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Active Voice: Exercise and Alzheimer's Disease

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Hyunsik Kang, Ph.D., is a professor and research director in exercise physiology and sports medicine at the College of Sport Science, Sungkyunkwan University, Republic of Korea. His research focuses on the integrative biological mechanisms that mediate physiological and cognitive changes with aging (i.e., mild cognitive impairments and dementia) and the effects of modulating influences and interventions on those neurodegenerative diseases. He has been a member for 16 years.

This commentary presents Dr. Kangs view on the topic of a research article which he and his colleagues published in the September 2015 issue of Medicine & Science in Sports & Exercise (MSSE).

Alzheimer's disease (AD) is a devastating brain disorder that is characterized by cognitive decline usually beginning with impairment in the ability to retain recent memories, but inevitably affecting all intellectual functions and leading to complete dependence for basic functions of daily life and premature death. Although three cholinesterase inhibitors (donepezil, galantamine and rivastigmine) are currently approved for use in AD by the U.S. Food and Drug Administration (FDA) to relieve the symptoms of AD and dementia, they do not significantly slow disease progression and may have severe side effects. On the other hand, a promising evidence-based and relatively side-effect-free lifestyle approach such as physical activity is emerging as either an alternative or adjunct to anticholinesterase therapies.

The triple transgenic AD (3x-Tg AD) mouse over-expresses human amyloid precursor protein, presenilin-1 and tau, and develops age-dependent and progressive amyloid beta (Aß) plaque and tangle pathology. These are two of the hallmarks of AD that contribute to the degradation of the nerve cells in the brain and the subsequent symptoms of AD. These factors make the transgenic mouse a valuable model for clinical intervention studies. In an experimental study involving the 3x-Tg AD mice, published in the September 2015 issue of *MSSE*, we investigated the therapeutic effects of treadmill running on cognitive decline and the two hallmarks of AD pathology, such as extracellular Aß plaques and intracellular neurofibrillary tangles.

This study investigated the effect of treadmill running on cognitive performance (i.e., spatial learning and short- and long-term memories) in the early and advanced stages of AD in these 3xTg-AD mice. At four (equivalent to an early stage) and 24 months (equivalent to an advanced stage) of age, the AD mice were assigned to control or exercise groups. Then, the AD mice in the exercise group were subjected to 20-30 minutes of treadmill running per day with a frequency of five days per week for 12 weeks. At each pathologic stage, background strain mice were included as wild type normal control.

At the early stage, the AD mice had impaired short- and long-term memory along with greater Aß and tau pathology and lower pre- and post-synaptic markers, as compared to the wild type mice. A 12-week treadmill running reversed the impaired cognitive declines and significantly improved the tau pathology and synaptic stability. At the advanced stage of AD, the AD mice had impaired short- and long-term memory along with greater Aß and tau pathology, lower pre- and post-synaptic markers and lower brain-derived neurotrophic factor (BDNF), as compared to the wild type mice. A 12-week treadmill running reversed the impaired cognitive declines, significantly reduced evidence of Aß and tau pathology, enhanced synaptic stability, and improved maintenance and/or survival of nerve cells.

The findings of this study suggest that, regardless of the severity of AD, physical activity should be recommended as an alternative or adjunct to the anticholinesterase therapies to combat cognitive declines due to AD pathology. In addition, the current findings are relevant to the ACSM Position Stand on Exercise and Physical Activity for Older Adults, in which a therapeutic role of physical activity is recognized in the treatment and management of mental and brain disorders, such as depression and dementia.