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Association of Daily Intellectual Activities With Lower Risk of Incident Dementia Among Older Chinese Adults

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IMPORTANCE Associations between late-life participation in intellectual activities and decreased odds of developing dementia have been reported. However, reverse causality and confounding effects due to other health behaviors or problems have not been adequately addressed.

OBJECTIVE To examine whether late-life participation in intellectual activities is associated with a lower risk of incident dementia years later, independent of other lifestyle and health-related factors.

DESIGN, SETTING, AND PARTICIPANTS A longitudinal observational study was conducted at all Elderly Health Centres of the Department of Health of the Government of Hong Kong among 15 582 community-living Chinese individuals age 65 years or older at baseline who were free of dementia, with baseline evaluations performed January 1 to June 30, 2005, and follow-up assessments performed from January 1, 2006, to December 31, 2012. Statistical analysis was performed from January 1, 2015, to December 31, 2016.

MAIN OUTCOMES AND MEASURES The main outcome was incident dementia as diagnosed by geriatric psychiatrists in accordance with the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision*, or a Clinical Dementia Rating of 1 to 3. At baseline and follow-up interviews, self-reported information on participation in intellectual activities within 1 month before assessment was collected. Examples of intellectual activities, which were described by a local validated classification system, were reading books, newspapers, or magazines; playing board games, Mahjong, or card games; and betting on horse racing. Other important variables including demographics (age, sex, and educational level), physical and psychiatric comorbidities (cardiovascular risks, depression, visual and hearing impairments, and poor mobility), and lifestyle factors (physical exercise, adequate fruit and vegetable intake, smoking, and recreational and social activities) were also assessed.

RESULTS Of the 15 582 individuals in the study, 9950 (63.9%) were women, and the median age at baseline was 74 years (interquartile range, 71-77 years). A total of 1349 individuals (8.7%) developed dementia during a median follow-up period of 5.0 years. Multivariable logistic regression analysis showed that the estimated odds ratio for incident dementia was 0.71 (95% CI, 0.60-0.84; $P < .001$) for those with intellectual activities at baseline, after excluding those who developed dementia within 3 years after baseline and adjusting for health behaviors, physical and psychiatric comorbidities, and sociodemographic factors.

CONCLUSIONS AND RELEVANCE Active participation in intellectual activities, even in late life, might help delay or prevent dementia in older adults.

Invited Commentary page 703

Supplemental content

CME Quiz at jamanetwork.com/learning and CME Questions page 764

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Dementia is a major public health concern worldwide.[1] Finding ways to delay or prevent the clinical onset of dementia is now a key priority, as disease-modifying treatment is lacking and populations are rapidly aging.[2-4] Increasing evidence suggests that active participation in intellectual activities such as reading books and playing games can help reduce the risk of dementia among older adults,[5-13] possibly through improving cognitive reserve and strengthening resilience against stress.[14-17] However, several questions remain unanswered. First, people with a high level of intellectual activities are often more health conscious and live a healthier life such as exercising regularly, eating a balanced diet, and refraining from smoking.[18,19] Whether participation in intellectual activity can prevent dementia independent of these healthy lifestyle practices, which themselves have already been shown to be useful in lowering the risk of dementia, has yet to be determined. Second, intellectual leisure activities often encompass a mixture of cognitive, social, and recreational components.[20] With a lack of standardized classification of intellectual activities and failure to adjust for other aspects of leisure activities, it remains uncertain whether it is the cognitive training, social engagement, or positive experience of intellectual activities that contributes most to better cognitive health.[8,9,11,21] Third, although previous longitudinal studies of intellectual activities and incidence of dementia excluded participants with dementia at baseline, individuals in the preclinical stage of dementia might have already experienced difficulty in performing more complicated hobbies and engaging in intellectual interests. Such reverse causation might introduce bias in the observed association.[22] A longer interval between assessment of activities and diagnosis of dementia might allow us to be more confident about the temporality of the association.[14]

In this study, we followed the cognitive status of a large well-characterized cohort of community-living older adults in Hong Kong who were free of dementia at baseline. The objective was to examine whether late-life participation in intellectual activities was associated with a lower risk of dementia years later, independent of other lifestyle and health-related factors. The findings might support and extend the previous literature suggesting that active participation in intellectual activities is important for reducing the risk of dementia.

Key Points

Question Does participation in intellectual activity reduce the risk of dementia in older adults, independent of other healthy lifestyle practices such as regular physical exercise, adequate fruit and vegetable intake, and not smoking?

Findings In this population-based study, 15 582 community-living Chinese individuals age 65 years or older who were free of dementia were followed up for a median period of 5 years. Daily participation in intellectual activities was associated with a significantly lower risk of dementia several years later independent of other health behaviors, physical health limitations, and sociodemographic factors.

Meaning Active participation in intellectual activities, even in late life, might help prevent dementia in older adults.

Methods

Study Design, Setting, and Participants

This was a longitudinal observational study based on all individuals presenting to the Elderly Health Centres (EHCs) of the Department of Health of the Government of Hong Kong from January 1 to June 30, 2005 (N = 18 298). The EHCs provide regular primary health care assessments and cognitive screening for local residents aged 65 years or older. Inclusion criteria for this study were age 65 years or older, Chinese ethnicity, and living in the community. Exclusion criteria were non-Chinese ethnicity; living in care homes; having history of stroke, Parkinson disease, or clinical dementia; scoring below the education-specific cutoff on the Cantonese version of the Mini-Mental State Examination (C-MMSE) at baseline (≤18 for individuals without education; ≤20 for those with 1-2 years of education; and ≤22 for those with >2 years of education)[23]; or not providing a description of their leisure activity pattern. In this study, participants were followed up for 6 years to the outcome of incident dementia. To minimize loss to follow-up, those who missed follow-up assessments after 2008 were traced and interviewed by geriatric psychiatrists (A.T.C. Lee and W.C.C.) either at the EHCs, at their homes, or by telephone between October 25, 2011, and December 31, 2012. Written informed consent was obtained from the participants, or from their relatives if they were mentally incapable to give consent, before the follow-up assessment was conducted. This study was approved by both the Department of Health of the Government of Hong Kong and the Joint Clinical Research Ethics Committee of the Chinese University of Hong Kong and the New Territories East Cluster of the Hospital Authority.

Evaluation of Intellectual and Other Types of Leisure Activities

During health assessments at baseline and follow-up interviews, nurses used a questionnaire to ascertain the frequency and type of leisure activities that the participants practiced in the prior month. Using a leisure activity classification system already validated for Hong Kong Chinese older people, the activities were classified as intellectual (reading books, newspapers, or magazines; playing board games, Mahjong, or card games; and betting on horse racing), social (joining a social center, participating in voluntary work, meeting relatives or friends, and attending religious activities), and other recreational (watching television, listening to radio, shopping, and going to a teahouse).[24]

Assessment of Other Variables

Participants' demographics (age, sex, and educational level), physical and psychiatric comorbidities (hypertension, diabetes, hypercholesterolemia, obesity, heart diseases, stroke, Parkinson disease, depression, visual and hearing impairments, and poor mobility), and lifestyle (regular physical exercise, current smoking, and adequate daily consumption of fruits and vegetables) were examined during the health assessment. All diseases were verified and classified by primary care physicians at the EHCs in accordance with the *International Statistical Classification of Diseases and Related Health Problems,*

Tenth Revision. Obesity was defined as body mass index equal to or greater than 25 (calculated as weight in kilograms divided by height in meters squared), in accordance with the local references.[25] Visual impairment was defined as visual acuity of 20/100 or less in both eyes despite best correction. Hearing impairment was defined as 1- and 2-kHz loss of more than 40 decibels in the better ear during audiometric testing (Audioscope, Welch Allyn). Poor mobility was defined as needing an aid to walk or being chairbound. Regular physical exercise, adequate daily consumption of fruits and vegetables, and current smoking were defined as previously reported.[26,27]

Identification of Dementia Cases

Participants received comprehensive clinical examination by physicians at the EHCs at baseline and follow-up, including a detailed history and cognitive screening such as the Delayed Recall Test, the Abbreviated Mental Test, and the C-MMSE. Those who missed these but agreed to a follow-up interview underwent the C-MMSE, clinical examination, and/or Clinical Dementia Rating by geriatric psychiatrists (A.T.C. Lee and W.C.C.), depending on the nature of the interview. A clinical diagnosis of dementia was made in accordance with the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision,* or a Clinical Dementia Rating of 1 to 3.[28,29] A panel of geriatric psychiatrists (A.T.C. Lee, W.C.C., H.F.K.C., and L.C.W.L.) blinded to the participants' other records reviewed the diagnosis independently. For cases whose diagnosis was uncertain or in disagreement, the principal investigator (L.C.W.L.) adjudicated the final diagnosis. The outcome of this study was incident dementia in 6 years.

Sample Size Estimation

Sample size estimation was performed using the Power and Precision software, version 3.0 (Biostat). Sample size was calculated based on estimates of incidence rate of dementia (6% in 6 years) and odds ratios (ORs) for major protective and risk factors (0.75 for intellectual activities) from our previous studies.[26,27] With α set at 0.05, a baseline sample of 10 000 participants would yield at least 80% power for detection of dementia at follow-up.

Statistical Analysis

Statistical analysis was performed from January 1, 2015, to December 31, 2016, using IBM SPSS Statistics, version 22.0 (IBM Corp). The number of participants with follow-up during the 6-year study period was expressed as person-years, which was calculated by summing each participant's contribution of follow-up time (ie, from baseline to the year of assessment when the participant was found to have dementia, or to the year of the last assessment if the participant remained free of dementia). Comparison of participation in intellectual activity and other variables at baseline between participants with and without incident dementia was analyzed by the Mann-Whitney test for continuous variables or the χ^2 test for categorical variables. The level of statistical significance was set at $P < .05$ (2-tailed).

To ascertain whether incident dementia was associated with a lower level of intellectual activities at baseline rather than a longitudinal decrease in practice, participants who remained free of dementia by year 3 but developed dementia at years 4 to 6 were selected, and the proportion of those not having activity participation at baseline was compared with that at year 3 using the McNemar test. To investigate if maintaining participation in intellectual activity in late life was associated with lower incidence of dementia, participants with participation in intellectual activity at baseline were selected, and the proportion of those who had continuous participation 3 years after baseline was compared between those with and without incident dementia at years 4 to 6. To test if baseline participation in intellectual activities was associated with lower risk of dementia years later, participants who were assessed to be free of dementia at year 3 were selected, and the proportion of participants participating in regular activities was compared between those with and without incident dementia at years 4 to 6.

Multivariable logistic regression analysis was performed on the same subgroup to test if participation in intellectual activity at baseline was associated with lower incidence of dementia, after adjusting for age, sex, educational level, cardiovascular risk factors, visual and hearing impairments, poor mobility, depression, smoking, adequate fruit and vegetable intake, regular physical exercise, and other types of leisure activities. The ORs were computed to yield point estimates with 95% CIs.

Results

Incidence of Dementia

A total of 15 582 older adults (85.2%) were included in this study (eFigure 1 in the Supplement). They had a median follow-up period of 5.0 years (interquartile range, 3.0-6.0 years), contributing to a response rate of 82.2%, or 68 919 person-years of follow-up over the 6-year study period (eFigures 2 and 3 in the Supplement). A total of 1349 participants (8.7%) developed incident dementia during the study period. As summarized in **Table 1**, those who developed incident dementia were older than those who remained free of dementia and were predominantly female, with lower educational attainment and a higher prevalence of physical and psychiatric comorbidities such as hypertension, diabetes, heart diseases, visual and hearing impairments, poor mobility, and depression. They also had lower adherence to healthy lifestyle practices, with less participation in physical exercise and lower intake of fruits and vegetables, than those who remained free of dementia. There was no significant difference in the prevalence of smoking between those with and without incident dementia.

Participation in Intellectual Activity at Baseline in Cognitively Stable Participants and Those With Incident Dementia

At baseline, almost all participants (n = 15 574) reported engaging in some kind of leisure activities every day. However, there was a difference in the number and type of activities in which they participated between those with and without incident dementia. Those who remained free of dementia engaged in more varieties of leisure activities at baseline (3 vs 2 activities; $P < .001$), with a larger proportion performing intellectual activities than those who developed dementia (9521

Table 1. Comparison of Baseline Characteristics Between Participants With and Without Incident Dementia in 6 Years of Follow-up

Characteristic	Incident Dementia, No. (%)		P Value
	No (n = 14 233)	Yes (n = 1349)	
Age, median (IQR), y	74 (71-77)	76 (73-80)	<.001[a]
Female sex	8970 (63.0)	980 (72.6)	<.001[b]
No schooling received	3660 (25.7)	511 (37.9)	<.001[b]
Hypertension	9083 (63.8)	943 (69.9)	<.001[b]
Type 2 diabetes	2112 (14.8)	246 (18.2)	.001[b]
Hypercholesterolemia	6002 (42.2)	584 (43.3)	.43[b]
Obesity	5392 (37.9)	526 (39.0)	.43[b]
Heart disease	1576 (11.1)	188 (13.9)	.002[b]
Depression	517 (3.6)	73 (5.4)	.001[b]
Visual problem	1217 (8.6)	196 (14.5)	<.001[b]
Hearing problem	3195 (22.4)	337 (25.0)	.03[b]
Poor mobility	991 (7.0)	168 (12.5)	<.001[b]
Physical exercises	7209 (50.6)	550 (40.8)	<.001[b]
Adequate intake of fruits and vegetables	7112 (50.0)	622 (46.1)	.007[b]
Smoking	699 (4.9)	59 (4.4)	.38[b]
Intellectual activities	9521 (66.9)	684 (50.7)	<.001[b]
Social activities	11 053 (77.7)	1065 (78.9)	.28[b]
Other recreational activities	13 890 (97.6)	1327 (98.4)	.07[b]

Abbreviation: IQR, interquartile range.

[a] Determined by the Mann-Whitney test.

[b] Determined by the χ^2 test.

Table 2. Longitudinal Changes of Proportion of Participants Who Did Not Engage in Leisure Activities During First 3 Years Among Those With Incident Dementia at Years 4 to 6

Type of Leisure Activities	Participants, No. (%) (n = 299)		P Value[a]
	Baseline	Year 3	
Intellectual	131 (43.8)	121 (40.5)	.31
Social	66 (22.1)	42 (14.0)	<.01
Other recreational	4 (1.3)	7 (2.3)	.55

[a] Determined by the McNemar test.

Table 3. Comparison of Maintenance of Leisure Activity in First 3 Years Between Participants With and Participants Without Incident Dementia in Subsequent Years

Type of Leisure Activities	Incident Dementia, No. (%)		P Value[a]
	No	Yes	
Intellectual	4050/4555 (88.9)	134/168 (79.8)	<.001
Social	4615/5111 (90.3)	206/233 (88.4)	.34
Other recreational	6312/6457 (97.8)	288/295 (97.6)	.89

[a] Determined by the χ^2 test.

of 14233 [66.9%] vs 684 of 1349 [50.7%]; $P < .001$) (Table 1). The proportion of participants engaging in social or other recreational activities was not significantly different between the 2 groups. Older age, female sex, and lower educational level were associated with fewer types of activities at baseline compared with the counterparts (2 vs 3 activities).

Longitudinal Changes of Intellectual Activity Participation Before Dementia Onset

Among those who developed incident dementia at years 4-6, there was no change in the frequency of leisure activity participation from baseline to year 3, with almost all individuals still reporting engaging in leisure activity daily over the years. There was also no increase in disengagement of intellectual activities over time prior to the clinical onset of dementia (**Table 2**).

Maintenance of Participation in Intellectual Activity and Incidence of Dementia

The proportion of participants who continued participating in daily intellectual activities 3 years after baseline was larger in those who remained free of dementia than in those who developed dementia at years 4 to 6. No associations were found between maintenance of social or other recreational activities and lower incidence of dementia (**Table 3**).

Participation in Intellectual Activity at Baseline and Future Risk of Dementia

Given the possible bidirectional association between participation in activity and dementia, the association between intellectual activities and risk of incident dementia was reexamined by excluding participants who developed dementia within 3 years after baseline (n = 588) and those who could not

be confirmed to be still free of dementia by year 3 owing to missing follow-up (n = 3483). Consistent with the above findings, those who remained free of dementia performed more types of activities at baseline than those who developed dementia (3 vs 2 activities; $P < .001$). Also, the proportion of participants with daily participation in intellectual but not recreational or social activities at baseline was significantly larger in the cognitively stable group (**Table 4**).

The estimated OR for incident dementia was significantly lower in those participating in intellectual activities daily (0.71; 95% CI, 0.60-0.84; $P < .001$), even after controlling for demographics, physical and psychiatric comorbidities, lifestyle factors, and other types of leisure activities (**Table 5**). Neither recreational nor social activities were associated with a lower OR for incident dementia. The OR for physical exercise was 0.79 (95% CI, 0.68-0.92; $P = .003$).

Engaging in more types of activities was associated with a lower OR for incident dementia (95% CI, 0.86; 0.77-0.96; $P = .01$) after adjustment for the same demographics, health problems, and lifestyle factors. It remained significant after additional adjustment for social activities (0.78; 95% CI, 0.67-0.91; $P = .001$) or recreational activities (0.83; 95% CI, 0.73-0.93; $P = .002$) but not intellectual activities (1.03; 95% CI, 0.86-1.22; $P = .78$).

Discussion

By observing the cognitive status of a large cohort of older adults who were free of dementia, we found that late-life participation in intellectual activities was associated with lower risk of incident dementia several years later. This association was not fully explained by other health lifestyle practices (regular physical exercise, adequate fruit and vegetable intake, and not smoking) nor by a wide range of physical health problems and limitations (cardiovascular risk factors, depression, sensory impairments, and poor mobility). The association also did not appear to be explained by reverse causality (participants with preclinical dementia disengaging from intellectual activities). These findings suggest that active participation in intellectual activities can reduce the risk of, or delay the onset of, dementia.

Comparison With Previous Studies

The present findings are consistent with the past epidemiologic observation that participation in intellectual activities, even in late life, is associated with better cognitive functioning in older adults.[30] However, to our knowledge, previous studies did not adequately examine other health behaviors and impairments, both of which are potential confounding factors in the observed association. Nor did they address the possibility of bidirectionality between participation in intellectual activity and preclinical dementia. Based on the past findings, it was therefore uncertain whether participation in intellectual activity could independently reduce the risk of dementia. The present study is better controlled than previous studies, with consideration of these important confounders and limitations in the study design and analysis. Our findings highlight the importance of active participation in intellectual activities in dementia prevention and, from the public health perspective, the need to promote inclusion of these activities into the multidomain lifestyle intervention for better brain health in older populations.

In this study, we found that not all types of leisure activities were associated with decreased risk of dementia. In particular, we did not identify an association between social or recreational activities and lower risk of dementia. It may be that, given the very high level of participation in recreational and social activities in our cohort, a ceiling effect might mask any association with risk of dementia. However, as these activities are in general more passive and less cognitively demanding than intellectual activities, we speculate that recreational and social activities might not be as effective as intellectual activities in preventing dementia.

Although participants who remained free of dementia performed more varieties of leisure activities at baseline, the association with lower risk of dementia was no longer significant after adjusting for intellectual activities. This finding suggests that choosing the right kind of activity appears to be more important than engaging in various nonintellectual leisure activities in preventing dementia.

We had previously reported that older adults who engage in regular physical activities, in particular aerobic

Table 4. Differences in Proportion of Participants Participating in Different Types of Leisure Activities at Baseline Between Those With and Those Without Incident Dementia at Years 4 to 6

Type of Leisure Activities	Incident Dementia, No. (%)		
	No (n = 10 750)	Yes (n = 761)	*P* Value[a]
Intellectual	7414 (69.0)	430 (56.5)	<.001
Social	8371 (77.9)	592 (77.8)	.96
Other recreational	10 498 (97.7)	749 (98.4)	.17

[a] Determined by the χ^2 test.

Table 5. Estimated ORs for Incident Dementia After Excluding Participants Who Developed Incident Dementia Within 3 Years After Baseline

Type of Leisure Activities	Model 1		Model 2[a]	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Intellectual	0.59 (0.50-0.68)	<.001	0.71 (0.60-0.84)	<.001
Social	1.00 (0.83-1.19)	.96	0.97 (0.81-1.17)	.78
Other recreational	1.50 (0.84-2.69)	.18	1.56 (0.86-2.81)	.14

Abbreviation: OR, odds ratio.

[a] Adjusted for age, sex, educational level, cardiovascular risk factors, visual and hearing impairments, poor mobility, depression, smoking, adequate consumption of fruits and vegetables, regular physical exercise, and other types of leisure activities.

and mind-body exercises, are at a lower risk of developing dementia.[26] Not only is this association replicated in the present study, but we find that it remains robust after controlling for intellectual activities. Although this study did not investigate possible causal mechanisms for the association of intellectual and physical activities with cognitive function, we speculate that being mentally and physically active may slow onset of clinical dementia by improving cognitive reserve. According to cognitive reserve theory, people with a higher level of cognitive reserve have larger brain anatomical substrate and greater dynamic neural network compensation in the face of neuropathologic characteristics, thus being more able to withstand brain insults before cognitive or functional impairment becomes clinically evident.[31,32] A recent study by Suo et al[33] shows that cognitive training is associated with enhanced functional connectivity between the hippocampus and superior frontal cortex, whereas physical training is associated with positive structural plasticity, such as increased cortical thickness of the posterior cingulate and reversed progression of white matter hyperintensities. These data, which suggest that physical and cognitive training improve cognition possibly through different neuromodulatory mechanisms, are in line with our findings that intellectual and physical activities modulate the risk of dementia independent of each other.

Strengths and Limitations

Regarding the strengths of this study, we followed a large territory-wide community cohort for a long time. The attrition rate was low, with most participants having a recent cognitive examination by physicians. Also, we quantified in sufficient detail a wide range of physical health problems and limitations; various health behaviors including physical exercise, diet, and smoking; and different types of leisure activities practiced at baseline and at follow-up.

Given the nature of our study design, however, care needs to be taken when making an inference about a causal association between participation in intellectual activity and prevention of dementia. The possibility of reverse causation, although minimized in this study, could not be completely excluded because the baseline cognitive capacity and the duration and intensity of participation in intellectual activity prior to this study were unknown. Although the observed association remained significant after excluding participants who developed dementia shortly after baseline, and we did not find disengagement of activities prior to onset of dementia among those who subsequently developed dementia, the potential confounding problem of people engaging in fewer activities owing to some cognitive dysfunction even though they were screened negative might still be present. Another limitation is that, for participants who did not complete the study who were previously free of dementia but were found on tracing to have dementia, we could not be completely certain when their clinical manifestation of dementia was; therefore, we defined the study outcome as incident dementia in 6 years and used a more conservative analytic model in this study. Objective measurements of leisure activities, genotyping, and neuroimaging were also not feasible in this study setting. Moreover, direct application of our findings to older populations of other ethnicities, with more comorbidities, and from later generations requires caution, as our participants were ethnic Chinese, relatively healthy and active, and had a lower educational level.

Conclusions

This study provides evidence that late-life participation in intellectual activities is independently associated with a lower risk of dementia in older adults. Given the growing older population worldwide, promoting regular engagement in intellectual activities might help delay or prevent dementia.

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REFERENCES

1. World Health Organization and Alzheimer's Disease International. Dementia: a public health priority. http://www.who.int/mental_health/publications/dementia_report_2012/en. Published 2012. Accessed November 2, 2017.

2. Brookmeyer R, Johnson E, Ziegler-Graham K, Arrighi HM. Forecasting the global burden of Alzheimer's disease. *Alzheimers Dement*. 2007;3(3):186-191.

3. Barnes DE, Yaffe K. The projected effect of risk factor reduction on Alzheimer's disease prevalence. *Lancet Neurol*. 2011;10(9):819-828.

4. Norton S, Matthews FE, Barnes DE, Yaffe K, Brayne C. Potential for primary prevention of Alzheimer's disease: an analysis of population-based data. *Lancet Neurol*. 2014;13(8):788-794.

5. Wilson RS, Mendes De Leon CF, Barnes LL, et al. Participation in cognitively stimulating activities and risk of incident Alzheimer disease. *JAMA*. 2002;287(6):742-748.

6. Wilson RS, Bennett DA, Bienias JL, et al. Cognitive activity and incident AD in a population-based sample of older persons. *Neurology*. 2002;59(12):1910-1914.

7. Verghese J, Lipton RB, Katz MJ, et al. Leisure activities and the risk of dementia in the elderly. *N Engl J Med*. 2003;348(25):2508-2516.

8. Karp A, Paillard-Borg S, Wang HX, Silverstein M, Winblad B, Fratiglioni L. Mental, physical and social

components in leisure activities equally contribute to decrease dementia risk. *Dement Geriatr Cogn Disord*. 2006;21(2):65-73.

9. Akbaraly TN, Portet F, Fustinoni S, et al. Leisure activities and the risk of dementia in the elderly: results from the Three-City Study. *Neurology*. 2009;73(11):854-861.

10. Paillard-Borg S, Fratiglioni L, Winblad B, Wang HX. Leisure activities in late life in relation to dementia risk: principal component analysis. *Dement Geriatr Cogn Disord*. 2009;28(2):136-144.

11. Valenzuela M, Brayne C, Sachdev P, Wilcock G, Matthews F; Medical Research Council Cognitive Function and Ageing Study. Cognitive lifestyle and long-term risk of dementia and survival after diagnosis in a multicenter population-based cohort. *Am J Epidemiol*. 2011;173(9):1004-1012.

12. Paillard-Borg S, Fratiglioni L, Xu W, Winblad B, Wang HX. An active lifestyle postpones dementia onset by more than one year in very old adults. *J Alzheimers Dis*. 2012;31(4):835-842.

13. Yates LA, Ziser S, Spector A, Orrell M. Cognitive leisure activities and future risk of cognitive impairment and dementia: systematic review and meta-analysis. *Int Psychogeriatr*. 2016;28(11):1791-1806.

14. Scarmeas N, Stern Y. Cognitive reserve and lifestyle. *J Clin Exp Neuropsychol*. 2003;25(5):625-633.

15. Fratiglioni L, Paillard-Borg S, Winblad B. An active and socially integrated lifestyle in late life might protect against dementia. *Lancet Neurol*. 2004;3(6):343-353.

16. Valenzuela MJ, Sachdev P. Brain reserve and dementia: a systematic review. *Psychol Med*. 2006;36(4):441-454.

17. Valenzuela MJ, Breakspear M, Sachdev P. Complex mental activity and the aging brain: molecular, cellular and cortical network mechanisms. *Brain Res Rev*. 2007;56(1):198-213.

18. Lövdén M, Xu W, Wang HX. Lifestyle change and the prevention of cognitive decline and dementia: what is the evidence? *Curr Opin Psychiatry*. 2013;26(3):239-243.

19. Di Marco LY, Marzo A, Muñoz-Ruiz M, et al. Modifiable lifestyle factors in dementia: a systematic review of longitudinal observational cohort studies. *J Alzheimers Dis*. 2014;42(1):119-135.

20. Leung GT, Lam LC. Leisure activities and cognitive impairment in late life: a selective literature review of longitudinal cohort studies. *Hong Kong J Psychiatry*. 2007;17:91-100.

21. Cheng ST. Cognitive reserve and the prevention of dementia: the role of physical and cognitive activities. *Curr Psychiatry Rep*. 2016;18(9):85.

22. Sajeev G, Weuve J, Jackson JW, et al. Late-life cognitive activity and dementia: a systematic review and bias analysis. *Epidemiology*. 2016;27(5):732-742.

23. Chiu HF, Lam LC, Chi I, et al. Prevalence of dementia in Chinese elderly in Hong Kong. *Neurology*. 1998;50(4):1002-1009.

24. Leung GT, Leung KF, Lam LC. Classification of late-life leisure activities among elderly Chinese in Hong Kong. *East Asian Arch Psychiatry*. 2011;21(3):123-127.

25. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet*. 2004;363(9403):157-163.

26. Lee AT, Richards M, Chan WC, Chiu HF, Lee RS, Lam LC. Intensity and types of physical exercise in relation to dementia risk reduction in community-living older adults. *J Am Med Dir Assoc*. 2015;16(10):899.e1-899.e7.

27. Lee ATC, Richards M, Chan WC, Chiu HFK, Lee RSY, Lam LCW. Lower risk of incident dementia among Chinese older adults having three servings of vegetables and two servings of fruits a day. *Age Ageing*. 2017;46(5):773-779.

28. World Health Organization. *International Statistical Classification of Diseases and Related Health Problems, 10th revision*. http://apps.who.int/classifications/apps/icd/icd10online2004/fr-icd.htm. Accessed November 2, 2017.

29. Morris JC. Clinical dementia rating: a reliable and valid diagnostic and staging measure for dementia of the Alzheimer type. *Int Psychogeriatr*. 1997;9(suppl 1):173-176.

30. Leung GT, Fung AW, Tam CW, et al. Examining the association between participation in late-life leisure activities and cognitive function in community-dwelling elderly Chinese in Hong Kong. *Int Psychogeriatr*. 2010;22(1):2-13.

31. Richards M, Deary IJ. A life course approach to cognitive reserve: a model for cognitive aging and development? *Ann Neurol*. 2005;58(4):617-622.

32. Stern Y. Cognitive reserve in ageing and Alzheimer's disease. *Lancet Neurol*. 2012;11(11):1006-1012.

33. Suo C, Singh MF, Gates N, et al. Therapeutically relevant structural and functional mechanisms triggered by physical and cognitive exercise. *Mol Psychiatry*. 2016;21(11):1633-1642.

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.

Related article page 697

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-