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Review Article

Exercise Training Could Improve the Cognitive Function in the Elderly

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Abstract

Increasing the lifespan of a population is often a marker of a country's success. With the percentage of the population over 65 year of age increasing, maintaining the health and independence of this population is an ongoing concern. Advancing age is associated with an increasing in cognitive function that affects quality of life ultimately. Understanding potential adverse effects of aging on brain blood flow and cognitive ability may help to determine effective strategies to mitigate these effects on the aging population. Exercise may be one strategy to delay cognitive decline. Regular exercise has been found to improve cognitive ability, and this occurs through beneficial adaptations in vascular physiology and improved neurovascular coupling. In this review we mainly highlight the potential mechanisms of how the exercises regulate age-associated variables especially cognitive dysfunction.

INTRODUCTION

Age is the greatest risk factor for nearly every major cause of mortality in developed nations. While increasing life expectancy is certainly an encouraging trend, substantial social and economic implications will ensue if this increase in lifespan is accompanied by poor health. The challenge for the medical study is working to maintain a high quality of life and lowering morbidity in older adults. Advancing age is associated with an increasing disease risk for cognitive dysfunction [1]. In addition, aging is associated with a decrease in cognitive function that ultimately affects quality of life. Understanding such adverse effects of aging on cognitive dysfunction may help to determine effective strategies to mitigate these effects on the population. Regular exercise is one intervention that is associated with better cognitive function [2], yet the physiology underlying the benefit of exercise is unknown. Studies showed that Exercise could improve cardiovascular function, and blood flow within the CNS, and is associated with improved cognitive, sensory, and motor test outcomes, angiogenesis. In this review we mainly summarize how the exercises regulate age-associated cognitive dysfunction.

AGING AND COGNITION

Aging is a manifestation of progressive, time-dependent failure of molecular mechanisms that creates disorder within a system of DNA and its environment (nuclear, cytosolic, tissue, organ, organism, other organisms, society, terra firma, atmosphere, and universe) [3]. Cognitive deficits are observed in aging.

Changes in the central nervous system (CNS) have been associated with functional deficits in the aging brain [4]. For example, alterations in synaptic morphology and activity of neurons, especially in the hippocampus and prefrontal cortex, have been associated with impairments in cognition during the process of aging [5]. Chronic inflammatory changes in the innate immune system during aging, such as microglia/monocytes and astrocytes may predispose to neural pathology in the CNS [6]. In addition, changes to the neurovascular unit in aging, and associated cerebrovascular alterations, have also been showed as impacting neural integrity and function [7]. In addition to the changes of CNS, decline of brain vascular is another cause of cognitive dysfunction. Although vascular hyperpermeability is associated with injuries in all age groups, its effect in the aging population is severe and warrants urgent attention. Aging elicits several changes in the vascular endothelium that effect permeability regulation. And age-related oxidative stress, via ROS, is one of the major contributing factors in the loss of endothelial cell function in advanced age. This oxidative stress, in addition to inflammatory molecules, may be involved in endothelial aging by affecting vascular function, endothelial gene expression, the activation of the apoptotic signaling pathways, as well as breaking down barrier integrity and deregulating permeability [8].

The impacts of exercise on age-related cognitive decline

Interestingly, the mechanisms underlying effects of factors that reduce the impact of aging on the brain are similarly opaque. Example shows that physical exercise, which is strongly

associated with protection against age-related decline in cognitive function [9]. Studies also showed that exercise training increased hippocampal volume by 2%, effectively reversing age-related loss in volume by 1 to 2 year [10]. As is known exercise could improve cardiovascular function, and blood flow within the CNS, and is associated with improved cognitive, sensory, and motor test outcomes, angiogenesis. We mainly summarize the molecular events that drive these protective effects through exercise.

Angiogenesis is a main factor that controls the aging of cognition. The effect that exercise has on angiogenesis in the aging rat is unknown. Yun-Hong Ding et al. [11], initiated this study with the intent to determine if exercise could induce angiogenesis in model of aging rats. Results demonstrates significant angiogenesis coupled to expression of vascular endothelial growth factor (VEGF) and angiopoietin 1 and 2 in aged rats after physical exercise for 3 weeks. Other study also proved that exercise could promote angiogenesis in brain [12]. During exercise, brain blood flow increases, which dependent on the mode and intensity of exercise. During steady-state cycling, for example, global brain blood flow increases in parallel with cardiac output and O_2 consumption [13]. Studies showed that the increases in regional brain blood flow correspond to the neural networks associated with central command and skeletal muscle afferents [14]. Central command in the brain initiates activation of skeletal muscle contraction and autonomic nervous system changes at the start of exercise. In summary the upregulation in brain blood flow at the onset of exercise is not simply due to the increase in cardiac output but also due to changes in brain metabolism to supply increased neural activation. All the results suggest that impaired angiogenesis in aging is restored, at least, partially, by physical exercise.

With continued debate over the functional significance of adult neurogenesis, identifying a correlate between exercise and neurogenesis has become an important goal. Findings show that, within the hippocampal formation, exercise targets the dentate gyrus with regional selectivity. In addition, results identify that, in mice, dentate gyrus cerebral blood volume (CBV) is an imaging correlate of exercise-induced neurogenesis [15]. Consistent with this, E Lezi et al., showed that exercise could activate a partial mitochondrial biogenesis in aged mice, and a gene (VEGF-A) known to support neurogenesis [16]. So exercise could promote the neurogenesis and regulate the cognitive dysfunction in aged model.

Studies showing forearm blood flow responses have provided insights into age-related changes in blood flow regulation and vascular function. DeSouza et al. [17], demonstrated an age-associated reduction in vascular function in healthy adults between 50 and 76 year of age. In contrast, there was no age-related reduction in vascular function in older adults who regularly performed structured endurance exercise training. In addition, when sedentary adults were enrolled in a 3-mo aerobic exercise training program, their vascular function improved, highlighting the plasticity of the vascular system. These evidences indicate that regular physical activity and exercise training can ameliorate or delay the negative effects of advancing age on the vasculature. Also human and animal studies indicate that exercise targets many aspects of brain function and have broad effects on cognitive dysfunction, particularly in elderly populations. Exercise sets into motion an interactive cascade of growth factor signaling that has the net effect of stimulating plasticity, enhancing cognitive function, stimulating neurogenesis and improving cerebrovascular perfusion. Growth factor including brain-derived neurotrophic factor (BDNF) and insulin-like growth factor-1 (IGF-1) might be a hub for effects of exercise on learning and depression. In addition to central mechanisms, exercise reduces several peripheral risk factors for cognitive dysfunction. A common mechanism between many of these peripheral risk factors is inflammation. Inflammation could interfere with growth factor signaling in the periphery and in the brain. Exercise might improve growth factor signaling by both reducing pro-inflammatory conditions and directly increasing growth factor levels [18,19]. So the results showed that exercise could improve the cognition through inhibiting the inflammation.

Another mechanism that improves the cognition is apolipoprotein E (ApoE). Dysfunction of the neurovascular unit in the aging and aged brain is of great interest, since numerous studies have independently correlated the development of AD with vascular dysfunction during aging, but the mechanisms involved are not very clear [20]. We return to ground familiar to those in the fields of neuro-degeneration. Findings implicate the Alzheimer disease (AD) risk factor ApoE as also regulating neurovascular integrity during aging and, moreover, suggest involvement of ApoE in the protective effects of exercise. Studies found that ApoE as a strong candidate for mediating age-related neurovascular unit decline; ApoE expression decreases in the cortex of aged mice, ApoE expression is preserved by exercise, and exercise has little to no effect on behavioral deficits, neurovascular dysfunction, and innate immune responses in aged ApoE-deficient mice. Given that mice deficient in Apoe show vascular permeability decreased CBF, synapse loss, and cognitive impairments, a decrease in ApoE expression in the aging brain would be predicted to impact the health of the neurovascular unit [21]. Data shows that astrocytic ApoE decreases in aged mice concomitant with age-related neurovascular decline and complement activation, and that this effect is prevented by exercise [22]. These data extend previous studies showing that ApoE deficiency in mice leads to progressive age-related neurovascular dysfunction [23-25] and suggest a potential link between astrocytic ApoE, cognitive dysfunction and exercise.

CONCLUSIONS

Human and other animal studies demonstrate that exercise targets many aspects of brain function and have broad effects on cognition. The benefits of exercise have been best defined for learning and memory, protection from neuro-degeneration and alleviation of depression, particularly in elderly populations. Exercise increases the cognition by promoting neurogenesis, increase angiogenesis, and reduce inflammation which could be a strategy for the cognitive dysfunction in the elderly.

DISCLOSURES

Presentation at a conference statement

The manuscript is an original work and has not been previously submitted or is under consideration for publication in another journal. The study complies with current ethical consideration.

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