Cardiorespiratory fitness and cognition in the elderly

Can you outrun cognitive impairment?

The identification of lifestyle choices that reduce dementia risk remains of considerable interest. Both exercise and nonexercise physical activity have been associated with better cognition and reduced dementia risk. One hypothesis for this association relates to the cardiovascular benefits on reduction of cerebrovascular disease, but few studies have generated data on cardiovascular fitness, neuroimaging, and cognition from a sufficiently large number of persons to test this theory. In this issue of Neurology®, Freudenberger et al. present such data from a community-based study of nearly 900 participants.

The authors assessed cardiorespiratory fitness with estimated maximum oxygen consumption ($\dot{V}O_2$max) based on a formula that incorporated weight, resting heart rate, and maximum heart rate from a graded treadmill stress test. They quantified lacunar infarct burden, white matter lesions (WMLs), and atrophy from MRIs. Cognition was assessed with a battery of tests and converted to summary measures. In multivariable analyses, the authors found that $\dot{V}O_2$max was directly associated with global and domain-specific cognition and this association was modified by body mass index (BMI) with stronger beneficial effect seen in persons with lower BMI. $\dot{V}O_2$max was also indirectly associated with WMLs, but not lacunes. WMLs did not mediate the association of $\dot{V}O_2$max with cognition.

The study has strengths including a large sample of community-dwelling participants with very good measures of $\dot{V}O_2$max and cognition, with standard measures of WMLs. Although this is not the first study to link measures of cardiorespiratory fitness to neuroimaging and cognition, the sample size and study design make it stand out.

One prior study of nearly 150 persons found that cardiorespiratory fitness was associated with better performance on cognitive function tests and higher volumes of several regions of gray matter. Of note, volumes in different regions were differentially associated with different aspects of cognition. A second study of more than 80 people found that cardiovascular fitness was positively associated with cognitive performance and greater gray matter volumes in several regions, and with lower WMLs.

The authors did not perform a mediation analysis. Taken together, the findings are certainly intriguing although limited by the cross-sectional design.

The current study also has limitations. Most important, similar to the earlier studies, the cross-sectional nature of the association limits causal inferences. The authors acknowledge this, but the other issues remain. Their associations were not robust, they treated all WMLs equally (did not consider anatomical distribution), and they did not look at the effects on gray matter. Perhaps some important associations were missed.

Based on these data, are we ready to recommend vigorous exercise to improve cardiorespiratory fitness to maintain cognition? The short answer is no. Perhaps the decision can be informed with data from randomized trials. A randomized clinical trial of more than 1,600 sedentary persons conducted earlier this year, the LIFE (Lifestyle Interventions and Independence for Elders) study, evaluated the efficacy of the moderate physical activity program on cognition. After 2 years, the intervention group did not perform better on cognitive function tests that served as the primary outcomes. There also was no effect on incident mild cognitive impairment or dementia. Perhaps a broader lifestyle intervention approach is required with physical activity as one of many lifestyles that promotes health. Also earlier this year, the results of a randomized clinical trial of more than 1,200 persons with a poor cardiovascular risk profile were reported. Participants were randomized to a multidomain intervention consisting of diet, exercise, cognitive training, and vascular risk monitoring; the primary outcome was change in a composite measure of cognition. The intervention group declined more slowly, suggesting a benefit of the intervention.

Of note, the study by Freudenberger et al. revealed an interaction with BMI, but one in which lower BMI had a more protective effect of cardiovascular fitness on cognition. It should be noted that both trials...
enrolled subjects with an at-risk profile. Furthermore, in neither trial was the intervention designed to maximize cardiovascular fitness. Physical activity and cardiorespiratory fitness are related but not the same.10

Thus, at this point we are left—as we are with most lifestyle risk factors—without the ability to make solid recommendations regarding the cognitive health benefits of cardiovascular fitness. However, there are many other very good reasons to recommend activities that promote cardiovascular fitness to our patients, and their family members. Better cardiovascular fitness is associated with better cardiovascular health and with reduced risk of all-cause mortality.10 Therefore, within the limits of one’s cardiovascular health, it seems like a good idea to engage in activities that promote cardiorespiratory fitness, because with few exceptions, “Every creature is better alive than dead…” (Henry David Thoreau, The Maine Woods).

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DISCLOSURE
L. Roever and D. Bennett report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

REFERENCES