

New Perspective of the Beneficial Effect of Exercise on Alzheimer's Disease: Vascular Theory

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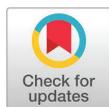
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Alzheimer's disease (AD) is a neurodegenerative brain disease with cognitive impairment and memory loss. Worldwide, at least 50 million people are living with AD or other dementias, and it is projected it would exceed 152 million by 2050 [1]. AD is characterized by the accumulation of extracellular amyloid and intraneuronal tau tangles. To date, underlying mechanisms for AD have not been clearly determined. A new approach to fight AD has been suggested as the "Vascular Theory of AD", which hypothesizes that malfunction of the cerebrovascular system induces cerebral amyloid angiopathy [2]. Various epidemiological studies have reported that cardiovascular risk factors are closely linked to the development and progression of AD. Chronic impairment of cerebral blood flow results in blood-brain-barrier dysfunction that ultimately causes neuronal injury/loss and the development of cognitive impairment [3]. Brain vessels maintain homeostasis of the brain through blood flow regulation, clearance of toxins, and transportation of oxygen/energy sources to brain cells. Cerebrovascular dysfunction in AD is characterized as impaired maintenance of vasodilation and vasoconstriction which is determined by communication between vascular endothelial (ECs) and smooth muscle cells (VSMCs) [4].

Exercise and physical activity have been known as non-pharmaceutical therapeutic strategies for the pathogenic phenotypes of AD. Previous studies showed that exercise training reduced AD pathology through a decrease in amyloid peptide accumulation, neuron cell death, and cognitive decline [5]. In addition, it has been well documented that exercise has beneficial effects on various vascular dysfunctions in diseases, especially through the endothelial cell. Last few decades, the positive effect of exercise on AD pathologies has been widely investigated, especially through the modulation of multiple processes in brain vessels [6]. Recently, we reported that exercise ameliorates cerebrovascular dysfunction and AD pathologies in AD mice by modulating, a novel target, purinergic receptor-mediated vasodilation. These findings suggest that exercise training, which regulates purinergic receptor-mediated vascular function in the AD brain, is a critical therapeutic strategy for AD [7].

It's been well known that regular physical exercise appears to be one of the best ways to

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reduce the risk of dementia and AD. However, its underlying mechanism is unclear. A new perspective, the vascular theory of AD, is important knowledge that Kinesiologists need to understand so that they can explain to older individuals how exercise is protective for their brain health to reduce the risk of AD.

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