The Role of Mobility as a Protective Factor of Cognitive Functioning in Aging Adults: A Review

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Context: Over 33 chronic disease states and health disorders, including obesity and type 2 diabetes, are grouped into what is known as sedentary death syndrome. All these conditions are positively affected by 30 minutes of brisk exercise daily. In addition, only 30% of aging is based on genetics, with 70% on lifestyle. Therefore, a large majority of aging is controlled by individual health behaviors. Exercise is a powerful tool for healthy aging of the body and the mind. Courses of short- and long-term exercise provide benefits to musculoskeletal and cardiovascular health and can prevent age-related brain structural and functional losses. This review examines the evidence in support of mobility as an inexpensive and effective protective factor in maintaining brain health and preventing cognitive decline in aging adults.

Evidence Acquisition: A PubMed search was performed for articles in English from 1990 to 2012. Reference lists were also reviewed and relevant articles obtained.

Level of Evidence: Level 4.

Results: Evidence suggests that maintaining a high level of cardiopulmonary fitness and mobility exhibits protective effects on structural changes that occur with aging in areas of the brain associated with memory, attention, and task completion. Chronic exercise is also associated with preservation of overall cognitive functioning and prevention of dementia.

Conclusion: In combination with other preventative measures, physical mobility can assist in preventing or slowing cognitive decline in aging adults.

Keywords: mobility; exercise; aging; master athlete; cognitive function
Table 1. Literature summary of mobility and exercise benefits on brain structure and cognitive function

|                                                          | Improved Cognitive Function |
|-----------------------------------------------------------|----------------------------|
|                                                            | Brain Volume Increase<sup>a</sup> | Reduced Cognitive Dysfunction | In Setting of Cognitive Decline | Decreased Risk<sup>b</sup> |
| Barnes et al<sup>2</sup>                                  | ×                           |                               |                               |                            |
| Bixby et al<sup>4</sup>                                   | ×                           |                               |                               |                            |
| Brown et al<sup>5</sup>                                   | ×                           |                               |                               |                            |
| Coelho et al<sup>9</sup>                                  | ×                           | ×                              |                               | ×                           |
| Colcombe et al<sup>12</sup>                               | ×                           |                               |                               |                            |
| Colcombe et al<sup>13</sup>                               | ×                           | ×                              |                               |                            |
| Erickson et al<sup>17</sup>                               | ×                           |                               |                               |                            |
| Fabre et al<sup>18</sup>                                  | ×                           |                               |                               |                            |
| Gordon et al<sup>20</sup>                                 | ×                           | ×                              |                               |                            |
| Hamer et al<sup>21</sup>                                  | ×                           |                               | ×                              | ×                           |
| Hillman et al<sup>23</sup>                                | ×                           |                               |                               |                            |
| Hopkins et al<sup>24</sup>                                | ×                           |                               |                               |                            |
| Langdon and Corbett<sup>27c</sup>                         | ×                           | ×                              |                               |                            |
| Laurin et al<sup>28</sup>                                 | ×                           |                               |                               | ×                           |
| Lautenschlager et al<sup>29</sup>                         | ×                           | ×                              |                               | ×                           |
| Lindwall et al<sup>30</sup>                               | ×                           |                               |                               |                            |
| Maki et al<sup>31</sup>                                   | ×                           |                               |                               | ×                           |
| Marks et al<sup>32</sup>                                  | ×                           |                               |                               |                            |
| Richards et al<sup>34</sup>                               | ×                           |                               | ×                              | ×                           |
| Rovio et al<sup>35</sup>                                  | ×                           |                               |                               | ×                           |
| Siette et al<sup>36c</sup>                                | ×                           | ×                              |                               |                            |
| Szabo et al<sup>38</sup>                                  | ×                           | ×                              |                               |                            |
| van Boxtel et al<sup>40</sup>                             | ×                           |                               |                               |                            |
| Voss et al<sup>43</sup>                                   | ×                           | ×                              |                               |                            |
| Weuve et al<sup>44</sup>                                  | ×                           |                               | ×                              | ×                           |
| Yaffe et al<sup>45</sup>                                  | ×                           |                               |                               | ×                           |

<sup>a</sup> With attenuated brain volume decrease.
<sup>b</sup> Decreased risk of cognitive disorders and mental decline.
<sup>c</sup> Animal study.
RESULTS
Effects of Exercise on Brain Structure and Cognition

Chronic exercise imparts greater cardiovascular fitness, which is associated with physical changes in brain structure and measurable differences in brain function when compared with conditions of sedentary living and reduced physical activity.2,10,21 Animal studies demonstrated structural differences in parts of the brain used in cognitive tasks; there is an increase in size for areas involved with memory, such as the hippocampus, which correlates with improved performance in cognitive tasks.42 Similar changes in brain structure and function were also noted during investigation of the human population.

Fitness and Structural Brain Changes

Examination of magnetic resonance images from 55 older adults (age range, 55-79 years; mean, 66.5 years) without cognitive impairment (Mini-Mental State Examination range, 24-30; mean, 28.6) exhibited a loss of gray and white matter that correlated with increased age, specifically in the prefrontal, superior parietal, and middle/inferior temporal cortices.12 However, when these images were analyzed to assess the degree to which fitness level moderated the change in tissue loss, the same areas affected by age-related decline exhibited the greatest sparing effects due to cardiovascular fitness.12,20 Ccolcombe et al also demonstrated that older adults with high cardiovascular fitness, compared with those with low cardiovascular fitness, had greater activation in areas of the brain related to effective attentional control, which is important in successful task completion.13 Fitness level can be a valid parameter in predicting structural changes related to improved cognitive function in areas such as memory and task completion, emphasizing the significance of exercise’s role in maintaining these functions.

Fitness and Increased Hippocampal Volume

One area of the brain that shows significant exercise-related size differences is the hippocampus, which is responsible for spatial navigation and the consolidation of short- to long-term memory. A cross-sectional investigation of older adults (n = 158; mean age, 66.49 years) showed that those with higher fitness levels also had greater preservation of hippocampal volume.38 This leads to increased accuracy and speed of spatial memory and reduced forgetfulness. Increased hippocampal size, due to exercise, is thought to be the result of exercise-induced increases in levels of brain-derived neurotrophic factor (BDNF).42 Decreased levels of BDNF are linked to age-related hippocampal dysfunction and related memory impairment, whereas increased levels of BDNF owing to exercise slow or prevent hippocampal degeneration and improve memory function.36

BDNF and IGF-1 Mediate Exercise-Induced Structural Changes in the Brain

Exercise-induced increase in levels of BDNF is one of the primary mechanisms mediating improved cognitive function through its effects on increasing hippocampal size, improving memory function, and reducing depression.16,41 Insulin-like growth factor 1 (IGF-1) plays a role in this protective BDNF-mediated mechanism. As with BDNF, levels of IGF-1 increase as a result of physical activity; IGF-1 interacts with BDNF, modulating downstream signaling and subsequent improvements in cognitive function associated with increased hippocampal size. Blocking IGF-1 receptors in the hippocampus resulted in a decrease in exercise-induced increase in BDNF levels and memory retention but not in learning acquisition; the blockade also reduced levels of downstream proteins related to cortical plasticity and memory processes, such as synapsin I, mitogen-activated protein kinase II, and calcium/calmodulin protein kinase II, which have been shown to be elevated as a result of exercise.15 Thus, exercise induces a biological change involving both BDNF and IGF-1, and these 2 proteins play important roles in mediating downstream effects of exercise-induced improvements in cortical plasticity, hippocampal size, and memory function.

Mobility and Preservation of White Matter

In addition to increased hippocampal size and the preservation of specific areas of cortical gray matter, exercise helps to preserve white matter. Anterior white matter tract loss is associated with cognitive impairment, dementia, and Alzheimer disease1 and is one of the main mechanisms behind cognitive aging. Anterior white matter tracts experienced greater age-related decline than posterior and temporal regions, but this loss was spared by increased aerobic fitness.12 The cingula, in particular, are white matter tracts that facilitate communication between areas of the limbic system involved in executive function and memory formation. (Executive function refers to cognitive processes such as planning, working memory, attention, problem solving, verbal reasoning, inhibition, and task monitoring.) A cross-sectional study of older adults (66 ± 6 years old) revealed that those with high physical fitness, as measured by maximal oxygen consumption, had greater white matter integrity in areas of the cingulum compared with older adults who were sedentary.32 Increased physical activity aids in the preservation of white matter tracts and is one mechanism that can help slow down the process of cognitive aging and prevent debilitating mental decline. (Another mechanism was seen through education effects: higher education was associated with preserved white matter in inferior frontal areas, which mildly differs from the effects seen with exercise.39) While different levels of fitness and education can lead to different structural changes in the brain, they are both predictive of cognitive function preservation through the enhancement of white matter integrity.

Mobility and Improved Cognitive Function

Exercise-induced changes in brain structure are predictive of improved cognitive functions related to those areas.7,46,42 These effects on cognitive function are evaluated via neurocognitive and neuropsychological tests that measure parameters such as verbal memory, visual memory, reaction time, and information-
processing speed. Physically fit older adults perform better than their less-fit counterparts at simple cognitive tasks. A study on 42 women aged 50 to 90 years revealed that higher cardiorespiratory fitness was a significant predictor of increased overall cognitive function, cognitive speed, verbal memory, and attention. Higher levels of physical activity and increased maximal oxygen consumption scores were positively associated with tasks that reflected information-processing speed, such as the Stroop color-word and interference task and concept shifting test. There is specificity to how physical activity can benefit cognitive function, particularly in the frontal lobe areas that mediate executive function. Also, increased aerobic capacity with increased age seemed to have the greatest influence on improved cognitive function, especially in areas related to memory and effortful cognitive processing. These results correlate with structural changes seen in the hippocampus and areas mediating executive function. In addition, physical mobility improves executive control function in older adults by affecting the distribution of cortical signaling related to memory and attentional processes. Data indicate that exercise has a selective beneficial effect in those tasks requiring cognitive effort and that it demonstrates significant application in promoting healthy cognitive aging.

The effects seen in van Boxtel's study correlate with an earlier hypothesis by Chodzko-Zajko: tasks that require significant cognitive processing would be more sensitive to the effects of fitness than tasks that can be performed with or without minimal attention. To investigate this task-dependent association between physical fitness and cognitive performance, Chodzko-Zajko suggested investigating molecular level differences and responses to various cognitive challenges between individuals of high and low fitness as well as before and after a structured program of exercise training. In the past 20 years since Chodzko-Zajko's suggestion, a wealth of information has been gathered. Results from studies investigating individuals of high and low fitness show that the biological impact of exercise on the brain and cognition includes structural and cognitive changes that facilitate healthy brain aging.

**Therapeutic Effects of Short-Term Exercise Interventions on Brain Structure and Cognition**

The human brain gradually grows and develops through the second or even third decade of life and then slowly decreases in size upon the later years of life. Exercise and maintained physical activity are implicated in slowing down the gradual progression of brain structural and cognitive decline. A number of longitudinal studies and randomized control trials investigated the effects of varying lengths of exercise interventions on brain structure and neurocognitive function, as well as mood and depression status, which are major determinants of quality of life. Generally, these studies show that adding physical activity to one's daily routine can result in significant biological changes that can improve one's overall physical as well as mental health.

**Exercise-Induced Changes in the Brain**

Exercise has an immediate biological effect on brain composition and structure. A regimen of physical activity for 2 hours per day at 5 days per week for either 4 or 8 weeks produced a significant increase in rat hippocampal BDNF, compared with only cognitive activity treatment. Similarly in humans, 6-month and 1-year aerobic exercise interventions, resulting in increased fitness in participants, were associated with an increase in serum BDNF levels and hippocampal size, greater levels of task-related activity in attentional control areas of the brain, increased white matter integrity in the frontal and temporal lobes, and greater improvement in short-term memory. Specifically, Erickson found that aerobic training for 1 year mediated hippocampal growth by 2%, which reversed age-related loss by 1 to 2 years. Also, higher preinterventional fitness was able to counter age-related hippocampal volume decline. Therefore, age-related loss of brain volume can be attenuated by high levels of lifelong fitness or starting and maintaining a chronic exercise regimen regardless of prior fitness level.

**Exercise-Induced Improvements in Cognitive Tasks in Healthy Brains**

Even short-term exercise interventions improved cognitive function. In older adults aged 60 to 77 years, 2 months of aerobic training significantly improved memory and learning ability, whereas the control group did not see such improvements. Walking 90 minutes once a week for 3 months was associated with improvements in frontal lobe function, perceived quality of life, and motor function compared with those who did not walk. Healthy young adults who exercised for 4 weeks improved in object recognition memory compared with those who did not exercise consistently or at all. The results of these exercise interventions support the evidence that executive functions are selectively maintained or enhanced in humans who exercise regularly and thus have higher levels of fitness. Specific improvements are associated with exercise-induced neurogenesis in the frontal lobe and hippocampal regions of the brain.

The conclusions of several meta-analyses on the wealth of research regarding the effect of exercise interventions on cognitive processes support the notion that exercise is beneficial and selective in which processes that experience the most age-related protection and improvement. Colcombe and Kramer’s analysis of 18 interventional studies involving older adults (55 years and older) conducted between 1966 and 2001 showed that fitness training has strong and selective benefits for cognition: the largest fitness-induced benefits were seen in executive control processes, and the degree of fitness effects was moderated by length, type, and duration of fitness training. A meta-analysis of 20 randomized control trials between 1982 and 2009 that included younger participants (18 years and older) demonstrated that individuals randomly assigned to aerobic exercise training had modest improvements in attention and processing speed, executive function, and memory.
Short-Term Exercise Can Improve Cognitive Function in Diseased States

In addition to reducing age-related declines in brain volume and cognitive function, exercise can reduce the risk of age-related neurologic disorders. Randomized control trials involving 4 to 6 months of physical activity intervention showed improved frontal cognitive functions in elderly patients with Alzheimer disease and significant improvement in Alzheimer’s Disease Assessment Scale–Cognitive subscale scores in older adults with memory problems compared with those who did not engage in physical activity interventions. In a study investigating the dose-response relationship of self-reported exercise and mental health in individuals aged 16 years and older, increased mental health benefits were seen at as little as 20 minutes of exercise per week. A strong dose-response relationship was observed in individuals that participated in high-volume activities such as sports. In a randomized trial, individuals who had memory problems and were at risk for dementia started a 6-month physical activity regimen and followed it for 18 months; those who received the physical activity intervention demonstrated a mild but important improvement on cognitive functioning tests at 6 months compared with the control group. This improvement continued for another 12 months following the discontinuation of the intervention.

Exercise May Be Less Effective in Mood Disorders

Exercise seems to have less of a beneficial effect in improving cognition in individuals with mood disorders. In a recent study involving middle-aged and older adults with major depressive disorders who engaged in an exercise intervention for 4 months, no significant difference between the exercise group and control group was seen in performance on neuropsychological tests of executive function, verbal memory, verbal fluency, and working memory. These results are in discordance with the depression reduction hypothesis, which states that depression suppresses cognitive ability but can be alleviated by physical activity, subsequently improving cognitive function. A depressive mood and emotional state may diminish the beneficial effects of exercise, but if exercise is able to reduce the depressive state, the beneficial effects on neurocognition may be more pronounced. A longer randomized clinical trial may be necessary for the effects of exercise on alleviating depression to be realized before improvements in neurocognition are examined.

Impact of Long-Term Exercise and Fitness on Executive Function

Higher Fitness in Older Age Mediates Improved Cognitive Function

Several studies have established that higher levels of activity and fitness over extended periods have positive effects on cognitive functioning in older adults. In a longitudinal study examining activity in more than 16,000 US women between the ages of 70 and 81 years, a higher level of self-reported activity was associated with higher cognitive performance. Individuals with the highest reported activity levels had a 20% lower risk of cognitive impairment than individuals with the lowest reported activity levels. Walking as little as 1.5 hours per week was associated with improved cognitive function. A longitudinal study of individuals in their 70s examining predictors of maintaining cognitive function over 8 years found that weekly moderate to vigorous exercise predicted higher cognitive functioning at follow-up. In addition to weekly exercise, younger age, white race, high school education level or greater, ninth-grade literacy level or greater, and not smoking predicted increased cognitive functioning, suggesting that a variety of factors are at play but that exercise is still a significant contributor to neuroprotection. A cohort study of men and women enrolled in the MRC National Survey of Health and Development (the British 1946 birth cohort) that evaluated the relationship between physical exercise and mental health benefits of participating in light exercise and exercise regimens of 4 to 6 months of physical activity intervention showed improved frontal cognitive functions in elderly adults at risk for dementia started a 6-month physical activity regimen and followed it for 18 months; those who received the physical activity intervention demonstrated a mild but important improvement on cognitive functioning tests at 6 months compared with the control group. This improvement continued for another 12 months following the discontinuation of the intervention.

Chronic Exercise Can Reduce the Risk of Cognitive Disorders

In addition to preserved cognitive functioning and decreased levels of psychological distress, long-term exercise and higher activity levels can decrease the risk of dementia in older adults. In a 5-year longitudinal study of individuals aged 65 years and older, physical activity was associated with a decreased risk of cognitive impairment, Alzheimer disease, and dementia, and greater protection against dementia was found in individuals with the highest activity levels. A 21-year longitudinal study involving 4 to 6 months of physical activity intervention showed improved frontal cognitive functions in elderly adults at risk for dementia started a 6-month physical activity regimen and followed it for 18 months; those who received the physical activity intervention demonstrated a mild but important improvement on cognitive functioning tests at 6 months compared with the control group. This improvement continued for another 12 months following the discontinuation of the intervention.
also found that physical activity of at least 2 times per week during midlife was associated with a reduced risk of dementia and Alzheimer disease at later ages.35

**Future Directions**

Studies regarding the effects of exercise on cognitive function provide promising results and pave the way for future research, especially with applications to aging adults. However, there have been several criticisms regarding the methods of past studies and their attempts to establish a causal relationship between exercise and improved cognitive functioning.33 More consistent measures and evaluations of cognitive functioning and a standard measure for exercise and fitness level would allow for study reproducibility among many different study populations. A more standardized approach to studying exercise and fitness level in relation to cognition would allow for a more quantitative evaluation of dose-response relationships.

A consideration for continued research includes directly studying a very physically active older population, such as masters athletes, and comparing them to a sedentary control group to determine the impact of high-level chronic exercise in preserving mental function. Examining the effects of physical activity in addition to other neurocognitive-stimulating processes, such as mental and social activity, will help researchers determine the various combinations of modalities that are most effective at preserving brain function and mental capabilities. Both animal and human studies have found that physical and cognitive interventions in combination may be more beneficial to cognitive function than either type of intervention alone,16,27 but more specific details regarding which activities are more neuroprotective and which cognitive processes are more impacted have yet to be elucidated.

**CONCLUSION**

Chronic exercise exhibits positive effects on many areas of the human body, including the cardiovascular and musculoskeletal systems.3 Recent research demonstrates that participating in a chronic exercise regimen can improve an individual’s cognitive functioning and reduce the risk of dementia and other neurodegenerative diseases. Maintaining mobility through exercise helps maintain brain fitness by preserving hippocampal volume and white matter tract integrity, which are important for memory processing, prevention of age-related cognitive decline, and even prevention of dementia.2,22,26,31,34,37

As we age, mobility is important not only for our bodies but for our minds as well.

### Clinical Recommendations

| Clinical Recommendation                                                                 | SORT Evidence Rating |
|----------------------------------------------------------------------------------------|----------------------|
| Engaging in regular exercise, especially during the later decades of life, is recommended for maintaining brain health by attenuating age-associated volume decline and white matter losses. | A                    |
| Maintained regular exercise increases cardiopulmonary fitness and can help improve executive cognitive functions such as memory. | A                    |
| Physical mobility is recommended in older adults to help reduce the risk of dementia and other age-associated cognitive disorders. | A                    |

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