifestyle could delay the aging of cognitive-control areas in the brain, and exercise can significantly improve brain health in patients with Alzheimer's disease and schizophrenia (Falkai et al., 2017; Frederiksen et al., 2018). Colcombe et al. (2003; 2006) used high-resolution magnetic resonance imaging (MRI) to scan the brain of 55 healthy people aged from 55 to 79 years old and observed a decrease in tissue density in the frontal and temporal lobes with age. The important point is that brain structure atrophy was related to aerobic fitness. In another study, 59 healthy people aged from 60-79 years old were divided into exercise training groups and control group. In the exercise training group, aerobic exercise intervention was conducted for 6 months. The results showed that the volume of gray matter and white matter was significantly increased in the exercise training group, and the researchers concluded that aerobic training could effectively delay brain aging process and lead to promote brain health (Colcombe et al., 2003; Colcombe et al., 2006; Colcombe & Kramer, 2003).

In terms of the mechanism based on which exercise training may enhance cognitive ability and delay brain aging, it has been proved that exercise training can induce fibronectin type III domain-containing protein 5 (FNDC5) expression in skeletal muscle which will be released into the circulation with Irisin variant (Wrann et al., 2013). Spiegelman found that exercise training for 30 days in mice increased the activity of peroxisome

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proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α), which is a metabolic regulatory molecule in skeletal muscle. PGC-1α could stimulate the upregulation of FNDC5 expression, and when FNDC5 enters the hippocampus through the blood-brain barrier, it enhanced the expression of BDNF in the dentate nucleus of the hippocampus (responsible for learning and memory). Interestingly, the study on sedentary mice injected with FNDC5 produced by exercise showed it activated gene for the brain health and improved the growth of new neurons involved in learning and memory. This new discovery links FNDC5, PGC-1α and BDNF in the cross talk between the brain and skeletal muscle upon exercise (Wrann et al., 2013). In addition to PGC-1 α/FNDC5 signaling on other molecules have also been found to affect BDNF expression in cognitive impairment.

In a cell model simulating the effect of exercise by adding AMPK agonist to L6 myoblasts rat, proteomics and mass spectrometry were performed to screen the factors secreted by myoblasts. Data showed that Cathepsin B (CTSB) increased after treatment while other cytokines did not changed. Meanwhile, CTSB levels also increased in gastrocnemius muscle and plasma of rats after voluntary wheel running exercise, anti-fatigue ability; spatial memory ability and coordinated movement improved in the exercised rats compared to the sedentary control group. However, these beneficial effects were absent in CTSB knockout rat. In addition, intravenous injected CSTB is able to enter the brain through blood-brain barrier and upregulate DCX and BDNF expression and thus enhancing hippocampal nerve growth (Moon et al., 2016).

Aerobic Training not only promotes physical health of people, but also prevents mental illness and effectively delays brain aging process, prevents brain structure atrophy, promotes volume gray and white matter and promotes cognitive ability in patients with Age-induced cognitive impairment. Therefore, it is very important to conduct original and cross-sectional research in order to discover relevant and new mechanisms.

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