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Never Too Fit for Body and Mind

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There is a tidal wave of evidence about the benefits of physical fitness in several health areas across the life span, including benefits on cognition and prevention of dementia. The evidence comes in many forms, such as epidemiologic studies identifying associations between physical activity or fitness measures and cognitive performance, clinical studies measuring the association between fitness and biomarkers of cognition and brain function, clinical trials demonstrating improvements in cognition associated primarily with aerobic activity interventions, and basic in vitro and in vivo biological studies implicating neuromechanisms affected by aerobic activity.

In this issue, the work presented by DeFina and colleagues (1) provides an interesting addition to this body of work. Here, cardiorespiratory fitness levels in midlife, measured by exercise stress testing, were found to lower the risk for diagnoses of dementia later in life. Specific details of the study include the impressively large sample size of more than 19 000 persons and more than 9 years of follow-up. Dementia diagnoses were based on Medicare claims data, which may have minimal precision in detection of dementia type or mild impairment but surely capture clinically significant disease. Most strikingly, the population, captured from a preventive medicine practice, was very healthy, highly educated, and primarily white. The take-away finding from this study is that better fitness levels in midlife were associated in decreased risk for all-cause dementia nearly a decade later. The association remained even after control for hypertension, diabetes, and hyperlipidemia, which is consistent with the report that the effect size was similar when dementia was considered both with and without stroke.

The beneficial effect of fitness has been demonstrated on many outcomes, and the benefit seems to be independent from and perhaps greater than many other factors, such as diabetes and hypertension control. For example, a greater reduction in mortality risk has been noted in fit persons than those who are “unfit,” regardless of body mass index. In fact, fit overweight persons have a lower risk for death than “unfit” normal-weight persons (2).

Many findings in DeFina and colleagues’ report have been described in previous studies. First, it has been established that midlife health and behaviors can influence future

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outcomes. For example, midlife depression, smoking, and high body mass index, as well as other cardiovascular risk factors, increase the risk for dementia in later life, and it has been suggested that modification of these risks can decrease the risk for dementia (3). Further, physical activity and fitness have been shown to affect dementia-related mortality (4). Cognition, as well as dementia, both immediately (5) and remotely (3), have been associated with physical activity. DeFina and colleagues' study confirms these previous observations. Although the objective measure of fitness using cardiorespiratory testing adds some conviction to the association between fitness levels and cognitive benefits, the association was also apparent in studies that relied on self-reported physical activity. An important and possibly unique contribution of the current study is the fact that, even in this healthy elite cohort, higher fitness levels yield greater protection against dementia.

Previous studies have demonstrated the benefit of fitness on cognition among those with comorbid conditions, such as obesity and diabetes. Levels of ideal or maximum fitness in many of these studies (>8 maximal metabolic equivalents) (6, 7) overlap with the lowest level of fitness of the participants in the current study (8.1 maximal metabolic equivalents). It is interesting that the association of fitness with reduced risk for dementia exists in these "super healthy" persons as well as those with comorbid conditions and suggests that there may be a dose-response relationship between fitness and cognitive health.

What are the secrets to midlife fitness that will provide maximal protection against dementia? Of note, the highest fitness level was the oldest, suggesting that these individuals may have a fitness "habit." Health behaviors are often longstanding. For example, among a large, well-characterized cohort of women, self-reported physical activity at earlier times in life (that is, adolescent years) correlated with the likelihood of reporting being physically active later in life. Further, physical activity in the early adolescent years was associated with the greatest reduction in dementia risk (8). These findings suggest that behaviors established early in life may persist and benefits may be due to the intensity of the behavior as well as the length of time one has engaged in it.

The authors write that fitness is modifiable through physical training. The hope is that any modifiable risk offers a path to better health outcomes. Unfortunately, adherence to exercise regimens is notoriously difficult. DeFina and colleagues point to reports estimating that 150 minutes per week of moderate intensity could improve fitness by 1 to 2 maximal metabolic equivalents. However, we must keep in mind that the lowest quintile of performance in the study cohort was already at a level that is likely to require this amount of activity, so even a small risk reduction in dementia would require an estimate of 5 hours or more per week. The national trends in physical activity are quite poor. A 2011 report suggests that less than 10% of the population achieves the 150-minutes-per-week guideline when measures of accelerometry were used (9). Even more disturbing from this report is that self-reported estimates of physical activity exceed the objective measures by 6-fold, indicating a lack of recognition of the problem at the individual level. Although physician recommendations may provide motivation to engage in physical activity as a health behavior for disease prevention, focus groups indicate that behavioral change is most likely to occur only in the face of health problems. Physicians' efforts to promote physical activity may have less effect when directed at healthy persons (10). Nevertheless, Alzheimer disease is the second

most feared disease among U.S. adults, behind only cancer (11). This fear may provide both the context for physicians to introduce the topic of physical activity and the motivation for patients to heed advice to increase physical activity. Given the evidence that physical activity is associated with a lower risk for cognitive decline, the relative safety of the intervention, and the other benefits it provides, physical activity seems to be a reasonable prescription for dementia prevention.

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