

High-intensity Physical Activity Is Not Associated With Better Cognition in the Elder: Evidence From the China Health and Retirement Longitudinal Study

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Research

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Abstract

Objective To evaluate the association of physical activity (PA) intensity with cognitive performance at baseline and during follow up.

Methods A total of 4 039 participants aged 45 years or above from the China Health and Retirement Longitudinal Study were enrolled in visit 1 (2011-2012), and followed for cognitive function in visit 2 (2013-2014), visit 3 (2015-2016) and visit 4 (2017-2018). We analyzed the association of PA intensity with global cognition, episodic memory and mental intactness at baseline using adjusted regression methods, and evaluated the long-term effect of PA intensity using multiple measures of cognition scores by mixed effect model.

Results Compared with individuals without PA, those with mild PA had 0.42 (3.7%) higher global cognition, and 0.20 (5.9%) higher episodic memory, while individuals with moderate PA had 0.59 (5.3%) higher global cognition, 0.25 (7.1%) higher episodic memory, and 0.34 (4.4%) higher mental intactness at baseline. The vigorous PA was not associated with better global cognition, episodic memory and mental intactness (all $P > 0.05$). The results remained almost consistent in multiple sensitivity analyses. In addition, mild and moderate PA, rather than vigorous PA, was beneficial to long-term cognitive performance.

Conclusions Our study indicates that mild and moderate PA could improve cognitive performance, rather than the vigorous activity. The targeted intensity of PA might be more effective to achieve the greatest cognition improvement considering age, overweight and depressive status.

Background

Decline in cognitive function is one of the main causes of disability and even death in the elderly, which has a pernicious impact on physical and mental health, independent living ability and social function. In China, the prevalence rates of mild cognitive impairment (MCI) and dementia are rapidly rising along with the population aging, and approximately 5.14% of people over 65 years had dementia.¹ Dementia has caused a heavy socio-economic burden, with the global cost of dementia is reported to be US \$957.56 billion in 2015, set to reach US \$2.54 trillion by 2030 and US \$9.12 trillion by 2050². Aging is a major risk factor of cognitive function decline and cognitive impairment progression, and evidence suggests that some important cognitive functions such as episodic memory decline with age even in the middle-aged people³. Thus, strengthening the prevention of cognitive decline and proposing the valid strategy to avoid cognitive impairment is of great public health significance.

Physical activity (PA) is associated with various health benefits, including cardiopulmonary capacity and muscular endurance, and the reduced risk of overall mortality, cardiovascular diseases, metabolic syndrome, and psychiatric disorders⁴⁻⁶. As a modifiable factor, PA acts as a non-pharmacological strategy to mitigate the age-related impairment on cognitive performance⁷. However, there exists a large

amount of variation in its effect on cognition improvement^{8,9}. The effects of PA on improving cognitive function have been extensively studied in different populations⁷. In a meta-analysis of 39 randomized controlled trials (RCT), the results showed that PA interventions are effective for improving cognitive function in older adults regardless of the baseline cognitive status¹⁰. In addition, a RCT in older adults aged 55 to 80 years without psychiatric or neurological diseases showed a positive association of cognitive improvement with aerobic fitness and training-induced neuroplasticity. However, in another RCT of exercise interventions, the researchers did not find sufficient evidence that PA or aerobic fitness could improve the cognitive performance in older adults over 50 years¹¹. The dose of PA volume, duration, frequency, or intensity, together with the population features, are possible factors contributing to this variation⁹, and the dose-response relationship between PA and the positive outcome was always argued^{10,12,13}. The 2018 Physical Activity Guidelines stated that little is known about the dose of PA intensity needed to improve cognitive function yet, and there lacks strong evidence that moderate-to-vigorous PA could improve the cognition, especially in the middle-aged adults⁷. Sammi et al. found that more exercise is not always better for the self-reported mental health burden⁶. However, it remains unknown whether or not high intensity PA is related with better cognitive performance^{14,15}. The long-term effect of PA on cognitive performance remains unclear neither.

In this study, we explored the association of PA intensity with global cognition, episodic memory and mental intactness both at baseline and during follow up, after accounting for a range of sociodemographic characteristics and physical health conditions. In addition, we examined the effect in certain populations characterized by age, sex, body mass index (BMI) and depression status.

Method

Data sources and study design

This current study was a secondary analysis of the China Health and Retirement Longitudinal Study (CHARLS), which is a national prospective cohort collecting a wide range of social and economic data, personal health information for geriatric and health policy research (<http://charls.pku.edu.cn/>). A total of 17 705 participants from 150 counties or districts within 28 provinces in China were recruited in the demographic background survey at baseline (visit 1: 2011-2012), and followed up every two years at visit 2 (2013-2014), visit 3 (2015-2016), and visit 4 (2017-2018). Details of the cohort design have been described previously¹⁶. The CHARLS study was approved by the institutional review board of Peking University (IRB00001052-11015). Written informed consent was obtained before participation. At each visit, the trained staff conducted face-to-face interviews to collect the sociodemographic characteristics, medical history, health behavior, cognitive function and depressive status using standardized questionnaire.

Of 17 705 participants at baseline, we excluded 832 individuals without age and sex information, or younger than 45 years. Then, 5 970 and 6 733 participants lacking cognitive function data or PA intensity

information were excluded, as the activity investigation was limited to a randomly selected subgroup in the CHARLS study. We excluded 47 individuals of Alzheimer's disease, brain atrophy or Parkinson's disease, and 84 individuals with history of stroke attack. Finally, 4 039 participants were included for this current analysis, and 2 319, 2 184, and 1 557 of them provided cognitive function data during follow up at visit 2, visit 3, and visit 4, respectively. The flow chart of this study was shown in Figure 1.

Cognition measurement

In accordance with previous studies¹⁷⁻¹⁹, the cognitive performance was tested by two cognition measures in this study: episodic memory and mental intactness. The episodic memory reflects an individual's ability to immediately repeat ten Chinese words just read to them in any order (referred as immediate recall) and to recall the same words four minutes later (referred as delayed recall). The episodic memory score is the mean value of immediate and delayed recall scores, and ranges from 0 to 10. The mental intactness reflects the mental status based on several questions of the Telephone Interview of Cognitive Status (TICS) battery, including serial subtraction of 7 from 100 (up to five times), the date (month, day, year and season), the day of week, and the ability to redraw a picture shown to the individual. Answers to these questions are summed into the mental intactness score ranging from 0 to 11. The global cognition score is calculated as the sum of episodic memory score and mental intactness score, which ranges from 0 to 21.

Definition of PA intensity

PA was quantified via a modified short form of the physical activity questionnaire²⁰. Participants were asked to report the number of days and typical spent time-per-day for three activity types (mild, moderate and vigorous) during the previous week. Participant were classified into 'none', 'mild', 'moderate' and 'vigorous' PA intensity, according to whether they had the corresponding activity type on three or more days per week and for at least 10 minutes at every time. The vigorous activities make breathe much harder than normal and include heavy lifting, digging, plowing, aerobics, fast bicycling, and cycling with a heavy load; the moderate activities make you breathe somewhat harder than normal and include carrying light loads, bicycling at a regular pace, mopping the floor, doing Taiji and walking fast; spend walking in a usual week; the mild activity refers to waking at work, at home, walking to travel from place to place, and any other walking that you might do solely for recreation, sport, exercise, or leisure. Participants without any of these activity types or not meeting the relevant standards were classified as 'none' PA intensity.

Covariates

Baseline measurements of age, sex, education level, marital status, residence location, BMI, smoking, drinking, self-reported health conditions and medication use, and depression status were included as covariates in the current study. Educational level was categorized as 'primary education', 'secondary education', and 'third education'. Marital status included 'married' and 'others'. Residence location included 'urban' and 'rural'. Smoking status was defined as 'never smoking', 'current smoker', and 'former smoker'. Drinking status was defined as 'current drinking more than once per month', 'current drinking

once or less than once per month', and 'no current drinking'. Self-reported health conditions included the diagnosis of hypertension, diabetes, dyslipidemia, and heart diseases (heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems). Medication use included the use of anti-hypertensive and anti-diabetic drugs. Depressive symptoms were assessed using the 10-item version of the Epidemiologic Studies Depression Scale (CES-D), and a score of ≥ 12 indicated the presence of depressive symptoms²¹.

BMI was calculated as weight (in kilograms)/height² (in metre squared), and grouped into underweight (BMI: <18.5 kg/m²), normal weight (BMI: 18.5-23.9 kg/m²), overweight (BMI: ≥ 24.0 kg/m²) according to the overweight and obesity standard²².

Statistics analysis

Baseline characteristics are presented as the mean (standard deviation, SD), median [interquartile range, IQR] or number (percentage), as appropriate. To show the distribution differences, we compared the scores of global cognition, episodic memory and mental intactness among those with different PA intensity by Kruskal-Wallis test, both with the population without PA and the whole population as reference.

To investigate the association of PA intensity and cognitive performance at baseline, we performed adjusted analyses using the regression models for the individual-level factors: **model 1** was adjusted for age; **model 2** was adjusted for age, sex, BMI, education level, marital status, residence location, health conditions, smoking, current drinking and CES-D score. To validate the findings, we did multiple sensitivity analyses. First, 37.5% (1 515 of 4 039) of total data items were missing at residence type (n of missing: 1 397), health conditions (n of missing: 16 for hypertension, 63 for dyslipidemia, 26 for diabetes, 21 for heart diseases) or CES-D assessment (n of missing: 103). Thus, we repeated the analyses using the imputed data by multiple imputation of chained equations method. We created five imputed data sets and pooled the results. Second, to account for the imbalanced self-select probability into different PA intensity group, we applied a multinomial propensity score weighting procedure using the tree-based regression model. The covariate set of age, sex, BMI, education, marital status, residence and CES-D score, which were significantly associated with cognitive performance in the analyses, were considered in this weighting procedure. The 'es.mean' and 'ks.mean' parameters were chosen as the stopping rule, which refer to the mean of absolute standardized mean difference and the mean of Kolmogorov-Smirnov statistic for measuring the balance across the covariates. The max number of trees was set as 10000 iterations. The balance measures of interest corresponding with iterations were shown in **Figure S1** to ensure that the parameter was reasonable. Then, we analyzed the effect of PA intensity in certain subgroups, according to age (<60 years and ≥ 60 years), sex (male and female), smoking, drinking, BMI level and depression status (CES-D <12 and CES-D ≥ 12).

To investigate the long-term effect of PA intensity on cognitive performance during follow up, we analyzed the association of PA intensity at baseline with multiple measures of cognition scores using

mixed effect model. The main effect of PA intensity and visit time, together with the interaction term, were fitted in the mixed model. Mixed effect model offers a better way to deal with missing data, and subjects with more missing values have a weaker impact on parameter estimation. The same covariates were adjusted as in **model 2**, and the individual difference was considered as random effect term in the analyses. Furthermore, the subgroup analyses were performed as mentioned above. All the analyses presented above were conducted using packages of 'mice', 'twang', 'survey', and 'lmerTest' by R software (version 4.1.0).

Data Availability

The CHARLS dataset is freely available to all researchers in related fields on request. Researchers can gain access to the data (<http://charls.pku.edu.cn/>). And the datasets used and/or analysed in this current study are available from the corresponding author (Dr. Lixin Tao) on reasonable request.

Results

Participant Characteristics

Our study was based on 4 039 participants, and 2 050 (50.8%) were male. The mean age was 58.12 (SD 9.12) years. The population level of global cognition, episodic memory and mental intactness were 11.71 (SD 3.57), 3.71 (SD 1.67), and 8.01 (SD 2.64). Vigorous PA was reported by 1 306 (32.3%) participants, while 1 263 (31.3%), 1 002 (24.8%) and 468 (11.6%) reported moderate, mild and none PA, respectively. Full demographic characteristics and health conditions of the study population are presented in Table 1. Individuals with moderate PA showed higher global cognition, episodic memory and mental intactness scores, both compared with those of none PA and the whole population. Noticeably, there were no significant differences regarding cognitive performance in individuals of vigorous PA as shown in Fig. 2.

Table 1
Baseline characteristics of the study population.

	Overall (n = 4039)	Male (n = 2050)	Female (n = 1989)	P value
Cognitive function				
episodic memory	3.71(1.67)	3.72(1.62)	3.69(1.73)	0.605
metal intactness	8.01(2.64)	8.46(2.41)	7.54(2.78)	< 0.001
global cognition	11.71(3.57)	12.18(3.30)	11.23(3.76)	< 0.001
Physical activity				< 0.001
none	468(11.6)	211(10.3)	257(12.9)	
mild	1002(24.8)	471(23.0)	531(26.7)	
moderate	1263(31.3)	577(28.1)	686(34.5)	
vigorous	1306(32.3)	791(38.6)	515(25.9)	
Age (years)	58.12(9.12)	59.26(9.01)	56.95(9.10)	< 0.001
Education level				
primary	2536(62.8)	1128(55.0)	1408(70.8)	< 0.001
secondary	1421(35.2)	865(42.2)	556(28.0)	
third	82(2.0)	57(2.8)	25(1.3)	
Marital status				< 0.001
married	3613(89.5)	1874(91.4)	1739(87.4)	
other	426(10.5)	176(8.6)	250(12.6)	
Residence				< 0.001
urban	589(22.3)	251(17.5)	338(28.0)	
rural	2053(77.7)	1186(82.5)	867(72.0)	
BMI (kg/m²)	23.49(4.00)	23.39(3.92)	23.59(4.07)	0.101
Health conditions				
hypertension	929(23.1)	493(24.9)	436(21.4)	0.009
diabetes	224(5.6)	92(4.5)	132(6.7)	0.004
dyslipidemia	366(9.2)	170(8.4)	196(10.0)	0.096
Data are the mean (SD), median [IQR] or number (%), as appropriate.				

	Overall (n = 4039)	Male (n = 2050)	Female (n = 1989)	P value
heart diseases	447(11.1)	184(9.0)	263(13.3)	< 0.001
Medication use				
anti-hypertensive	744(80.1)	339(77.8)	405(82.2)	0.111
anti-diabetic	167(74.6)	70(76.1)	97(73.5)	0.776
Smoking status				< 0.001
current	1298(32.1)	1180(57.6)	118(5.9)	
former	365(9.0)	327(16.0)	38(1.9)	
never	2376(58.8)	543(26.5)	1833(92.2)	
Current drinking				< 0.001
>once a month	1115(27.6)	961(46.9)	154(7.7)	
≤once a month	335(8.3)	213(10.4)	122(6.1)	
no current drinking	2589(64.1)	876(42.7)	1713(86.1)	
CES-D score	6.00[3.00,11.00]	6.00[3.00,10.00]	7.00[4.00,12.00]	< 0.001
Data are the mean (SD), median [IQR] or number (%), as appropriate.				

Association between PA intensity and cognition scores at baseline

Based on the adjusted regression model, compared with individuals without PA, those with mild PA had 0.42 (3.7%) higher global cognition, and 0.20 (5.9%) higher episodic memory, while individuals with moderate PA had 0.59 (5.3%) higher global cognition, 0.25 (7.1%) higher episodic memory, and 0.34 (4.4%) higher mental intactness at baseline. Vigorous PA was not associated with better global cognition, neither its components (all $P > 0.05$) as shown in Table 2. In the multivariate model, age and CES-D score had negative effects on the cognitive performance, while those of male, higher education, married status, living in urban area, nondrinker had better cognitive performance (**Table S1**).

Table 2

Association of physical activity intensity with global cognition, episodic memory and mental intactness at baseline.

	model 1			model 2		
	β	95% CI	P value	β	95% CI	P value
Global cognition						
physical activity (ref: none)						
mild	0.575	0.197–0.953	0.003	0.421	0.0734–0.768	0.018
moderate	0.631	0.265–0.998	<0.001	0.59	0.255–0.926	<0.001
vigorous	-0.124	-0.490-0.242	0.506	0.133	-0.209-0.474	0.447
Episodic memory						
physical activity (ref: none)						
mild	0.268	0.091–0.445	0.003	0.204	0.0330–0.375	0.020
moderate	0.259	0.088–0.431	0.003	0.248	0.082–0.413	0.003
vigorous	-0.018	-0.190-0.153	0.835	0.128	-0.040-0.297	0.135
Mental intactness						
physical activity (ref: none)						
mild	0.307	0.023–0.592	0.034	0.217	-0.050-0.483	0.111
moderate	0.372	0.096–0.648	0.008	0.343	0.085–0.601	0.009
vigorous	-0.106	-0.381-0.169	0.451	0.004	-0.258-0.266	0.975
model 1: adjusted for age;						
model 2: adjusted for age, sex, BMI, education level, marital status, residence location, health conditions, smoking, current drinking and CES-D score.						

The results did not significantly change using the imputed data set. Compared with individuals without PA, those of mild PA owned 0.44 (before imputation: 0.42) higher global cognition score, and 0.22 (before imputation: 0.20) higher episodic memory, while individuals of moderate PA had 0.63 (before imputation: 0.59) higher global cognition, 0.26 (before imputation: 0.25) higher episodic memory, and 0.37 (before imputation: 0.34) higher mental intactness. Vigorous PA was still not associated with global cognition

and its components (all $P > 0.05$) as shown in Fig. 3 (A). In the propensity score weighted population, the effective sample size was 3 482, and the matched covariates were balanced among groups of different PA intensity (**Table S2**). Figure 3 (B, C) showed that mild PA was only associated with higher episodic memory ('es.mean': $\beta = 0.20$, $P = 0.041$; 'ks.mean': $\beta = 0.20$, $P = 0.041$), and moderate PA was associated with improved global cognition ('es.mean': $\beta = 0.46$, $P = 0.022$; 'ks.mean': $\beta = 0.46$, $P = 0.022$) and episodic memory ('es.mean': $\beta = 0.23$, $P = 0.016$; 'ks.mean': $\beta = 0.23$, $P = 0.015$). Vigorous PA was not significantly associated with global cognition, episodic memory and mental intactness (all $P > 0.05$).

Figure 4 (A) summarizes the subgroup analyses of the cognitive performance, and the associations varied in certain populations. The protective effects of mild and moderate PA were not significant in the middle-age (< 60 years), underweight and depressive populations. In the elder adults, mild and moderate PA were associated with 0.72 and 0.95 higher global cognition scores compared to individuals of none PA. Only moderate PA could improve the global cognition in individuals of overweight ($\beta = 0.78$, $P = 0.022$). Similar results were found when we analyzed the episodic memory and mental intactness.

Long term effect of PA intensity on cognition scores

During the follow up, 2 319, 2 184, and 1 557 participants provided cognitive performance data at visit 2, visit 3, and visit 4, as shown in **Figure S2**. Compared with individuals without PA, those with mild PA had 0.56 (95 CI: 0.12–0.99) higher global cognition score, 0.23 (95 CI: 0.01–0.46) higher episodic memory score, and 0.33 (95 CI: 0.01–0.64) higher mental intactness score considering multiple measurements and the long-term effect. Individuals with moderate PA had 0.74 (95 CI: 0.32–1.17) higher global cognition score, 0.32 (95 CI: 0.09–0.54) higher episodic memory score, and 0.43 (95 CI: 0.12–0.74) higher mental intactness score. Vigorous PA was not associated with long-term improved global cognition and its components (all $P > 0.05$) as shown in Table 3. Subgroup analyses of the associations varied in certain populations are shown in Fig. 4 (B). The protective effects of mild and moderate PA were significant dominantly in the elder adults (≥ 60 years), and non-depressive populations. In the elder adults, mild and moderate PA were associated with 0.47 (95% CI: 0.02–0.91) and 0.50 (95CI: 0.06–0.95) higher global cognition scores compared to individuals of none PA. Among non-depressive population, global cognition was 0.49 (95% CI: 0.15–0.82) higher for those with mild PA, and 0.34 (95% CI: 0.02–0.67) higher for those with moderate PA, compared with those without PA.

Table 3

The effect of physical activity intensity on the long-term cognitive performance during follow up.

	model 1			model 2		
	β	95% CI	P value	β	95% CI	P value
Global cognition						
physical activity (ref: none)						
mild	0.545	0.178–0.912	0.004	0.556	0.119–0.993	0.013
moderate	0.869	0.514–1.224	< 0.001	0.744	0.317–1.171	0.001
vigorous	0.200	-0.153-0.553	0.267	0.24	-0.187-0.667	0.272
Episodic memory						
physical activity (ref: none)						
mild	0.253	0.065–0.441	0.008	0.23	0.005–0.457	0.048
moderate	0.376	0.194–0.558	< 0.001	0.316	0.093–0.539	0.005
vigorous	0.141	-0.039-0.321	0.128	0.11	-0.113-0.333	0.336
Mental intactness						
physical activity (ref: none)						
mild	0.292	0.029–0.555	0.029	0.325	0.007–0.643	0.045
moderate	0.493	0.238–0.748	< 0.001	0.429	0.117–0.741	0.007
vigorous	0.059	-0.194-0.312	0.646	0.13	-0.182-0.442	0.413
model 1: the main effect of PA intensity and visit time plus the interaction were fitted;						
model 2: model 1 and adjusted for age, sex, BMI, education level, marital status, residence location, health conditions, smoking, current drinking and CES-D score.						

Discussion

In this cohort study, we found that the mild and moderate intensity of PA are associated with better cognitive performance, rather than vigorous. The results were almost consistent in multiple sensitivity analyses. In addition, the long-term effects of mild and moderate PA on cognitive performance are significant, instead of vigorous activity. The associations of mild and moderate PA are predominant in the elder (≥ 60 years), normal weight and non-depressive populations.

To date, numerous studies have examined the relationship between PA and cognitive function, but the results are contradictory^{7,23}. Results of a meta-analysis of 36 RCTs showed that only moderate (0.17, 95CI: 0.03–0.33) to vigorous (0.16, 95CI: 0.04–0.27) activity improved cognitive function in older

adults¹⁰. While another meta-analysis of prospective studies showed that low to moderate intensity was also associated with a significantly lower risk of cognitive decline compared to inactivity individuals²³.

The association between vigorous PA and cognition in the present study was consistent with several RCTs and meta-analyses that have demonstrated an inverted U-shaped dose-response relationship between PA intensity and cognitive performance¹⁴. This relationship was first proposed from arousal performance theory by Yerkes et al. in 1908²⁴. In recent years, Dietrich et al. proposed that moderate PA could activate the arousal mechanism of the reticulum system, thus improving several domain-specific cognition²⁵. However, vigorous PA requires greater activation of the premotor cortex and supplementary motor areas at the expense of the prefrontal cortex, resulting in the disengagement of higher-order functions in the prefrontal cortex. This model provides a neurobiological basis for the dose-response relationship. On the other hand, studies on mental health have also found that more activity does not necessarily translate into better mental well-being⁶.

The underlying mechanisms by which PA promotes the improvement of cognitive function have not been determined yet⁹. One of the key hypotheses is that activity of the sympathetic adrenal system induced by PA increases plasma catecholamine (E) and norepinephrine (NE) concentrations, which feed back to the hypothalamus via the autonomic nervous system, leading to an increase in the catecholamine neurotransmitters (NE) and dopamine (DA) in the brain^{26,27}. The norepinephrine system activated by NE and the dopaminergic pathway activated by DA are both important neurotransmitters related to cognitive function in humans²⁸. Furthermore, studies suggest that brain-derived neurotrophic factor (BDNF) also plays an important role in the improvement of cognitive function caused by PA²⁹. BDNF can promote neuronal differentiation and survival, which is an important regulator of synaptic plasticity²⁹⁻³¹. PA can increase the expression of BDNF genes and proteins in the cerebellum, cerebral cortex, and hippocampus^{32,33}, and induces hippocampal angiogenesis by promoting insulin-like growth factor (IGF-1) and vascular endothelial growth factor (VEGF) production in the periphery^{34,35}. Intervention trials in the elderly have shown that these neurotrophins contribute to the positive effects of PA on cognition^{36,37}. In the existing RCTs of cognitive change caused by PA, the duration of follow up is generally less than 1 year^{13,15}. Compared with measuring the immediate response of cognition to a single PA experience or the effect of PA on cognition over a short period (weeks or months), long-term follow-up is more likely to reflect real changes in the individual's cognitive level and the cumulative effect of PA on cognitive function. In this current study, we reported the long-term effect of mild and moderate activity on cognition and validated the observed results.

The stratified analysis results showed that there was a dominantly significant association of mild and moderate activity with cognitive performance among people aged 60 and older, rather than people younger than 60. Most systematic review or meta-analysis of the association between PA and cognitive performance in older adults have yielded positive results⁷ and numerous studies have identified the neurobiological mechanisms of cognitive decline in the elder^{12,13,38}. Strong evidence for biomarker

analysis of DA indicates that the density of postsynaptic D1 and D2 receptors in the substantia nigra striatum DA system decreases with age³⁹, while PA is positively associated with dopamine receptor availability⁴⁰⁻⁴². This may explain the greater benefits of PA on cognitive function in the elderly with aging-related impaired DA systems. The results also indicate a gender differences in response to PA intensity. Correspondingly, a meta-analysis of RCTs suggests that the greater benefit of PA in enhancing cognitive function is observed in female, as evidenced by the higher cognitive performance benefit of PA in studies with a higher proportion of female⁸. For the overweight people, only moderate PA showed a positive association with cognitive performance. And in the stratified analysis of depressive status, no significant association between PA and cognitive performance was observed in individuals with depressive symptoms: the neuroplasticity damage caused by depression as well as neuronal atrophy and synaptic loss in the hippocampus leads to poor cognitive performance⁴³. In summary, results showed that maintaining a good physical and mental status is significant for the cognitive performance.

The strengths of this study include that we used repeated and well-validated measures of cognitive performance from a national longitudinal cohort. We applied the adjusted regression method and mixed model to analyze the association of PA intensity with cognitive performance at baseline and during follow up. In addition, we used the multinomial propensity score weighting procedure to account for a range of confounding factors.

We acknowledge several limitations in this study. First, this study is an observational study, and the causality or the intervention effect could not be referred, although we used a series of method to mitigate the confounding bias. Our findings need further validation in other population-based cohort or intervention research. Second, although the frequency and duration time of PA were measured using a standard questionnaire, the self-reported PA intensity was not an objective measure of activity, and we failed to calculate the individual-level metabolic equivalent value (MET). Further work using more objective PA measures like wearable monitoring devices would hopefully validate this relation. Third, the no-response rate during follow up is high, and only 2 319, 2 184, and 1 557 of 4 039 participants enrolled at baseline provided cognitive function data during follow up at visit 2, visit 3, and visit 4, although the mixed effect model offers a better way to deal with missing data, and subjects with more missing values have a weaker impact on parameter estimation process.

Conclusions

In brief, our findings indicate that mild and moderate PA are associated with better cognitive performance, rather than vigorous activity. The significant association is still observed during the long-term follow up of cognitive function. The targeted intensity of PA might be more effective to achieve the greatest cognition improvement in certain population.

Declarations

Ethical Approval and Consent to participate

Ethical approval for all the CHARLS waves was granted from the Institutional Review Board at Peking University. The IRB approval number for the main household survey , including anthropometrics, is IRB00001052-11015.

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available in China Health and Retirement Longitudinal Study (CHARLS), at <http://charls.pku.edu.cn/>.

Materials are available on request to the corresponding author.

Competing interests

The authors declare that they have no competing interests.

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Figures

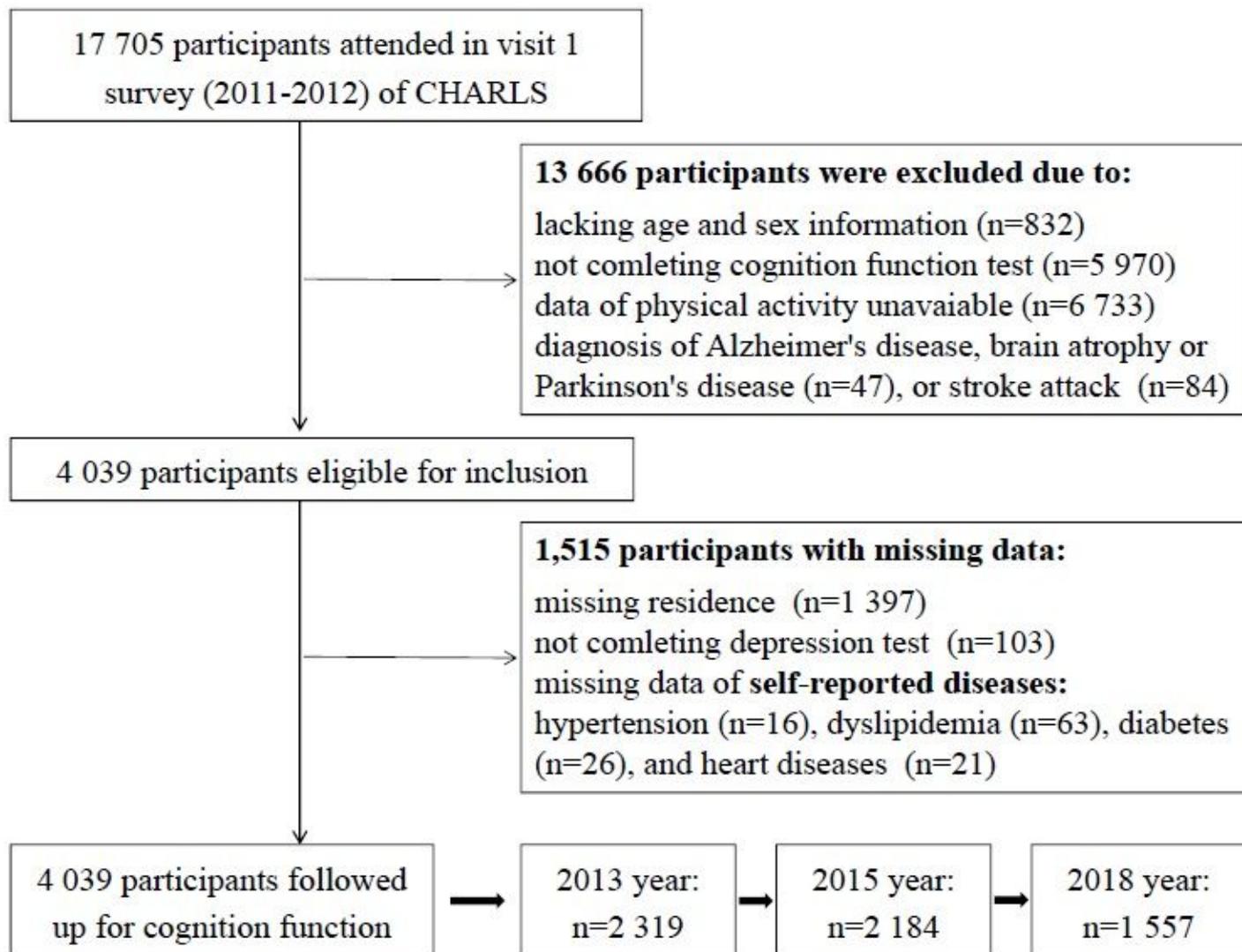


Figure 1

Flow chart of this current study.

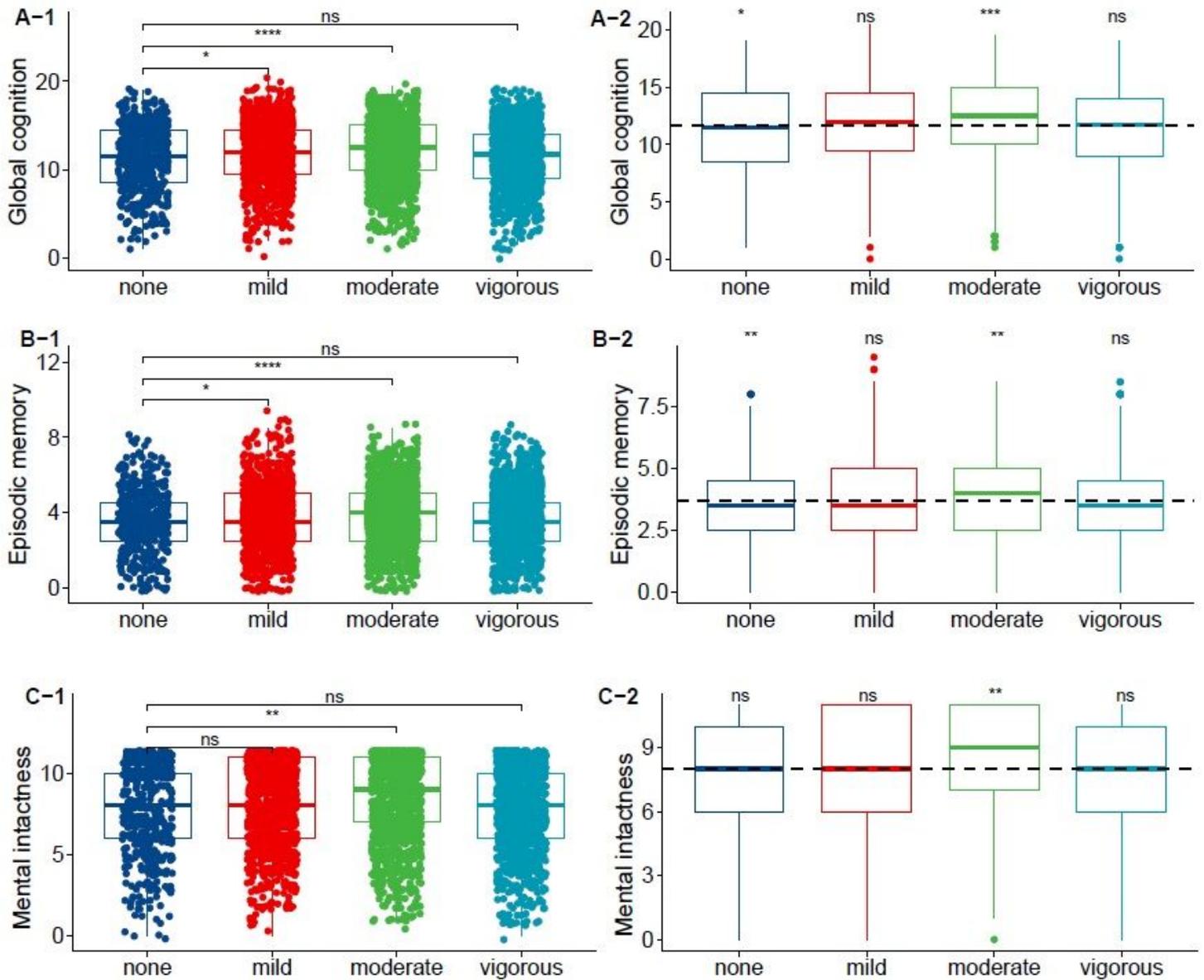


Figure 2

Distribution of global cognition score, episodic memory score and mental intactness score among groups of different physical activity intensity. The distributions were compared with the group without physical activity as reference (A-1, B-1, C-1); with the whole population as reference (A-2, B-2, C-2).

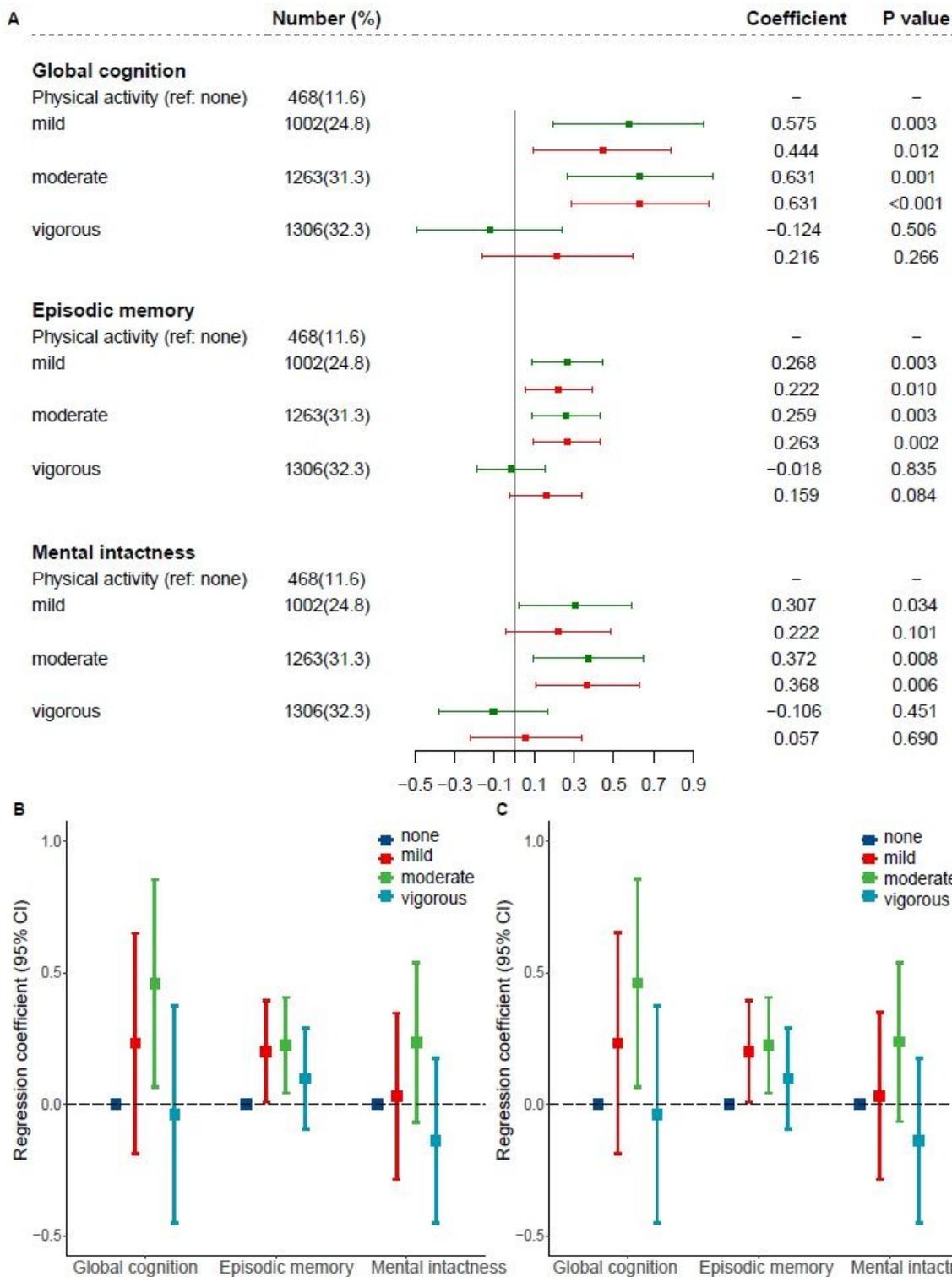


Figure 3

Results of sensitivity analyses. A: the pooled association of physical activity intensity with cognitive performance after data imputation. the green line refers to the fitted results adjusting for age; the red line refers to the results adjusting for age, sex, BMI, education level, marital status, residence location, health conditions, smoking, current drinking and CES-D score; B: the association between physical activity intensity and cognitive performance after the multinomial propensity score weighting procedure using the

'es.mean' as the stopping rule parameters; C: the association between physical activity intensity and cognitive performance after the multinomial propensity score weighting procedure using the 'ks.mean' as the stopping rule parameters; the variable set of age, sex, BMI, education, marital status, residence and CES-D score was adapted in the weighting procedure.

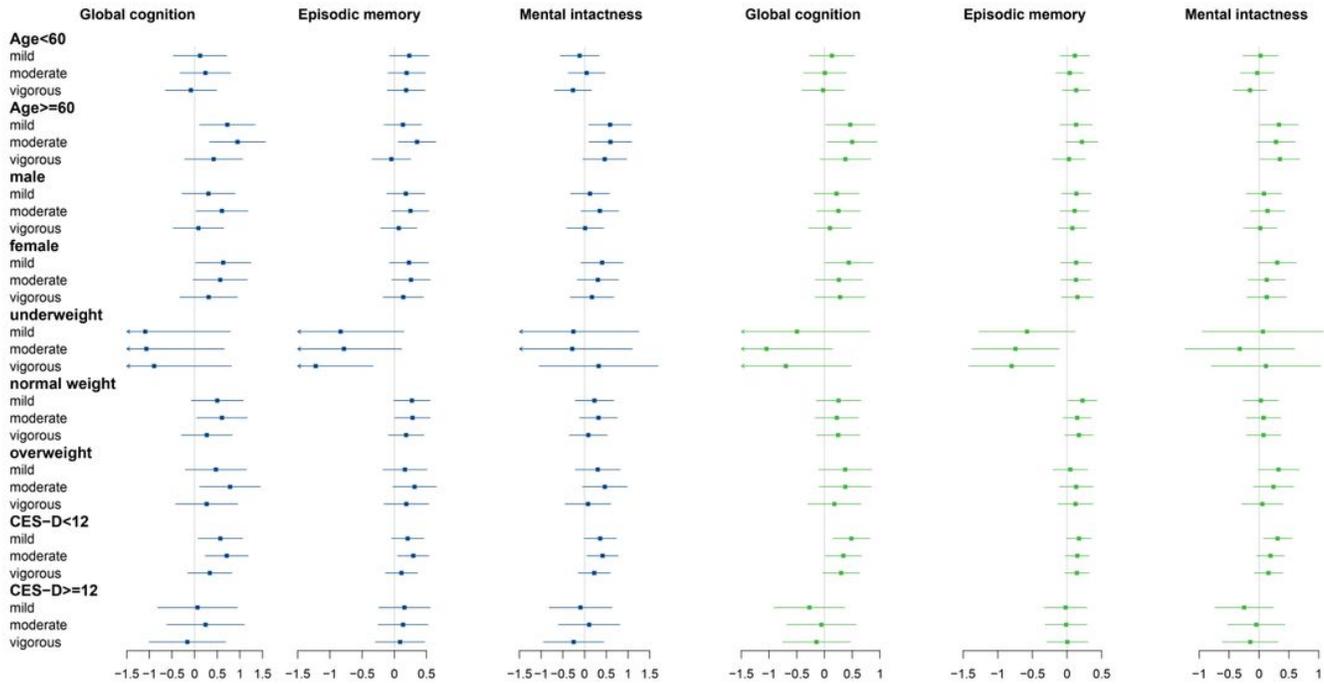


Figure 4

Stratified association of physical activity intensity with cognitive performance in subgroups at baseline (blue line) and during follow up (green line). adjusted for age, sex, BMI, education level, marital status, residence location, health conditions, smoking, current drinking and CES-D score.

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