The association between physical activity and cognitive function is partly explained by better sleep quality

For correspondence:
boris.cheval@unige.ch

Boris Cheval, PhD[1,2,*], Silvio Maltagliati, MSc[3], Stefan Sieber, MA[4,5], Stéphane Cullati, PhD[6,7], Liye Zou, PhD[8,9], Andreas Ihle, PhD [4,5,10], Arthur F. Kramer, PhD[11,12], Qian Yu, PhD[8,9], David Sander, PhD[1,2], Matthieu P. Boisgontier, PT, PhD[13,14]

[1]Swiss Center for Affective Sciences, University of Geneva, Switzerland. [2]Laboratory for the Study of Emotion Elicitation and Expression (E3Lab), Department of Psychology, University of Geneva, Switzerland. [3]Univ. Grenoble Alpes, SENS, F-38000 Grenoble, France. [4]Swiss NCCR "LIVES – Overcoming Vulnerability: Life Course Perspectives", University of Geneva, Switzerland. [5]Center for the Interdisciplinary Study of Gerontology and Vulnerability, University of Geneva, Switzerland. [6]Population Health Laboratory, University of Fribourg, Switzerland. [7]Department of Readaptation and Geriatrics, University of Geneva, Switzerland. [8]Institute of KEEP Collaborative Innovation, Shenzhen University, China. [9]Exercise Psychophysiology Laboratory, School of Psychology, Shenzhen University, China. [10]Cognitive Aging Lab, Department of Psychology, University of Geneva, Geneva, Switzerland. [11]Center for Cognitive and Brain Health, Department of Psychology, Northeastern University, Boston, MA, USA.[12]Beckman Institute, University of Illinois at Urbana-Champaign, Champaign, IL, USA. [13]School of Rehabilitation Sciences, Faculty of Health Sciences, University of Ottawa, Canada. [14]Bruyère Research Institute, Ottawa, Canada. [*]Corresponding author: Campus, Biotech, Chemin des mines 9, 1202 Genève, Switzerland; boris.cheval@unige.ch (@ChevalBoris)

Please cite as: Cheval, B., Maltagliati, S., Sieber, S., Cullati, S., Zou, L., Ihle, A., Kramer, A.F., Yu, Q., Sander, S., Boisgontier, M.P. (2021). The association between physical activity and cognitive function is partly explained by better sleep quality. *SportRxiv*. DOI: 10.51224/SRXIV.89

Abstract

Background: Physical activity has been associated with better cognitive functions and sleep quality. Yet, whether the effect of physical activity on cognitive functions could be explained by better sleep quality in adults who are 50 year of age or older is unclear.

Objective: To investigate whether sleep quality mediates the association between physical activity and cognitive functions in adults 50 year of age or older.

Methods: 97,767 community-dwelling 50 years-of-age or older European adults were included in the study. Physical activity and sleep quality were self-reported, and indicators of cognitive function (i.e., immediate recall, delayed recall, and verbal fluency) were assessed using objective tests. All measures were collected six times between 2004 and 2017. The mediation was tested using multilevel mediation analyses.

Results: Results showed that physical activity was associated with better sleep quality, which was associated in turn with better performance in all three indicators of cognitive function, thereby demonstrating an indirect effect of physical activity on cognitive function through sleep quality. However, the magnitude of this indirect effect was small in comparison to the magnitude of the direct effect of physical activity on cognitive function. Specifically, sleep quality explained 3.8%, 6.5%, and 9.0% of the total association of physical activity with verbal fluency, immediate recall, and delayed recall, respectively.

Conclusions: These findings suggest that self-reported sleep quality partly mediates the association between physical activity and cognitive function, but that the effect of self-reported physical activity on cognitive function is largely independent from self-reported sleep quality. Future studies using devices-based measures of physical activity and sleep quality are needed.

Keywords: physical activity, sleep quality, cognitive function, aging, mediation

Introduction

Worldwide, 35.6 million people have dementia, with a new case every four seconds [1, 2] and a prevalence that doubles every five years [3]. Thus, promoting cognitive health in aging is a public health priority [1] and non-pharmacological lifestyle interventions play a central role in this promotion [2]. Specifically, adopting a physically active lifestyle is considered a protective factor against cognitive decline and dementia [4-9]. For example, randomized controlled trials have shown that fitness training improves cognitive functions [10]. Prospective cohort studies have suggested that engaging in regular physical activity reduces the risk of dementia by 28% [11] and that meeting the recommended 150 min/week of moderate-to-vigorous physical activity could reduce up to 18% the prevalence of Alzheimer's disease cases among older adults [8]. Moreover, a recent Mendelian randomization study drawing on large-scale genome-wide association studies revealed that moderate physical activity improves cognitive functioning [6]. Overall, these findings consistently demonstrate how essential physical activity is for maintaining cognitive function in later life.

The protective effect of physical activity on cognitive functions can be explained by multiple mechanisms [12]. For example, at the molecular and cellular level, it has been suggested that physical activity induces an increased availability of growth factors such as the brain-derived neurotrophic factor (BDNF), insulin-like growth factor-1 (IGF-1), and vascular endothelial growth factor (VEGF), which have been associated with increased brain plasticity, synaptogenesis, and neurogenesis [13-16]. At the brain level, cross-sectional and experimental studies have shown that physical activity is associated with an increase volume of the hippocampus [17, 18], prefrontal cortex [19], and caudate nucleus [20]. Furthermore, better white matter integrity [21, 22] and functional connectivity [23-25] are thought to explain the positive effect of physical activity on cognitive function [21, 22]. Finally, at the behavioral and socioemotional level, current evidence suggests that physical activity improves sleep quality [24, 26-31], which promotes cognitive health [32-35].

Deterioration in sleep quality is common in older adults [36-38] and could explain the cognitive decline in aging [32, 39-41]. However, only few cross-sectional studies have tested the potential mediating role of sleep quality on the association between physical activity and cognitive function [40, 42, 43]. Some studies showed that sleep quality [43], sleep efficiency [42] and total sleep time [44] mediated the association between physical activity and executive functions. Other studies showed no evidence of a mediation by sleep quality [40, 45]. In sum, current evidence on the potential mediating role of sleep on the relationship between physical activity and cognitive function in later life fully relies on cross-sectional studies and is inconclusive. Studies which have utilized experimental designs did not conduct mediation analyses to examine the relationship between exercise, sleep, and cognition and there is no longitudinal study addressing this relationship [41].

To address this gap, the objective of this large-scale longitudinal study was to examine the associations between some indicators of physical activity, sleep quality, and cognitive function in adults aged 50 years of age or older. Based on the literature [42, 43], we hypothesized that sleep quality mediates the relationship between physical activity and that part of the effect of physical activity on cognitive function is independent from sleep quality (H2) [40].

Methods

Study design

Data were drawn from the Survey of Health, Ageing and Retirement in Europe (SHARE), a longitudinal population-based study on adults 50 years of age or older living in 27 European countries and Israel [46]. Data were collected every two years between 2004 and 2017 for a total of 7 measurement waves using computer-assisted personal interviewing (CAPI) in participants' homes. Physical activity, sleep quality, and cognitive function (immediate recall, delayed recall, and verbal fluency) were assessed at all measurement waves except wave 3. SHARE was carried out in accordance with the Declaration of Helsinki and has been approved by the Ethics Committee of the University of Mannheim (waves 1-4) and the Ethics Council of the Max Plank Society (waves 4-7). All participants provided a written informed consent. To be included in the present study, participants should be aged 50 years or older and have at least one measure of physical activity, sleep quality, and cognitive function. We excluded people with suspected dementia, as indicated by scores above two on the time orientation question [47], and people who reported more than two limitations in activities of daily living (ADL).

Measures

Outcome: Cognitive function. Cognitive function was derived from validated tests of verbal fluency, immediate recall, and delayed recall. In the verbal fluency test [48], participants were asked to name as many different animals as they could think of in one minute. The score was the total number of correctly named animals, with a higher score indicating better performance. Immediate and delayed recall were assessed using an adapted 10-word delayed-recall test [49]. In the immediate-recall test, participants first listened to a 10-word list that was read out loud by the interviewer. Immediately after reading the list, participants were asked to recall as many words as possible. At the end of the cognitive testing session, participants were asked again to recall the words from the list, which captured delayed recall. Both recall scores ranged from 0 to 10, with a higher score indicating better performance.

Independent variable: Physical activity. Physical activity was derived from two questions: "How often do you engage in vigorous physical activity, such as sports, heavy housework, or a job that involves physical labor?" and "How often do you engage in activities that require a low or moderate level of energy such as gardening, cleaning the car, or doing a walk?" [50-52]. Participants answered using a four-point scale: 1 = *Hardly ever, or never*; 2 = *One to three times a month*; 3 = *Once a week*; 4 = *More than once a week*. Participants who did not answer "more than once a week" to either item were classified as physically inactive. As described in previous research [53-55], this strategy reduces the potential misclassification bias which would lead to physically inactive participants being incorrectly classified as physically active.

Mediating variable: Sleep quality. Sleep quality was derived from the question: "Have you had trouble sleeping recently?" Participants who answered "Trouble with sleep or recent change in pattern" were classified as having poor sleep quality, whereas participants who answered "No trouble sleeping" were classified as having good sleep quality [56].

Covariates and potential confounders. The following covariates were included in the analysis: measurement wave (1 to 7), age group (50-64; 65-79; 80-96), sex (male, female), body mass index (underweight <18.5, normal: ≥18 and <25, overweight: ≥25 and <30, obese: ≥30 kg/m^2), education (7 categories based on the International Standard Classification of Education 1997) [57], ability to make ends meet (with great difficulty, with some difficulty, fairly easily, easily), birth cohort [war (between 1914 and 1918 and between 1939 and 1945), great depression (between 1929 and 1938), no war nor economic crisis (before 1913, between 1919 and 1928, and after 1945)], country of residence (Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Luxembourg, Netherlands, Poland, Portugal, Slovenia, Spain, Sweden, Switzerland), attrition [no dropout, dropout (participants who responded to neither wave 6 nor wave 7), death (participants who died during the follow-up)], number of chronic diseases, and depressive symptoms assessed with the EURO-D scale [58]. These variables were adjusted for in the models because they have been identified as potentially confounding factors in the associations between physical activity, sleep quality, and cognitive function.

Statistical analyses

Data were analyzed using linear and logistic mixed-effects models that account for the nested structure of the data (i.e., repeated measurement over time within a single participant) and provide acceptable type I error rates [59]. Participants with missing observations were included as mixed-effects models do not require an equal number of observations from all participants [60]. Specifically, to investigate the mediating role of sleep quality on the relationship between physical activity and cognitive function, we conducted mediation analyses using the component approach (i.e., testing individual parameters in the model) [61]. This approach operates by demonstrating that the two components of the indirect effect (i.e., from the independent variable to the mediator [the first component] and from the mediator to the outcome [the second component]) are both significant (Figure 1). This test, referred to as the joint-significant test [62] or the causal steps test [63], has proven to perform better in term of Type I errors rate compared with other tests like bootstrap-based methods [61].

The modeling strategy was the same across the three cognitive outcomes. Specifically, two mixed-effects models were computed to test the mediating role of sleep quality on the associations between physical activity and cognitive function. Model 1 tested the association between physical activity (i.e., exposure) and sleep quality (i.e., mediator) and was adjusted for the covariates. Model 2 tested the association between sleep quality (i.e., mediator) and cognitive function (i.e., outcome), adjusted for physical activity (i.e., the exposure) and the covariates. An indirect effect is established if both the association between physical activity and sleep quality (i.e., first component, Model 1) and between sleep quality and cognitive function (i.e., second component; Model 2) are significant. The total effect is estimated by summing the indirect effect and the direct effect. Confidence intervals around the indirect effects were computed using the RMediation package [64], which provided indirect effects using the distribution of product of coefficients [65]. Finally, the proportions of the total effect explained by the mediator was calculated as the difference between the total effect and the direct effect divided by the total effect. Estimates of the effect size for fixed effects were reported using the marginal and conditional pseudo-R^2 computed with the MuMin R package [66].

Sensitivity analyses

Three sensitivity analyses were conducted. In the first sensitivity analysis, we relied on a sample of participants with at least two measures of physical activity, two measures of sleep quality, and two measures of a given cognitive function. The second sensitivity analysis excluded participants who dropped out during the survey (i.e., participants who responded to neither wave 6 nor wave 7). The third sensitivity analysis excluded participants who died during the survey. These two last sensitivity analyses aimed to check if attrition due to dropout and death modified the results.

Robustness analyses

We performed a robustness analysis in which a time lag was created between the predictors (i.e., physical activity and sleep quality) and the outcome (i.e., cognitive function). Specifically, for a given wave (except for wave 1) the predictors were assigned the value of the preceding wave [67]. This approach aimed to minimize the impact of reverse causation bias on the associations observed.

Results

The study sample included 97,767 individuals (52,948 women). Table 1 summarizes the characteristics of the participants stratified by physical activity status at baseline. Simple association tests indicated that physically active (vs. physically inactive) participants showed better cognitive function (i.e., on all three indicators), better sleep quality, higher education, higher ability to make ends meet, and were less likely to be a woman, to be older, to have chronic condition, and to be obese.

Table 1. Baseline characteristics of the participants across the physical activity status

	Physically inactive (N = 26844)	Physically active (N = 70923)	*P* value
Cognitive functions outcomes			
Verbal fluency, mean ± SD	17.1 ± 7.8	20.6 ± 7.3	<0.001
Immediate recall, mean ± SD	2.8 ± 1.3	3.3 ± 1.0	<0.001
Delayed recall, mean ± SD	2.4 ± 1.5	2.9 ± 1.3	<0.001
Mediator			
Sleep quality, n (%)			
Good sleep quality	15930 (59)	48296 (68)	
Poor sleep quality	10914 (41)	22627 (32)	<0.001
Other covariates			
Age, n (%)			
50-64	12351 (46)	42651 (60)	
65-79	10747 (40)	24546 (35)	
80-96	3746 (14)	3726 (5)	<0.001
Women, n (%)	15319 (57)	37629 (53)	<0.001
Body mass index, n (%)			
Underweight	362 (1)	720 (1)	
Normal weight	8596 (32)	27082 (38)	
Overweight	11029 (41)	30027 (42)	
Obesity	6857 (26)	13094 (18)	<0.001
Education, n (%)			
Primary	8741 (33)	15119 (21)	
Secondary	13734 (51)	39837 (56)	
Tertiary	4369 (16)	15967 (23)	<0.001
Satisfaction with income			
With great difficulty, n (%)	4159 (16)	6395 (9)	
With some difficulty, n (%)	6981 (26)	14310 (20)	
Fairly easily, n (%)	8396 (31)	21631 (31)	
Easily, n (%)	7308 (27)	28587 (40)	<0.001
Number of chronic conditions, n (%)			
Less than two chronic conditions	12293 (46)	42691 (60)	
More than two chronic conditions	14551 (54)	28232 (40)	<0.001
Countries, n (%)			
Austria	1655 (6)	4107 (6)	
Belgium	2271 (8)	5585 (8)	
Denmark	739 (3)	4248 (6)	
France	2064 (8)	4955 (7)	
Germany	1725 (6)	6292 (9)	
Greece	966 (4)	2353 (3)	
Israel	1025 (4)	2257 (3)	
Italy	2499 (9)	4051 (6)	
Netherlands	986 (4)	4817 (7)	
Spain	2187 (8)	5312 (7)	

Sweden	804 (3)	5189 (7)	
Switzerland	822 (3)	3312 (5)	
Czech Republic	2765 (10)	5047 (7)	
Ireland	227 (1)	714 (1)	
Poland	1031 (4)	1422 (2)	
Estonia	1942 (7)	4726 (7)	
Hungary	1033 (4)	1815 (3)	
Portugal	835 (3)	931 (1)	
Slovenia	897 (3)	2657 (4)	
Luxembourg	371 (1)	1133 (2)	<0.001
Birth Cohort, n (%)			
After 1945	11222 (42)	38777 (55)	
Between 1939 and 1945	5246 (20)	14952 (21)	
Between 1929 and 1938	6812 (25)	13136 (18)	
Between 1919 and 1928	3564 (13)	4058 (6)	<0.001

Notes. Baseline = the first measurement occasion for each participant; SD = standard deviation; *p* values are based on the analysis of variance and chi-square tests for continuous and categorical variables, respectively, testing the effect of physical activity status at baseline (physically active vs. physically inactive) on these variables. The descriptive statistics are based on the larger sample size (i.e., 97,767 from the models testing verbal fluency).

Verbal fluency

Model 1 showed that physically active individuals had better sleep quality than physically inactive individuals (b = 0.22; odds ratio [OR] = 1.24, 95% confidence interval [95% CI] = 1.21–1.28, $p < .001$). Model 2 showed that better sleep quality was associated with better verbal fluency (b = 0.25, 95% CI = 0.19–0.30, $p < .001$). The two components of the mediation pattern being significant, results thus demonstrate an indirect effect of physical activity on verbal fluency through sleep quality. The confidence interval for this indirect effect did not cross zero (mean indirect effect = .054, 95% CI = 0.039–0.068). However, in Model 2 (i.e., with adjustment for sleep quality), the association of physical activity with verbal fluency was significant (b = 1.35, 95% CI = 1.30–1.41, $p < .001$), suggesting that the effect of physical activity on verbal fluency was not fully mediated by sleep quality. 3.8% of the total effect of physical activity on verbal fluency was mediated by sleep quality. Overall, the model explained 29.6% of the marginal variance and 61.3% of the conditional variance in verbal fluency.

Immediate recall

Model 1 showed that physically active individuals had better sleep quality than physically inactive individuals (b = 0.27; OR = 1.31, 95% CI = 1.27–1.35, $p < .001$). Model 2 showed that better sleep quality was associated with better immediate recall (b = 0.05, 95% CI = 0.04–0.06, $p < .001$). The two components of the mediation pattern being significant, results thus demonstrate an indirect effect of physical activity on immediate recall through sleep quality. The confidence interval for this indirect effect did not cross zero (mean indirect effect = 0.014, 95% CI = 0.011–0.017). However, in Model 2 (i.e., with adjustment for sleep quality), the association between physical activity and immediate recall was significant (b = 0.19, 95% confidence interval [95% CI] = 0.18–0.20, $p < .001$), suggesting that the effect of physical activity on verbal fluency was not fully mediated by sleep quality. 6.5% of the total effect of physical activity on immediate recall was mediated by sleep quality. Overall, the model explained 29.2% of the marginal variance and 54.2% of the conditional variance in immediate recall.

Table 2. Results of the mixed-effects models

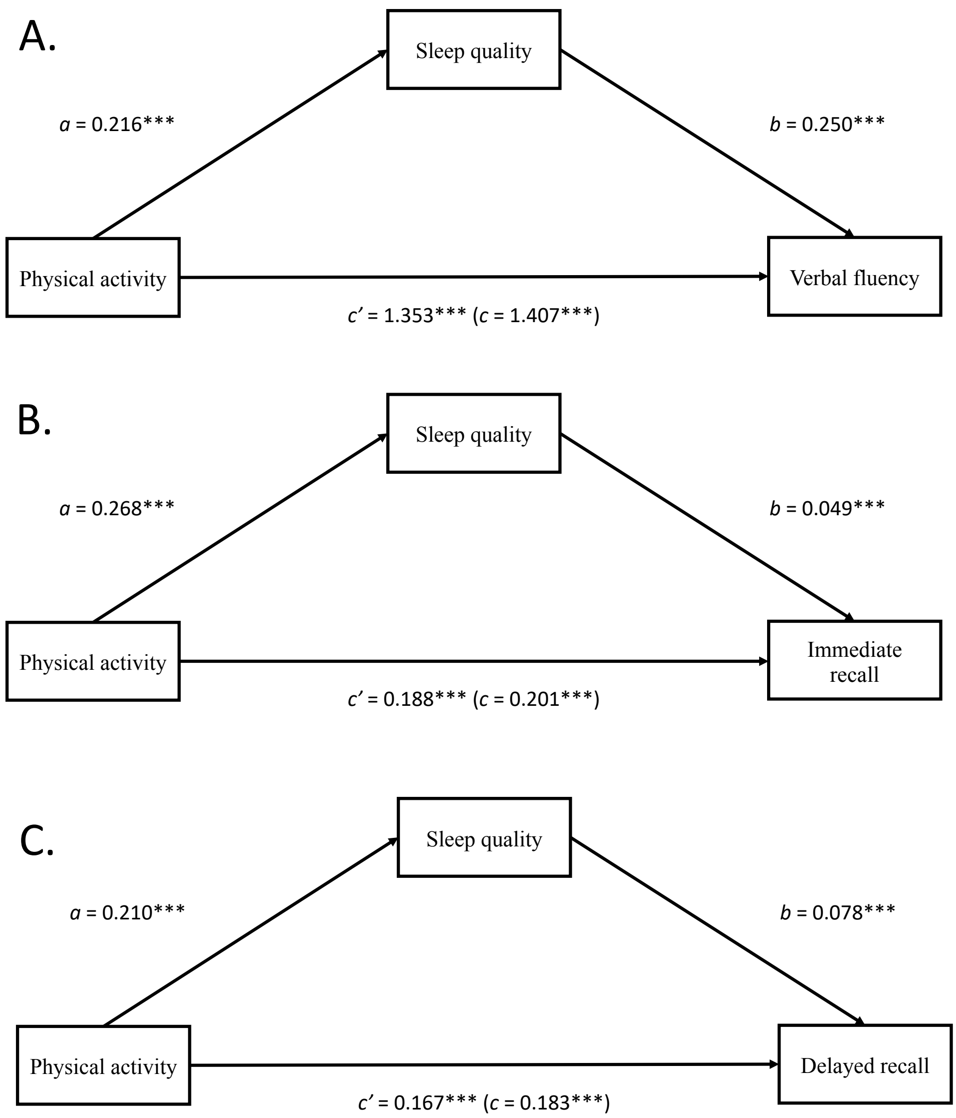
	Model 1 (sleep quality)		Model 2 (cognitive functions)	
	OR [b] (CI)	*p*	b (CI)	*p*
Verbal fluency (N = 97,767)				
Physical activity (ref. physically inactive)				
Physically active	1.24 [.22] (1.21;1.28)	<.001	1.35 (1.30;1.41)	<.001
Sleep quality (ref. poor sleep quality)				
Good sleep quality			0.25 (0.19;0.30)	<.001
Immediate recall (N = 88,963)				
Physical activity (ref. physically inactive)				
Physically active	1.31 [0.27] (1.27;1.35)	<.001	0.19 (0.18;0.20)	<.001
Sleep quality (ref. poor sleep quality)				
Good sleep quality			0.05 (0.04;0.06)	<.001
Delayed recall (N = 90,627)				
Physical activity (ref. physically inactive)				
Physically active	1.23 [.21] (1.20;1.27)	<.001	0.17 (0.15;0.18)	<.001
Sleep quality (ref. poor sleep quality)				
Good sleep quality			0.08 (0.07;0.09)	<.001

Notes. CI = confidence interval at 95%; OR = Odds Ratio. Results are derived from linear mixed effects models. Results of the Model 1 are derived from logistic mixed-effects models, while results of the Model 2 are derived from linear mixed-effects models. Models are adjusted for wave of measurement, age, sex, birth cohort, body mass index, education, satisfaction with household income, attrition, country of residence, number of chronic diseases, and depressive symptoms.

Delayed recall

Model 1 showed that physically active individuals had better sleep quality than physically inactive individuals (b = 0.21; OR = 1.23, 95% CI = 1.20–1.27, $p < .001$). Model 2 showed that better sleep quality was associated with better delayed recall (b = 0.08, 95% CI = 0.07–0.09, $p < .001$). The two components of the mediation pattern being significant, results thus demonstrate an indirect effect of physical activity on delayed recall through sleep quality. The confidence interval for this indirect effect did not cross zero (Mean indirect effect = 0.016, 95% CI = 0.013–0.020). However, in Model 2 (i.e., with adjustment for sleep quality), the association between physical activity and delayed recall was significant (b = 0.17, 95% confidence interval [95% CI] = 0.15–0.18, $p < .001$), suggesting that the effect of physical activity on verbal fluency was not fully mediated by sleep quality. 9.0% of the total effect of physical activity on delayed recall was mediated by sleep quality. Overall, the model explained 26.3% of the marginal variance and 53.4% of the conditional variance in delayed recall.

Figures 1. Mediation models



Notes. Coefficients are unstandardized regression coefficients obtained from the mixed-effects models. *a* represents the association between the exposure (i.e., physical activity) and the mediator (i.e., sleep quality). *b* represents the association between the mediator (i.e., sleep quality) and the outcome (i.e., cognitive function), c' represents the direct effect of the exposure on the outcome, after adjustment for the mediator. The unstandardized regression coefficient representing the total association (c) between physical activity and cognitive functions is in parentheses. *** p <.001. A. Results of the models for verbal fluency. B. Results of the models for immediate recall. C. Results of the models for delayed recall.

Sensitivity and robustness

The sensitivity (Table S2, S3, and S4) and robustness analyses (Table S5) yielded similar results as the main analyses. Specifically, physically active individuals had a better sleep quality than physically inactive individuals, and better sleep quality was associated with better performance on all three measures of cognitive functions. This effect was also observed in participants with a least two measurements and regardless the type of tested attrition. Moreover, physical activity and sleep quality were independently associated with all three measures of cognitive function, which suggested the association between physical activity and cognitive function was not fully mediated by sleep quality. Results of the robustness analysis, in which we introduced a time-lag between the predictors and outcomes, showed the same partial indirect effect, although the magnitude of the associations of physical activity and sleep quality with cognitive function were smaller.

Discussion

Our results showed that physical activity was positively associated with sleep quality and that sleep quality was positively associated with cognitive function, thereby indicating a significant indirect effect of physical activity on cognitive function through sleep quality. However, the magnitude of the indirect effects was relatively small (proportion of mediated effects < 10 %), with physical activity remaining significantly associated with all three domains of cognition after adjustment for sleep quality. Hence, our study lends support for the significant, although modest, mediating role of sleep quality on the relationship between physical activity and cognitive functioning. In the rest of the discussion, we compare our results with other literature and highlight the strengths and limitations of the present study.

Comparisons with other studies

Our results showed an association between physical activity and sleep quality that is consistent with earlier evidence indicating that physical activity improves sleep quality [24, 26-31]. To explain this association, at least three complementary explanations have been proposed [27, 68]. First, a higher level of physical activity may improve affective states and mental health [54, 69, 70]. Second, physically active individuals may have a better weight management than inactive individual [71-73]. Third, physically active individuals may exhibit better physical function [74]. All these factors could contribute to sleep quality [75-79]. Consequently, the conjunction of these three explanations can lead to better sleep quality in physically active than physical inactive individuals.

Our results also aligned with the mounting evidence showing that better sleep quality is associated with better cognitive function [42, 80-82]. Specifically, we observed that poor sleep quality was significantly associated with lower cognitive performance, thereby confirming the robustness of this association. Several biological mechanisms have been proposed to account for the link between sleep and cognitive function [32]. Specifically, studies suggested that sleep disturbance may favor cognitive impairment through increased amyloid-β concentrations [83], neurodegeneration [84, 85], or the alteration of specific neurotransmitter systems [86]. In sum, our findings confirm that sleep quality could contribute to maintaining cognitive health across aging. Nonetheless, it should be noted that the sizes of the observed associations in our study were small. For example, compared with participants who reported sleep problems, participants without sleep problems scored on average 0.25 more words for verbal fluency, 0.10 for immediate recall, and 0.05 for delayed recall. The significance of the observed effects should thus be interpreted in the context of the large-scale dataset.

These two previous results (i.e., significant links between physical activity and sleep quality, and between sleep quality and cognitive function) may suggest that physical activity has an indirect effect on cognitive function through the mediating role of sleep quality. However, although the indirect effects were significant for all three indicators of cognitive function, the proportion of the total effect of physical activity on cognitive function mediated by sleep quality was relatively small. Indeed, sleep quality explained only 3.8%, 6.5%, and 9.0% of the total association of physical activity with verbal fluency, immediate recall, and delayed recall, respectively. Furthermore, after adjustment for sleep quality, physical activity was still significantly associated with cognitive function. This result is consistent with the literature suggesting that the protective effect of physical activity on cognitive health in later life is independent from sleep quality [4-9]. Consequently, sleep quality mediates the association between physical activity and cognitive function in later life, but the weight of this pathway could be limited. Additional mechanisms likely play a more essential role.

Strengths and weaknesses

Among the strengths of the present study are the large sample size of community-dwelling middle-aged and older individuals living in 21 European countries, the reliance of a statistical approach suited to formally test mediation, and the use of three indicators of cognitive function providing consistent results. Moreover, the results remain similar across the sensitivity and robustness analyses. However, our findings need to be considered in light of the following features that limit the conclusions that can be drawn from our study. First, physical activity was assessed using a self-reported questionnaire, which may have reduced measurement validity and produced issues in the classification of active versus inactive individuals [87]. Ideally, future studies should include more objective measures such as accelerometry or VO_2 max. Similarly, sleep quality was assessed using a self-reported item. Finally, although we computed time-lagged analysis, we cannot exclude reverse causality from these correlational data, and thus cannot infer a causal relationship from physical activity to cognitive function through sleep quality.

Conclusion

This study highlights that the protective effect of physical activity on cognitive function in middle-age and older adults may be partly explained by sleep quality. However, the magnitude of this mediating effect was limited, thereby highlighting that an important part of the effect of physical activity on cognitive function was independent from sleep quality – though this finding needs to be confirmed using devices-based measure of physical activity and sleep quality. In general, our results confirm that public health policies and clinicians should promote a lifestyle that contains both physical activity and good sleep quality in later life to protect against the cognitive decline.

Author Contributions: B.C.: conceptualization, writing – original draft; S.S.: data curation, writing – review & editing; S.M.: writing – review & editing; S.C.: supervision, writing – review & editing; L.Z.: writing – review & editing; A.I.: writing – review & editing; A.F.K.: writing – review & editing D.S.: writing – review & editing; Q.Y.: writing – review & editing D.S.: writing – review & editing; M.P.B.: supervision, writing – original draft.

Ethical approval. This study was part of the SHARE study, approved by the relevant research ethics committees in the participating countries.

Informed consent: All participants provided written informed consent.

Funding: B.C. is supported by an Ambizione grant (PZ00P1_180040) from the Swiss National Science Foundation (SNSF). M.P.B. is supported by the Natural Sciences and Engineering Research Council of Canada (RGPIN-2021-03153) and by a grant from The Banting Research Foundation.

Data sharing: This SHARE dataset is available at http://www.share-project.org/data-access.html.

Acknowledgements: *This paper uses data from SHARE Waves 1, 2, 3 (SHARELIFE), 4, 5,6 and 7 (DOIs: 10.6103/SHARE.w1.600, 10.6103/SHARE.w2.600, 10.6103/SHARE.w3.600, 10.6103/SHARE.w4.600, 10.6103/SHARE.w5.600, 10.6103/SHARE.w6.600, 10.6103/SHARE.w7.711).* The SHARE data collection was primarily funded by the European Commission through FP5 (QLK6-CT-2001-00360), FP6 (SHARE-I3: RII-CT-2006-062193, COMPARE: CIT5-CT-2005-028857, SHARELIFE: CIT4-CT-2006-028812) and FP7 (SHARE-PREP: no.211909, SHARE-LEAP: no.227822, SHARE M4: no.261982). Additional funding from the German Ministry of Education and Research, the Max Planck Society for the Advancement of Science, the U.S. National Institute on Aging (U01_AG09740-13S2, P01_AG005842, P01_AG08291, P30_AG12815, R21_AG025169, Y1-AG-4553-01, IAG_BSR06-11, OGHA_04-064, HHSN271201300071C) and from various national funding sources is gratefully acknowledged (see www.share-project.org).

References

[1] WHO (2012) Dementia: a public health priority. Geneva, Switzerland, 2012. **112**.

[2] Maasakkers CM, Claassen JA, Gardiner PA, Rikkert MGO, Lipnicki DM, Scarmeas N, Dardiotis E, Yannakoulia M, Anstey KJ, Cherbuin N (2020) The association of sedentary behaviour and cognitive function in people without dementia: a coordinated analysis across five cohort studies from COSMIC. *Sports Med* **50**, 403-413.

[3] Cao Q, Tan C-C, Xu W, Hu H, Cao X-P, Dong Q, Tan L, Yu J-T (2020) The prevalence of dementia: A systematic review and meta-analysis. *J Alzheimers Dis* **73**, 1157-1166.

[4] Ten Brinke LF, Bolandzadeh N, Nagamatsu LS, Hsu CL, Davis JC, Miran-Khan K, Liu-Ambrose T (2015) Aerobic exercise increases hippocampal volume in older women with probable mild cognitive impairment: a 6-month randomised controlled trial. *Br J Sports Med* **49**, 248-254.

[5] Hamer M, Terrera GM, Demakakos P (2018) Physical activity and trajectories in cognitive function: English Longitudinal Study of Ageing. *J Epidemiol Community Health* **72**, 477-483.

[6] Cheval B, Darrous L, Choi KW, Klimentidis YC, Raichlen DA, Alexander GE, Cullati S, Kutalik Z, Boisgontier MP (2020) Physical activity and general cognitive functioning: A Mendelian Randomization study. *BioRxiv*.

[7] Baumgart M, Snyder HM, Carrillo MC, Fazio S, Kim H, Johns H (2015) Summary of the evidence on modifiable risk factors for cognitive decline and dementia: a population-based perspective. *Alzheimer Dement* **11**, 718-726.

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

[9] Piercy KL, Troiano RP, Ballard RM, Carlson SA, Fulton JE, Galuska DA, George SM, Olson RD (2018) The physical activity guidelines for Americans. *JAMA* **320**, 2020-2028.

[10] Colcombe S, Kramer AF (2003) Fitness effects on the cognitive function of older adults: a meta-analytic study. *Psychol Sci* **14**, 125-130.

[11] Hamer M, Chida Y (2009) Physical activity and risk of neurodegenerative disease: a systematic review of prospective evidence. *Psychol Med* **39**, 3-11.

[12] Stillman CM, Cohen J, Lehman ME, Erickson KI (2016) Mediators of physical activity on neurocognitive function: a review at multiple levels of analysis. *Front Hum Neurosci* **10**, 626.

[13] Cotman CW, Berchtold NC (2002) Exercise: a behavioral intervention to enhance brain health and plasticity. *Trends Neurosci* **25**, 295-301.

[14] Hillman CH, Erickson KI, Kramer AF (2008) Be smart, exercise your heart: exercise effects on brain and cognition. *Nat Rev Neurosci* **9**, 58-65.

[15] Cotman CW, Berchtold NC, Christie L-A (2007) Exercise builds brain health: key roles of growth factor cascades and inflammation. *Trends Neurosci* **30**, 464-472.

[16] Van Praag H (2008) Neurogenesis and exercise: past and future directions. *Neuromolecular Med* **10**, 128-140.

[17] Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, Kim JS, Heo S, Alves H, White SM (2011) Exercise training increases size of hippocampus and improves memory. *PNAS* **108**, 3017-3022.

[18] Makizako H, Liu-Ambrose T, Shimada H, Doi T, Park H, Tsutsumimoto K, Uemura K, Suzuki T (2015) Moderate-intensity physical activity, hippocampal volume, and memory in older adults with mild cognitive impairment. *J Gerontol A Biol Sci Med Sci* **70**, 480-486.

[19] Weinstein AM, Voss MW, Prakash RS, Chaddock L, Szabo A, White SM, Wojcicki TR, Mailey E, McAuley E, Kramer AF (2012) The association between aerobic fitness and executive function is mediated by prefrontal cortex volume. *Brain Behav Immun* **26**, 811-819.

[20] Verstynen TD, Lynch B, Miller DL, Voss MW, Prakash RS, Chaddock L, Basak C, Szabo A, Olson EA, Wojcicki TR (2012) Caudate nucleus volume mediates the link between cardiorespiratory fitness and cognitive flexibility in older adults. *J Aging Res* **2012**, 939285.

[21] Oberlin LE, Verstynen TD, Burzynska AZ, Voss MW, Prakash RS, Chaddock-Heyman L, Wong C, Fanning J, Awick E, Gothe N (2016) White matter microstructure mediates the relationship between cardiorespiratory fitness and spatial working memory in older adults. *Neuroimage* **131**, 91-101.

[22] Sexton CE, Betts JF, Demnitz N, Dawes H, Ebmeier KP, Johansen-Berg H (2016) A systematic review of MRI studies examining the relationship between physical fitness and activity and the white matter of the ageing brain. *Neuroimage* **131**, 81-90.

[23] Colcombe SJ, Kramer AF, Erickson KI, Scalf P, McAuley E, Cohen NJ, Webb A, Jerome GJ, Marquez DX, Elavsky S (2004) Cardiovascular fitness, cortical plasticity, and aging. *PNAS* **101**, 3316-3321.

[24] Hillman CH, Pontifex MB, Castelli DM, Khan NA, Raine LB, Scudder MR, Drollette ES, Moore RD, Wu C-T, Kamijo K (2014) Effects of the FITKids randomized controlled trial on executive control and brain function. *Pediatrics* **134**, e1063-e1071.

[25] Yu Q, Herold F, Becker B, Klugah-Brown B, Zhang Y, Perrey S, Veronese N, Müller NG, Kramer AF, Zou L (2021) Cognitive benefits of exercise interventions: an fMRI activation likelihood estimation meta-analysis. *Brain Struct Funct*, 1-19.

[26] Kredlow MA, Capozzoli MC, Hearon BA, Calkins AW, Otto MW (2015) The effects of physical activity on sleep: a meta-analytic review. *J Behav Med* **38**, 427-449.

[27] Youngstedt SD (2005) Effects of exercise on sleep. *Clin Sports Med* **24**, 355-365.

[28] King AC, Oman RF, Brassington GS, Bliwise DL, Haskell WL (1997) Moderate-intensity exercise and self-rated quality of sleep in older adults: a randomized controlled trial. *JAMA* **277**, 32-37.

[29] Singh NA, Clements KM, Fiatarone MA (1997) A randomized controlled trial of the effect of exercise on sleep. *Sleep* **20**, 95-101.

[30] Chennaoui M, Arnal PJ, Sauvet F, Léger D (2015) Sleep and exercise: a reciprocal issue? *Sleep Med Rev* **20**, 59-72.

[31] Holfeld B, Ruthig JC (2014) A longitudinal examination of sleep quality and physical activity in older adults. *J Appl Gerontol* **33**, 791-807.

[32] Yaffe K, Falvey CM, Hoang T (2014) Connections between sleep and cognition in older adults. *Lancet Neurol* **13**, 1017-1028.

[33] Walker MP (2009) The role of sleep in cognition and emotion. *Ann N Y Acad Sci* **1156**, 168-197.

[34] Ellenbogen JM (2005) Cognitive benefits of sleep and their loss due to sleep deprivation. *Neurology* **64**, E25-E27.

[35] McSorley VE, Bin YS, Lauderdale DS (2019) Associations of sleep characteristics with cognitive function and decline among older adults. *Am J Epidemiol* **188**, 1066-1075.

[36] Foley DJ, Monjan AA, Brown SL, Simonsick EM, Wallace RB, Blazer DG (1995) Sleep complaints among elderly persons: an epidemiologic study of three communities. *Sleep* **18**, 425-432.

[37] Crowley K (2011) Sleep and sleep disorders in older adults. *Neuropsychol Rev* **21**, 41-53.

[38] Neikrug AB, Ancoli-Israel S (2010) Sleep disorders in the older adult–a mini-review. *Gerontology* **56**, 181-189.
[39] da Silva RAPC (2015) Sleep disturbances and mild cognitive impairment: a review. *Sleep Sci* **8**, 36-41.
[40] Falck RS, Best JR, Davis JC, Liu-Ambrose T (2018) The independent associations of physical activity and sleep with cognitive function in older adults. *J Alzheimers Dis* **63**, 1469-1484.
[41] Sewell K, Erickson KI, Rainey-Smith SR, Peiffer JJ, Sohrabi HR, Brown BM (2021) Relationships between physical activity, sleep and cognitive function: A narrative review. *Neurosci Biobehav Rev* **130**, 369-378.
[42] Wilckens KA, Erickson KI, Wheeler ME (2018) Physical activity and cognition: a mediating role of efficient sleep. *Behav Sleep Med* **16**, 569-586.
[43] Li L, Yu Q, Zhao W, Herold F, Cheval B, Kong Z, Li J, Mueller N, Kramer AF, Cui J (2021) Physical Activity and Inhibitory Control: The Mediating Role of Sleep Quality and Sleep Efficiency. *Brain Sci* **11**, 664.
[44] Won J, Alfini AJ, Weiss LR, Nyhuis CC, Spira AP, Callow DD, Carson Smith J (2019) Caudate volume mediates the interaction between total sleep time and executive function after acute exercise in healthy older adults. *Brain Plast* **5**, 69-82.
[45] Yuan M, Fu H, Liu R, Fang Y (2020) Effect of frequency of exercise on cognitive function in older adults: Serial mediation of depression and quality of sleep. *Int J Environ Res Public Health* **17**, 709.
[46] Börsch-Supan A, Brandt M, Hunkler C, Kneip T, Korbmacher J, Malter F, Schaan B, Stuck S, Zuber S (2013) Data resource profile: the Survey of Health, Ageing and Retirement in Europe (SHARE). *Int J Epidemiol* **42**, 992-1001.
[47] Aartsen MJ, Cheval B, Sieber S, Van der Linden BW, Gabriel R, Courvoisier DS, Guessous I, Burton-Jeangros C, Blane D, Ihle A (2019) Advantaged socioeconomic conditions in childhood are associated with higher cognitive functioning but stronger cognitive decline in older age. *PNAS* **116**, 5478-5486.
[48] Rosen WG (1980) Verbal fluency in aging and dementia. *J Clin Exp Neuropsychol* **2**, 135-146.
[49] Harris S, Dowson J (1982) Recall of a 10-word list in the assessment of dementia in the elderly. *Br J Psychiatry* **141**, 524-527.
[50] Cheval B, Orsholits D, Sieber S, Courvoisier DC, Cullati S, Boisgontier MP (2020) Relationship between decline in cognitive resources and physical activity. *Health Psychol* **39**, 519-528.
[51] Cheval B, Rebar AL, Miller MM, Sieber S, Orsholits D, Baranyi G, Courvoisier DC, Cullati S, Sander D, Boisgontier MP (2019) Cognitive resources moderate the adverse impact of poor neighborhood conditions on physical activity. *Prev Med* **126**, 105741.
[52] de Souto Barreto P, Cesari M, Andrieu S, Vellas B, Rolland Y (2017) Physical activity and incident chronic diseases: a longitudinal observational study in 16 European countries. *Am J Prev Med* **52**, 373-378.
[53] Cheval B, Sieber S, Guessous I, Orsholits D, Courvoisier DC, Kliegel M, Stringhini S, Swinnen S, Burton-Jeangros C, Cullati S, Boisgontier MP (2018) Effect of early-and adult-life socioeconomic circumstances on physical inactivity. *Med Sci Sports Exerc* **50**, 476-485.
[54] Boisgontier M, Orsholits D, von Arx M, Sieber S, Courvoisier D, Iversen M, Cullati S, Cheval B (2020) Adverse Childhood Experiences, Depressive Symptoms, Functional Dependence, and Physical Activity: A Moderated Mediation Model. *J Phys Act Health* **17**, 79-799.

[55] Chalabaev A, Boisgontier M, Sieber S, Sander D, Cullati S, Maltagliati S, Sarrazin P, Cheval B (in press) Early-life socioeconomic circumstances and physical activity in older age: women pay the price. *Psychol Sci*.

[56] van de Straat V, Cheval B, Schmidt RE, Sieber S, Courvoisier D, Kliegel M, Burton-Jeangros C, Cullati S, Bracke P (2020) Early predictors of impaired sleep: a study on life course socioeconomic conditions and sleeping problems in older adults. *Aging Ment Health* **24**, 322-332.

[57] United Nations Educational (2006) International Standard Classification of Education 1997. UNESCO, Paris

[58] Prince MJ, Reischies F, Beekman AT, Fuhrer R, Jonker C, Kivela S-L, Lawlor BA, Lobo A, Magnusson H, Fichter M (1999) Development of the EURO–D scale–a European Union initiative to compare symptoms of depression in 14 European centres. *Br J Psychiatry* **174**, 330-338.

[59] Boisgontier MP, Cheval B (2016) The anova to mixed model transition. *Neurosci Biobehav Rev* **68**, 1004-1005.

[60] Raudenbush SW, Bryk AS (2002) *Hierarchical linear models: Applications and data analysis methods*, Sage.

[61] Yzerbyt V, Muller D, Batailler C, Judd CM (2018) New recommendations for testing indirect effects in mediational models: The need to report and test component paths. *J Pers Soc Psychol* **115**, 929-943.

[62] MacKinnon DP, Lockwood CM, Hoffman JM, West SG, Sheets V (2002) A comparison of methods to test mediation and other intervening variable effects. *Psychol Methods* **7**, 83-104.

[63] Biesanz JC, Falk CF, Savalei V (2010) Assessing mediational models: Testing and interval estimation for indirect effects. *Multivariate Behav Res* **45**, 661-701.

[64] Tofighi D, MacKinnon DP (2011) RMediation: An R package for mediation analysis confidence intervals. *Behav Res Methods* **43**, 692-700.

[65] MacKinnon DP, Lockwood CM, Williams J (2004) Confidence limits for the indirect effect: Distribution of the product and resampling methods. *Multivariate Behav Res* **39**, 99-128.

[66] Barton K (2018) MuMIn: Multi-model inference. R package version 1.42.1. https://CRAN.R-project.org/package=MuMIn.

[67] Cheval B, Maltagliati S, Sieber S, Beran D, Chalabaev A, Sander D, Cullati S, Boisgontier MP (2021) Why are individuals with diabetes less active? The mediating role of physical, emotional, and cognitive factors. *Ann Behav Med* **55**, 904-917.

[68] Buman MP, King AC (2010) Exercise as a treatment to enhance sleep. *Am J Lifestyle Med* **4**, 500-514.

[69] Rebar AL, Stanton R, Geard D, Short C, Duncan MJ, Vandelanotte C (2015) A meta-meta-analysis of the effect of physical activity on depression and anxiety in non-clinical adult populations. *Health Psychol Rev* **9**, 366-378.

[70] Cheval B, Sivaramakrishnan H, Maltagliati S, Fessler L, Forestier C, Sarrazin P, Orsholits D, Chalabaev A, Sander D, Ntoumanis N (2021) Relationships between changes in self-reported physical activity, sedentary behaviour and health during the coronavirus (COVID-19) pandemic in France and Switzerland. *J Sports Sci* **39**, 699-704.

[71] Goldberg JH, King AC (2007) Physical activity and weight management across the lifespan. *Annu. Rev. Public Health* **28**, 145-170.

[72] Lee I-M, Djoussé L, Sesso HD, Wang L, Buring JE (2010) Physical activity and weight gain prevention. *JAMA* **303**, 1173-1179.

[73] Swift DL, Johannsen NM, Lavie CJ, Earnest CP, Church TS (2014) The role of exercise and physical activity in weight loss and maintenance. *Prog Cardiovasc Dis* **56**, 441-447.

[74] Manini TM, Pahor M (2009) Physical activity and maintaining physical function in older adults. *Br J Sports Med* **43**, 28-31.

[75] Young T, Peppard PE, Taheri S (2005) Excess weight and sleep-disordered breathing. *J App Physiol* **99**, 1592-1599.

[76] Hung HC, Yang YC, Ou HY, Wu JS, Lu FH, Chang CJ (2013) The association between self-reported sleep quality and overweight in a Chinese population. *Obesity* **21**, 486-492.

[77] Rahe C, Czira ME, Teismann H, Berger K (2015) Associations between poor sleep quality and different measures of obesity. *Sleep Med* **16**, 1225-1228.

[78] Morin CM, Bootzin RR, Buysse DJ, Edinger JD, Espie CA, Lichstein KL (2006) Psychological and behavioral treatment of insomnia: update of the recent evidence (1998–2004). *Sleep* **29**, 1398-1414.

[79] Ensrud KE, Blackwell TL, Redline S, Ancoli-Israel S, Paudel ML, Cawthon PM, Dam TTL, Barrett-Connor E, Leung PC, Stone KL (2009) Sleep disturbances and frailty status in older community-dwelling men. *J Am Geriatr Soc* **57**, 2085-2093.

[80] Wilckens KA, Hall MH, Nebes RD, Monk TH, Buysse DJ (2016) Changes in cognitive performance are associated with changes in sleep in older adults with insomnia. *Behav Sleep Med* **14**, 295-310.

[81] Blackwell T, Yaffe K, Ancoli-Israel S, Schneider JL, Cauley JA, Hillier TA, Fink HA, Stone KL (2006) Poor sleep is associated with impaired cognitive function in older women: the study of osteoporotic fractures. *J Gerontol A Biol Sci Med Sci* **61**, 405-410.

[82] Nebes RD, Buysse DJ, Halligan EM, Houck PR, Monk TH (2009) Self-reported sleep quality predicts poor cognitive performance in healthy older adults. *J Gerontol B Psychol Sci Soc Sci* **64**, 180-187.

[83] Kang J-E, Lim MM, Bateman RJ, Lee JJ, Smyth LP, Cirrito JR, Fujiki N, Nishino S, Holtzman DM (2009) Amyloid-β dynamics are regulated by orexin and the sleep-wake cycle. *Science* **326**, 1005-1007.

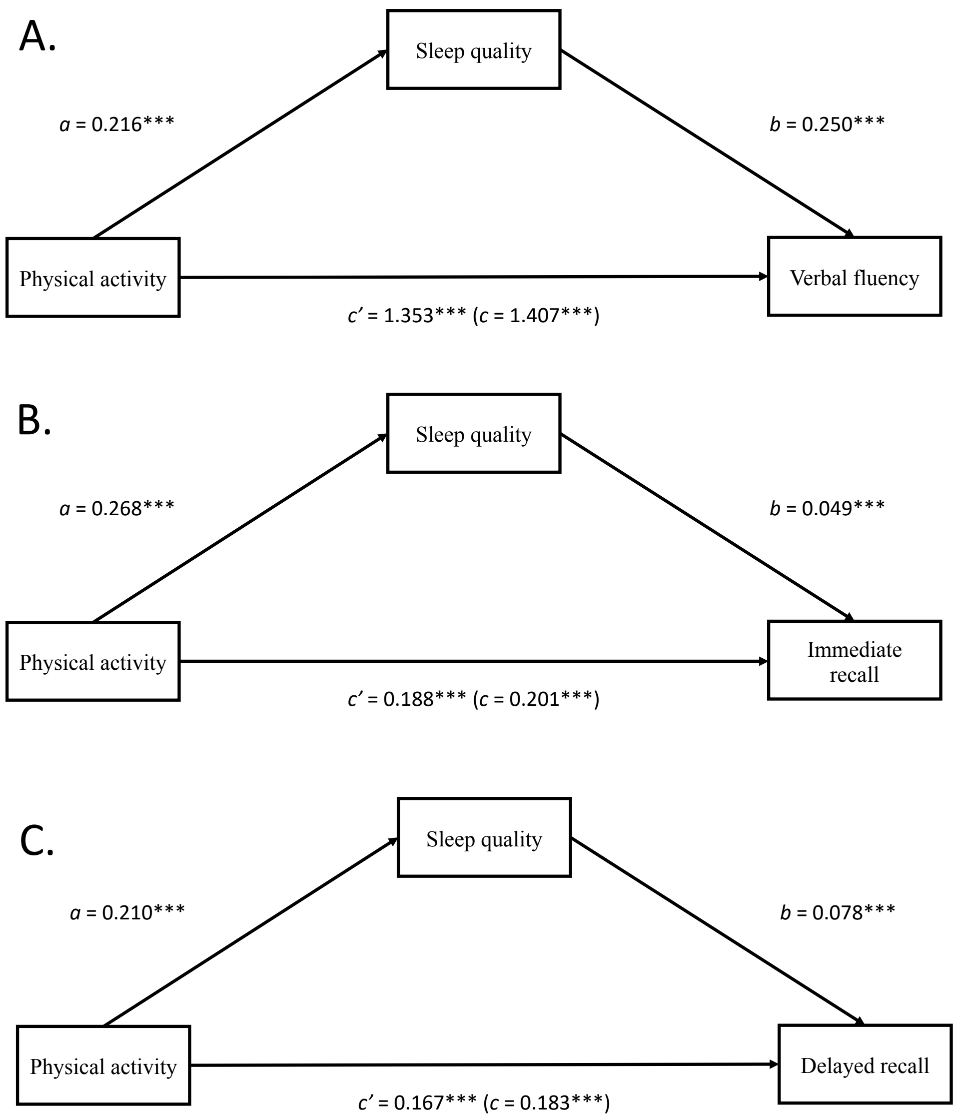
[84] Zhu B, Dong Y, Xu Z, Gompf HS, Ward SA, Xue Z, Miao C, Zhang Y, Chamberlin NL, Xie Z (2012) Sleep disturbance induces neuroinflammation and impairment of learning and memory. *Neurobiol Dis* **48**, 348-355.

[85] Meerlo P, Mistlberger RE, Jacobs BL, Heller HC, McGinty D (2009) New neurons in the adult brain: the role of sleep and consequences of sleep loss. *Sleep Med Rev* **13**, 187-194.

[86] Porkka-Heiskanen T, Zitting KM, Wigren HK (2013) Sleep, its regulation and possible mechanisms of sleep disturbances. *Acta physiologica* **208**, 311-328.

[87] Prince SA, Adamo KB, Hamel ME, Hardt J, Gorber SC, Tremblay M (2008) A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review. *Int J Behav Nutr Phys Act* **5**, 56.

Figures 1. Mediation models



Notes. Coefficients are unstandardized regression coefficients obtained from the mixed-effects models. *a* represents the association between the exposure (i.e., physical activity) and the mediator (i.e., sleep quality). *b* represents the association between the mediator (i.e., sleep quality) and the outcome (i.e., cognitive function), c' represents the direct effect of the exposure on the outcome, after adjustment for the mediator. The unstandardized regression coefficient representing the total association (c) between physical activity and cognitive functions is in parentheses. *** p <.001. A. Results of the models for verbal fluency. B. Results of the models for immediate recall. C. Results of the models for delayed recall.

Supplemental material

Sensitivity analyses

Table S1. Results based on participants with at least two measures of PA, sleep quality, and cognitive function.

Table S2. Results excluding participants who dropped out during the survey.

Table S3. Results excluding participants who died during the survey.

Sensitivity analyses

Table S4. Results based on data in which a time lag have been introduced between the predictors and the outcomes.

Table S1. Results based on participants with at least two measures of PA, sleep quality, and cognitive function.

	Model 1 (sleep quality)		Model 2 (cognitive functions)	
	OR [b] (CI)	*p*	b (CI)	*p*
Verbal fluency (N = 67,088)				
Physical activity (ref. physically inactive)				
Physically active	1.23 [.21] (1.20;1.27)	<.001	1.22 (1.16;1.28)	<.001
Sleep quality (ref. poor sleep quality)				
Good sleep quality			0.24 (0.18;0.30)	<.001
Immediate recall (N = 52,013)				
Physical activity (ref. physically inactive)				
Physically active	1.29 [0.25] (1.24;1.34)	<.001	0.17 (0.16;0.18)	<.001
Sleep quality (ref. poor sleep quality)				
Good sleep quality			0.04 (0.03;0.05)	<.001
Delayed recall (N = 54,664)				
Physical activity (ref. physically inactive)				
Physically active	1.24 [.22] (1.20;1.29)	<.001	0.16 (0.14;0.17)	<.001
Sleep quality (ref. poor sleep quality)				
Good sleep quality			0.07 (0.06;0.08)	<.001

Table S2. Results excluding participants who dropped out during the survey

	Model 1 (sleep quality)		**Model 2 (cognitive functions)**	
	OR [b] (CI)	*p*	b (CI)	*p*
Verbal fluency (N = 66,009)				
Physical activity (ref. physically inactive)				
Physically active	1.22 [.20] (1.19;1.27)	<.001	1.28 (1.21;1.34)	<.001
Sleep quality (ref. poor sleep quality)				
Good sleep quality			0.25 (0.19;0.31)	<.001
Immediate recall (N = 63,263)				
Physical activity (ref. physically inactive)				
Physically active	1.30 [.27] (1.26;1.35)	<.001	0.18 (0.17;0.20)	<.001
Sleep quality (ref. poor sleep quality)				
Good sleep quality			0.05 (0.04;0.06)	<.001
Delayed recall (N = 62,339)				
Physical activity (ref. physically inactive)				
Physically active	1.27 [0.24] (1.22;1.31)	<.001	0.16 (0.15;0.18)	<.001
Sleep quality (ref. poor sleep quality)				
Good sleep quality			0.08 (0.07;0.09)	<.001

Table S3. Results excluding participants who died during the survey.

	Model 1 (sleep quality)		**Model 2 (cognitive functions)**	
	OR [b] (CI)	*p*	b (CI)	*p*
Verbal fluency (N = 87,785)				
Physical activity (ref. physically inactive)				
Physically active	1.23 [.21] (1.19;1.27)	<.001	1.23 (1.17;1.29)	<.001
Sleep quality (ref. poor sleep quality)				
Good sleep quality			0.24 (0.18;0.30)	<.001
Immediate recall (N = 79,959)				
Physical activity (ref. physically inactive)				
Physically active	1.28 [0.25] (1.24;1.32)	<.001	0.17 (0.16;0.18)	<.001
Sleep quality (ref. poor sleep quality)				
Good sleep quality			0.05 (0.04;0.06)	<.001
Delayed recall (N = 81,258)				
Physical activity (ref. physically inactive)				
Physically active	1.23 [.21] (1.19;1.27)	<.001	0.15 (0.14;0.17)	<.001
Sleep quality (ref. poor sleep quality)				
Good sleep quality			0.08 (0.06;0.09)	<.001

Table S4. Results based on data in which a time lag have been introduced between the predictors and the outcomes.

	Model 1 (sleep quality)		**Model 2 (cognitive functions)**	
	OR [b] (CI)	*p*	b (CI)	*p*
Verbal fluency (N = 42,327)				
Physical activity (ref. physically inactive)				
Physically active	1.28 [.25] (1.22;1.35)	<.001	0.80 (0.70;0.89)	<.001
Sleep quality (ref. poor sleep quality)				
Good sleep quality			0.16 (0.07;0.25)	<.001
Immediate recall (N = 46,648)				
Physical activity (ref. physically inactive)				
Physically active	1.26 [0.23] (1.20;1.32)	<.001	0.10 (0.09;0.12)	<.001
Sleep quality (ref. poor sleep quality)				
Good sleep quality			0.02 (0.01;0.04)	<.001
Delayed recall (N = 47,921)				
Physical activity (ref. physically inactive)				
Physically active	1.23 [.21] (1.17;1.29)	<.001	0.10 (0.08;0.12)	<.001
Sleep quality (ref. poor sleep quality)				
Good sleep quality			0.04 (0.02;0.05)	<.001