

Being physically active may protect the brain from Alzheimer disease

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Neurology® 2012;78:1290–1291

Physical activity has been consistently associated with decreased risk for cognitive decline and dementia¹ and its positive effects are evident both for Alzheimer disease (AD)² and vascular dementia.³ In contrast to many other risk and protective factors for AD that have failed to show effectiveness when translated into clinical trials (e.g., vitamin E, statins),⁴ clinical trials investigating the effects of physical activity on cognitive outcomes have yielded mostly positive results,⁵ albeit with relatively small sample sizes. These effects are relevant for prevention in primary (normal), secondary (mild cognitive impairment), and tertiary (AD) patients. Potential mechanisms underlying the relationship of physical activity with AD include modification of levels of brain-derived neurotrophic and vascular endothelial growth factors, and improved glucometabolic functioning.⁶

A weakness of most prior studies was the use of self-reports of physical activity, which may be influenced by recall bias and usually omit low intensity, nonexercise activity. Only 2 published studies have used objective measures to confirm that physical activity is associated with current⁷ or future cognitive impairment.⁸

In this issue of *Neurology*®, Buchman et al.⁹ advance the field by reporting the relationship of total physical activity, objectively measured by actigraphy, with incident AD and cognitive decline in the Rush Memory and Aging Project. Subjects (n = 716) wore an actigraph on the nondominant wrist 24 hours/day for up to 10 days, while both exercise and nonexercise activity were continuously recorded. This is the first study to report prospective associations of physical activity with AD and cognitive decline using an objective measurement of physical activity, which importantly eliminates recall bias, and includes an all-encompassing measure of daily physical activity.

Subjects with lower overall physical activity had higher risk of AD and faster rate of cognitive decline after controlling for several confounders, including motor function. Importantly, additional accounting

for self-reported measures of exercise, physical activity, and socially and cognitively stimulating activities changed results only slightly, suggesting that total daily activity, including nonexercise physical activity, may be particularly important to augment cognition and forestall AD. Examination of 5 specific cognitive domains found significant associations for episodic memory, working memory, perceptual speed, and a possible but nonsignificant difference for visuospatial abilities, suggesting that the relationship of physical activity with an overall cognitive measure reflects a spread of benefits over several cognitive domains. This differs from other risk factors that are associated with specific domains, such as kidney function, which was associated only with memory in this same cohort.¹⁰

Since the follow-up period of this study was only 3.5 years, the question of reverse causality (i.e., incipient AD potentially contributing to physical deterioration) was well addressed by showing that baseline physical activity was not associated with prior cognitive decline, and that change in physical activity was not associated with baseline cognition. Clinical trials with positive results further support the view that low physical activity is deleterious to the brain rather than vice versa.⁵

The authors also examined the intensity of daily activity (steps per time in activity), which was consistently more strongly associated with improved cognitive outcomes than the primary overall daily activity measure. The difficulty with the interpretation of this result is that most daily activity is low intensity, and although not presented in the study, the daily volume and intensity of activity are probably positively correlated, so that their effects on cognition may be difficult to distinguish. This suggests the usefulness of a study monitoring both low intensity and higher intensity activity to clarify what activity to recommend.

These results may have substantial pragmatic implications for public health: motivating the elderly to be physically active, even if mobility is limited, may

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Go to Neurology.org for full disclosures. Disclosures deemed relevant by the authors, if any, are provided at the end of this editorial.

decrease their risk of developing AD. Since in the Buchman et al. study the actigraph was attached to the wrist, cooking, washing dishes, playing cards, and even activity in the setting of reduced mobility, such as moving a wheelchair with one's arms, constitute nonexercise physical activity from which elderly may benefit. Although the beneficial effects of physical activity may accumulate over many years, this study supports encouragement of physical activity at any age, including very old age (the sample was on average 82). In a world that is becoming progressively sedentary, and in the context of very limited success of the currently available medications to treat or delay AD, physical activity provides a promising, low-cost, easily accessible, and side-effect-free means to prevent AD. In addition, physical activity has other beneficial effects on quality of life, combatting cardiovascular disease, risk of falls, disability, and depression.

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