

Effect of physical activity, nutrient supplementation interventions on cognition

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Two studies in the August 25 issue of *JAMA* examine the effect of physical activity and nutrient supplementation on cognitive function.

In one study, Kaycee M. Sink, M.D., M.A.S., of the Wake Forest School of Medicine, Winston-Salem, N.C., and colleagues evaluated whether a 24-month [physical activity](#) program would result in better cognitive

function, lower risk of [mild cognitive impairment](#) (MCI) or dementia, or both, compared with a health education program.

Epidemiological evidence suggests that physical activity is associated with lower rates of cognitive decline. Exercise is associated with improved cerebral blood flow and neuronal connectivity and maintenance or improvement in brain volume. However, evidence from randomized trials has been limited and mixed, according to background information in the article.

Participants in the Lifestyle Interventions and Independence for Elders (LIFE) study (n = 1,635; 70 to 89 years of age) were randomly assigned to a structured, moderate-intensity [physical activity program](#) (n = 818) that included walking, resistance training, and flexibility exercises or a health education program (n = 817) of educational workshops and upper-extremity stretching. Participants were sedentary adults who were at risk for mobility disability but able to walk about a quarter mile. Measures of cognitive function and incident MCI or dementia were determined at 24 months.

The researchers found that the moderate-intensity physical activity intervention did not result in better global or domain-specific cognition compared with the health education program. There was also no significant difference between groups in the incidence of MCI or dementia (13.2 percent in the physical activity group vs 12.1 percent in the health education group), although this outcome had limited statistical power.

"Cognitive function remained stable over 2 years for all participants. We cannot rule out that both interventions were successful at maintaining cognitive function," the authors write.

Participants in the physical activity group who were 80 years or older

and those with poorer baseline physical performance had better changes in executive function composite scores compared with the health education group. "This finding is important because executive function is the most sensitive cognitive domain to exercise interventions, and preserving it is required for independence in instrumental activities of daily living. Future physical activity interventions, particularly in vulnerable older adult groups (e.g., ≥80 years of age and those with especially diminished physical functioning levels), may be warranted."

In another study, Emily Y. Chew, M.D., of the National Eye Institute/National Institutes of Health, Bethesda, Md., and colleagues tested the effects of oral supplementation with nutrients on cognitive function.

The prevalence of Alzheimer disease, estimated to have affected 5.2 million people in the United States in 2013, may triple in the next 4 decades. Epidemiologic studies have suggested that diets high in omega-3 long-chain polyunsaturated fatty acids (LCPUFAs) have a protective role in maintaining cognitive function. However, numerous randomized clinical trials (RCTs) failed to show omega-3 LCPUFAs to be effective in treating dementia, according to background in the article.

Participants in the Age-Related Eye Disease Study 2 [AREDS2]), who were at risk for developing late age-related macular degeneration (AMD), were randomly assigned to LCPUFAs (1 g) and/or the dietary supplements lutein (10 mg)/zeaxanthin (2 mg) vs placebo. All participants were also given varying combinations of vitamins C, E, beta carotene, and zinc. In addition to annual eye examinations, several validated cognitive function tests were administered via telephone by trained personnel at baseline and every 2 years during the 5-year study. A total of 89 percent (3,741/4,203) of AREDS2 participants consented to the ancillary cognitive function study and 94 percent (3,501/3,741) underwent cognitive function testing. The average age of the participants

was 73 years, and 57.5 percent were women.

There were no statistically significant differences in change of measures of cognitive function for participants randomized to receive supplements vs those who were not. The yearly change in the composite cognitive function score was -0.19 for participants randomized to receive LCPUFAs vs -0.18 for those randomized to no LCPUFAs. Similarly, the yearly change in the composite cognitive function score was -0.18 for participants randomized to receive lutein/zeaxanthin vs -0.19 for those randomized to not receive lutein/zeaxanthin.

Regarding the lack of effect of the supplements, the authors speculate that the supplements were started too late in the aging process and that supplementation duration of 5 years may be insufficient. "The process of cognitive decline may occur over decades, thus a short-term supplementation given too late in the disease may not be effective."

They add that the observational data regarding dietary intake of specific nutrients such as omega-3 LCPUFAs and antioxidants suggest strong inverse associations with dementia, yet the RCTs have failed to show beneficial effects. "It is possible that eating foods rather than taking any specific single supplement may have an effect."

"Although the well-designed RCTs presented by Sink and colleagues and Chew and colleagues failed to demonstrate significant cognitive benefits, these results should not lead to nihilism involving lifestyle factors in older adults. It is still likely that lifestyle factors such as diet and physical activity have important roles in the prevention of cognitive decline, dementia, and performance of the activities of daily living," write Sudeep S. Gill, M.D., M.Sc., and Dallas P. Seitz, M.D., Ph.D., of Queen's University, Kingston, Ontario, Canada, in an accompanying editorial.

"Physicians should encourage patients of all ages to optimize physical activity levels throughout their life, which may help to reduce the risk of developing dementia and many other adverse health outcomes. An active lifestyle throughout the lifespan may be more effective in preventing cognitive decline than starting physical activity after the onset of cognitive symptoms. Similarly, adherence to Mediterranean or heart healthy diets throughout life are likely to be most beneficial in preventing [cognitive decline](#) or the onset of dementia in contrast to isolated nutritional supplements initiated late in life."

More information: *JAMA*, [DOI: 10.1001/jama.2015.9617](https://doi.org/10.1001/jama.2015.9617)
JAMA, [DOI: 10.1001/jama.2015.9677](https://doi.org/10.1001/jama.2015.9677)
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