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Invited Commentary

# Brain Exercise and Brain Outcomes: Does Cognitive Activity Really Work to Maintain Your Brain?

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**A wide variety of cohort studies,** conducted primarily in Europe and North America, have reported that cognitive activity reduces the risk of dementia, Alzheimer disease, or cognitive decline.[1,2] In this issue of *JAMA Psychiatry*, Lee et al[3] report a similar finding in a different population: 15 582 older adult residents of Hong Kong who were dementia-free at baseline and followed up for a median of 5 years. The study is carefully done, with systematic evaluation of cognitive activity, careful baseline and follow-up cognitive assessments, collection of data on a wide variety of potential confounding factors, and efforts to limit loss to follow-up and missing data.

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The article[3] addresses limitations of the existing literature in several key ways. First, investigators have often defined cognitive activities based on their own experience, so there is a subtle (or unsubtle) bias favoring the leisure activities of more highly educated individuals. Although most articles adjust for educational attainment, this underlying measurement bias could contribute to significant residual confounding, given the potentially large effect of education on both cognitive activity (whether actual or measured) and dementia. Second, although definitions of cognitive activity can be narrow with respect to educational background, they are often so broad as to include passive TV-watching, attendance at social gatherings, and other less explicitly cognitive activities. Instead, Lee et al tried to focus on activities that clearly involve cognitive engagement. These investigators also used analytic tools to minimize the chances that any association between cognitive activity and dementia incidence is nonspecific, adjusting for social and physical activities, as well as for the general health factors that facilitate activity in general.

More critically, the analyses of Lee et al[3] carefully address the possibility of *reverse causation* (eg, that lower levels of participation in cognitive activities may be the result rather than the cause of incipient dementia). It is now well estab-

lished that common pathologies leading to dementia (eg, Alzheimer disease and macrovascular and microvascular diseases of the brain) accumulate over years, if not decades, before the patient develops symptoms, and that these symptoms accumulate for years before the patient crosses the functional impairment threshold for dementia. So these investigators looked to see if their findings held up when they excluded those who developed dementia in the first 3 years.

Do we believe that cognitive activity reduces risk of dementia after reading this article[3] in the context of the larger literature? We think that readers of this journal, who likely engage in a great many cognitive activities, will certainly want to believe that. Moreover, everyone wants to believe that specific efforts, particularly those undertaken later in life when the risk of dementia looms closer, might confer a real benefit. Overall, these authors buttress the findings through their careful efforts to address confounding by education, health behaviors, and health status; include a range cognitive activities of interest to those across the social spectrum; understand the effect of specifically cognitive activities independent of social and physical activity; and minimize outcomes associated with reverse causation.

Are there any other major limitations that threaten the validity of their conclusions?[3] In addition to residual confounding by education or reverse causation over the longer term, there is still a strong possibility that the salient factor is not late-life cognitive activity, but lifelong cognitive activity, because the 2 are probably highly correlated. That may still be good news for readers of *JAMA Psychiatry*, but perhaps less so for those seeking to reduce their risk by embarking on such activities late in life.

Do these findings generalize beyond the current generation of Chinese elders? The authors are careful to point out that the observed association between cognitive activity and dementia risk may be different in China or Hong Kong than elsewhere in the world, but, perhaps just as crucially, but, perhaps just as crucially, this association may differ markedly across generations. Readers will note that the categories of education for participants in the study by Lee et al are 0 years, 1 to 2 years, and more than 2 years. Given upward secular trends in literacy and education,[4] along with likely concomitant changes in workplace cognitive demands, cognitive activities are likely evolving in both nature and effect—in China, Hong Kong, and elsewhere in the world. Moreover, educational level also affects both dementia screening procedures and dementia risk via cardiovascular risk, health behaviors, and access to care.

What is the takeaway? The preponderance of the evidence suggests that cognitive activity may prevent the development of dementia, although in principle a randomized clinical trial would be required to confirm that finding. Trials to date have largely been limited to administering cognitive training and then assessing the short-term outcome on focused cognitive activities. Most such studies have shown an improvement in the practiced task and perhaps similar tasks, with limited if any generalization to overall cognition or functional status.[5] Even for late-life engagement, it would be difficult if not impossible to design a randomized clinical trial that truly asks the same question as the observational studies—about the outcome of real-world, freely chosen cognitive activities over months, years, or decades.

In the meantime, is there any reason not to pursue cognitive (and physical and social) activities that can enrich our lives and those of people around us? Chosen well, such activities improve quality of life, and they might reduce our risk of dementia, too. On the other hand, do these data support the purchase of brain games software or toys? Only if the users find that such activities are engaging and worth pursuing—and purchasing—for their own sake. There is no evidence that such activities offer more benefit than a book from the public library, a game of chess in the local park, a penny-ante poker game, or a wide variety of other highly cognitive but close-to-free activities on offer.

## ARTICLE INFORMATION

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