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Association of Objectively Measured Physical Activity with Cognitive Function in Older Adults - The REGARDS Study

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ABSTRACT

Objectives: To examine the relationship between objectively measured physical activity (PA) and cognitive function in white and black older adults.

Design: Cross-sectional.

Setting: REasons for Geographic and Racial Differences in Stroke (REGARDS) study

Participants: Older adults who provided valid data from accelerometer and cognitive function tests (N=7,098).

Measurements: Actical™ accelerometers provided estimates of PA variables for 4-7 consecutive days. PA count cut-points of 50 counts per minute (cpm) and 1065 cpm were applied to differentiate between being sedentary and light PA, and light and moderate-to-vigorous PA, respectively. Prevalence of cognitive impairment was defined by the Six-Item Screener (scored <4 out of 6). Letter fluency, animal fluency, word list learning and Montreal Cognitive Assessment (orientation and recall), were conducted to assess memory and executive function.

Results: Of 7,098 participants (70.1 ± 8.5 yr, 54.2% women, 31.5% black), 359 (5.1%) exhibited impaired cognition within ±12 months of PA measurement. The average proportion of time spent in moderate-to-vigorous PA (MVPA%) was 1.4 ± 1.9%. Participants in the highest quartile of MVPA% (approximately 258.3 min/wk of MVPA) were less likely to be cognitively impaired than those in the lowest quartile (OR [95%C.I.] = 0.65 [0.43-0.97]). MVPA% was also significantly associated with z-scores of executive function and memory (P<0.001). Similar analyses of proportion of time spent in light PA (LPA%) and sedentary time (ST%) showed no significant associations with cognitive function.

Conclusion: Higher levels of objectively measured MVPA%, rather than LPA% or ST%, were associated with lower prevalence of cognitive impairment and better performance in memory and executive function in aging people. The amount of MVPA associated with lower prevalence of cognitive impairment is consistent with meeting PA guidelines.

Key Words: Aging; Physical Activity; Accelerometry; Cognitive Function

INTRODUCTION

A growing body of evidence indicates increasing prevalence and incidence of cognitive impairment among older adults in the United States (U.S.).[1] A national study reported an estimated 5.4 million people in the U.S. age >70 years had mild cognitive impairment (MCI).[2] Among those who completed follow-up assessments in the study, 11.7% with MCI progressed to dementia annually. A recent study showed the prevalence of dementia among older adults in the U.S. in 2010 was 14.7%.[3] The monetary cost of dementia in 2010 was $157-215 billion, with $11 billion associated with direct medical care. Cognitive impairment represents a substantial financial liability on society that is similar to heart disease and cancer. Effective prevention strategies will have significant public health implications by improving quality of life and reducing economic cost and social burden.

Regular physical activity (PA) provides benefits for cognitive health and helps to improve or maintain quality of life among older adults.[4] Research suggests more active individuals have reduced risk of cognitive impairment or dementia.[5,6] Cognitive impairment was more prevalent in those reporting no PA versus moderate and high PA levels in community-dwelling older adults.[7] Higher self-reported PA levels at early life were associated with reduced risk of MCI in later life.[8,9] However, methodological differences in PA assessment preclude comparisons among studies of the optimal pattern of PA to reduce the risk of cognitive decline. Most previous studies were based on self-reported PA

assessments,[7,10,11] which are subject to reporting and recall biases. Furthermore, important differences exist in PA across racial groups,[12-14] with blacks significantly understudied in terms of the association between PA and cognitive function.[15]

Thus, the purpose of this study was to investigate the association between objectively-measured PA and cognitive function among older adults, and to explore the associations by sex and race. We hypothesized that a significant positive dose-response association would exist between PA measured by accelerometers and cognitive function in a representative sample of white and black older adults in the U.S.

METHODS

Design and Procedures

Our study was ancillary to the REasons for Geographic and Racial Differences in Stroke (REGARDS) study, a national epidemiological study that enrolled and is following a cohort of 30,239 black and white adults to assess the prevalence and incidence of stroke and cognitive decline in the continental U.S. The cohort was recruited by a combination of mail and telephone contact from January 2003-October 2007. A telephone interview assessed risk factors, followed by an in-person physical assessment 3-4 weeks later. Participants were contacted by telephone every 6 months for incident stroke events, annually for cognitive screening status, and every 2 years for more detailed cognitive assessments. The detailed design and methods for REGARDS have been described previously.[16]

Our ancillary study was conducted May 2009-January 2013 during follow-up of the cohort. A question was added to the 6-month telephone follow-up asking participants if they were willing to wear an accelerometer and complete a daily activity log for one week. Upon acceptance, a package including an accelerometer and log sheet were mailed to participants with instructions, and then mailed back for processing. Detailed design and methods for the ancillary study have been described elsewhere.[17] The study was approved by the institutional review boards of Arizona State University, University of South Carolina, University of Georgia, and University of Alabama at Birmingham.

Baseline information obtained from the parent REGARDS dataset included age, sex, race, region of residence (living within or outside the stroke belt), education, body mass index (BMI), smoking status (self-reported current smoking or not), hypertension (Hypertensive if SBP $\geq$ 140 or DBP $\geq$ 90mmHg or self-reported current medication use to

control blood pressure) and diabetes (self-reported disease or current medication use) for purposes of describing the sample and controlling for possible confounders.

PA Measures

Actical™ PA monitors (Mini Mitter Respironics, Inc. Bend, OR) provided real-time estimates of the frequency, intensity, and duration of PA. Accelerometers were worn over the right hip while attached to a neoprene waistband. Participants were asked to put on the device after waking up each morning and take it off just prior to going to bed each evening. Participants were instructed to wear the device for 7 consecutive days and return the device immediately after. For all participants with valid data, time in sedentary behavior, light (LPA) and moderate to vigorous intensity PA (MVPA), and proportions of total wear time spent in sedentary behavior (ST%), light PA (LPA%), and MVPA (MVPA%) were determined. Activity count cut-points of 50 counts per minute (cpm) and 1065 cpm were applied to differentiate between being sedentary and light PA, and light PA and MVPA, respectively.[18] Details of the accelerometer data management and analysis have been published previously.[17,18]

Cognition Assessment

Cognitive function was assessed during telephone interviews using standardized scripts and scoring methods described previously.[19] Cognitive impairment was defined by each participant's score on the SIS, which is a test of global cognitive function with established reliability and validity in community samples and among black and white adults.[20] The SIS included 6 questions: "1. What year is this? 2. What month is this? 3. What is the day of the week? 4-6. What were the three objects I asked you to remember (Apple, Table and Penny)?" Scores on the SIS range from 0 to 6, with a score of 4 or fewer correct responses indicating cognitive impairment.[20] We conducted sensitivity analyses (data not shown) and decided to use cognitive assessments within a time range of ±12 months of wearing the accelerometer to obtain the largest sample size and shortest time intervals between PA measurements and cognitive tests.

We also utilized four expanded cognitive battery tests with demonstrated usefulness in early identification of Alzheimer's disease or dementia.[21] These tests were Word List Learning (WLL) and semantic fluency (animals fluency, AF) from the Consortium to Establish a Registry for Alzheimer's Disease battery,[21] and letter fluency (LF), recall and orientation items from the Montreal Cognitive Assessment (MoCA-recall and orientation).[22]

These tests assess domains of memory (WLL, MoCA-recall and orientation) and executive function (AF, LF). Acceptable reliability and validity of these cognitive battery tests have been previously reported.[21,23] For these measures, we also restricted analyses to the most recent results obtained within ±12 months of PA measurement. Composite measures of two cognitive domains (memory and executive function) were created by converting each battery test into a z-score based on the mean and standard deviation for that specific test's results among all participants. The mean of the z-scores of memory and executive function was calculated as an overall cognitive z-score presenting the average level of memory and executive domains. For participants missing one test score or z-score, the other available records were used to calculate domain and cognitive battery z-scores.

Participants

Among the cohort of the parent REGARDS study, 12,146 (60.5%) agreed to complete the accelerometer protocol, 7,312 (36.4%) declined, and 618 (3.1%) were deferred and did not have the opportunity to be asked again during the enrollment period. Of the devices that were mailed, 972 (8.0%) were lost/not returned, 1,187 (9.8%) were returned not worn, 14 (0.11%) were returned and found to be defective such that no data could be downloaded, and 9,973 (82.1%) were returned with data. Of the 9,973 participants who returned and wore the accelerometer, 8,096 (81.1%) provided usable data, after exclusions for device error, missing log sheet, and wear time < 4 days and/or <10 hr/day.[17]

We included 7,098 participants of the 8,096 participants in the present analyses. Participants were excluded if they: 1. had self-reported stroke at baseline (n=264); 2. were identified as cognitively impaired >12 months prior to PA assessment (n=383); 3. had an incident stroke prior to wearing the accelerometer (n=6); 4. had no record of valid PA measurement associated with SIS assessment within ±12 months of PA assessment (n=345).

Statistical Analysis

Continuous data expressed as MVPA (min/wk) and MVPA% was extremely skewed (e.g., 20% of the entire sample recorded <1 min/day of MVPA), thereby violating the assumptions of linear regression and not providing a true measure of associations with the dependent variables. Thus, the primary independent variable of MVPA% was divided into quartiles allowing for group comparisons and investigation of possible dose-response associations in the presence of skewness. Due to inherent variability in daily accelerometer wear time, MVPA% rather than the absolute time spent in MVPA was used as the standard for quartiles

to render results comparable among individuals. Dependent variables were cognitive status (impairment or not) measured by SIS, and z-scores generated from WLL, AF, LF and MoCA-recall and orientation. Differences in demographic variables across quartiles were tested by Analysis of Variance (continuous variables) or Chi-square tests (categorical variables). Because the SIS was validated using dichotomous outcomes rather than continuous scores,[20] associations between MVPA% and cognitive impairment were examined using multivariable logistic regression models. In the logistic models, Model 1 was unadjusted. Model 2 adjusted for age, sex, race, region of residence, and education. Model 3 adjusted for age, sex, race, region of residence, education, ST%, BMI, hypertension, smoking, and diabetes. Odds ratios (ORs) and 95% confidence intervals (CIs) were generated. Linear regression models with similar adjustments for potential confounders mentioned above were used to assess the association between MVPA% and z-scores generated from WLL, AF, LF and MoCA-recall and orientation. Differences in z-scores of memory and executive function across quartiles and race/sex subgroups were examined after full adjustment of confounders. Analyses were conducted using SAS version 9.3 (SAS Institute, Cary, NC).

RESULTS

Demographics, PA and cognitive function status are shown in Tables 1 and 2 according to quartiles of MVPA%. Among the 7,098 participants, 54.2% were women, 31.5% were black, 54.9% were living in the Stroke Belt, and 5.1% exhibited impaired cognitive status at the assessment within ± 12 months of the PA measurement. The mean (±SD) time between PA assessment and each cognitive assessment was 5.4 ± 3.8 months. The mean (±SD) age of all participants was 70.1 ± 8.5 years, and they wore the accelerometer for 6.6 ± 0.8 days. Participants spent most of their wear time in sedentary behavior (69.9% ± 8.1%) and LPA (26.6% ± 7.7%). MVPA% was extremely limited (1.5% ± 1.9%). There were significant differences across quartiles of MVPA% in all variables listed in Table 2 ($P<0.001$). Participants with higher MVPA% were more likely to be men, white, younger, well-educated, non-smoker, without diabetes and hypertension, and cognitive impairment, and lower in BMI and systolic and diastolic blood pressure. Participants in the higher MVPA% quartiles also spent more time in LPA, and had higher raw scores in WLL, AF, LF, and MoCA-recall and orientation. A higher level of MVPA% was associated with lower prevalence of cognitive impairment as measured by SIS. There were fewer individuals with

cognitive impairment in the highest MVPA% quartile (2.9%) than in the lowest MVPA% quartile (15.0%).

Results of logistic regression analyses are displayed in Table 3. In the unadjusted model (Model 1), those participants in the highest MVPA% quartile were 63% less likely to have cognitive impairment compared with those in the lowest quartile. After adjustment for age, sex, race, region of residence, and education (Model 2), significance remained. Participants in the highest quartile were 36% less likely to have cognitive impairment (OR [95% CI] =0.64 [0.44-0.93]). There were no significant interactions (age*MVPA%, sex*MVPA%, race*MVPA%, education *MVPA%, region*MVPA%); thus, these were not included in the analytic models. In the fully adjusted model (Model 3), results were consistent with Model 2, with participants in the highest MVPA% quartile 37% less likely to have cognitive impairment (OR [95% CI] =0.63 [0.43-0.93]). Similar analyses with LPA% and ST% did not reveal any significant associations (P>0.05) with the odds of cognitive impairment. Additionally, logistic regression analysis categorizing participants as accumulating more or less than 150 min/wk of MVPA indicated older adults were 36% less likely to have cognitive impairment if they accumulated ≥150 min/wk of MVPA (OR [95% CI] =0.64 [0.44-0.91]) after full adjustment. Subgroup logistic analyses were conducted for each race/sex group, but significance was not maintained. When using MVPA% as a continuous variable, there was no significant association between MVPA% and the prevalence of cognitive impairment when adjusted for confounders in Models 2 and 3 (P>0.05).

There were 4,441 participants with at least one test of AF or LF in the domain of executive function (with 3,412 or 77% of those having both tests), 5178 participants having at least one test of WLL or MoCA items in the domain of memory (with 3,977 or 77% of those having both tests). Additionally, 5,188 participants had at least one z-score of memory or executive function (with 4,431 or 85% of those having both tests). Linear regression models (Table 4) revealed a significant association (P<0.001) between MVPA% and both cognitive function domains in the unadjusted model. These relationships remained significant when controlling for age, sex, race, region of residence, and education, and there were no significant interactions between MVPA% and these confounders, respectively (P>0.05). When analyses were further adjusted for BMI, hypertension, smoking and diabetes, MVPA% remained significantly associated with z-scores of executive function, memory, and their average combined score for overall cognitive function. Linear regression models using MVPA% as a continuous variable were also conducted. Significances were maintained for

the association between MVPA% and z-scores of executive function, memory, and overall cognitive function in all models (P<0.05).

The association between MVPA% and memory and executive function varied across different race/sex subgroups (Table 5). For white men, both memory and executive function z-scores were significantly positively associated with MVPA% (P<0.001). For white women, significant differences existed between Quartile 1 and 3 and Quartile 1 and 4 for executive function (P<0.001). For black men, significant differences existed between Quartile 1 and 3 and Quartile 1 and 4 for memory (P<0.001). No significance was observed for any domains among black women (P>0.05).

DISCUSSION

To our knowledge, this is one of the first studies to examine the dose-response association between objectively measured PA and cognitive function in a large and diverse older population. Objectively measured MVPA (both absolute min/wk and MVPA%) was independently associated with cognitive impairment and continuous measures of cognitive function among a population of 7,098 older white and black adults. The odds of cognitive impairment was significantly lower in those in the highest quartile which was associated with 36.9 min/day (258.3 min/wk) of MVPA, which is above that recommended in U.S. national guidelines (accumulating >150 min/wk).[24] Older adults with a greater proportion of accelerometer wear time spent in MVPA also had higher levels of memory and executive function than their less active peers.

Both cross-sectional and prospective studies[5,6] using self-reported PA measurements suggest more active individuals may be less likely to develop cognitive impairment and dementia. A meta-analysis of 16 prospective studies using self-reported PA indicated the relative risks of incident dementia and Alzheimer's disease in the highest PA category compared with the lowest were reduced by 28% and 45%, respectively.[25] However, most previous studies on the relationship between PA and cognitive function have been limited by the bias of self-report measures of PA, and also have difficulties identifying effects of LPA and sedentary time on cognitive function.

A few studies with objectively measured data have also reported that active older adults may have lower prevalence of cognitive impairment or dementia.[26-29] One cross-sectional study of 2,735 old women showed daytime PA measured by accelerometers was associated with lower odds of cognitive impairment in women.[26] Another cross-sectional study with 217

older adults indicated a dose response relationship between objectively measured PA intensity and cognitive function, with a stronger association between MVPA and cognitive function.[27] Buchman et al.[5] reported a higher level of total daily PA, measured by accelerometers, was significantly associated with a reduced risk of Alzheimer disease among 716 white older adults aged 55 and older during 4 years of follow up. Barnes et al.[28] also demonstrated higher levels of aerobic fitness at baseline predicted better performance on measures of attention and executive function 6 years later with 349 adults aged >55 years. However, the sample sizes of studies with objective PA assessment were relatively small and included fewer non-white participants.

To our knowledge, the association between PA and cognitive function remains robust in older adults when adjusted for race, sex, education, and age,[30-32] but few investigations have investigated the relationship between PA and cognitive function within specific race/sex subgroups. Although interaction terms were non-significant, our exploratory analyses (Table 5) indicated the association between MVPA% and memory and executive function may vary by race/sex subgroups. Additional prospective and intervention studies are needed to investigate the contributions of race and sex to the association between PA and cognitive function in diverse older adults.

Our findings regarding LPA% and ST% revealed no relationships to cognitive function. MVPA% was the only PA element displaying a significant dose-response relationship with cognitive function in this population, suggesting intensity may be an important factor influencing the relationship between PA and cognitive function in older adults. This finding was consistent with previous studies using self-reported PA.[33,34] There has been only one study using accelerometers reporting intensity of PA as important in the association between PA and cognitive function in older adults, with participants in the highest tertile of PA intensity performing better than those in the lowest tertile in cognitive tasks related to memory and executive function.[35]

The influence of LPA and sedentary behavior on cognitive function is not fully known. One cross-sectional study documented LPA was not significantly associated with memory and executive function after adjustments for confounders in older adults.[27] Another longitudinal study in Japan determined self-reported LPA and sedentary time were associated with cognitive impairment after 8 years of follow-up.[36] Previous research also indicated diverse types of sedentary behaviors might be differently associated with cognitive function.[37] Computer using time was positively associated with memory and executive function, while television viewing time was negatively associated with cognitive function in

older adults.[38,39] Unfortunately, we were not able to record the type of sedentary behavior in our study. Additional investigations are necessary to more fully explore the impact of sedentary behavior and LPA on cognitive function in older adults as this is how they spend the vast majority of their time.

PA may be related to cognitive function through different mechanisms. Research suggests PA is associated with greater brain volume in specific areas related to executive function and memory (e.g., hippocampus volume),[40,41] increased levels of brain-derived neurotrophic factor,[42,43] improved cerebrovascular function, and reduced vascular risk associated with hypertension, type 2 diabetes and obesity.[44] Moreover, studies suggest improved cognitive function and reduced risk of dementia may be mediated by significant changes in cardiorespiratory fitness.[45]

Our study has several strengths. First and most important, we used an objective measure of PA to examine the association of PA with cognitive function in a large population of older adults. This allowed for analyses with both absolute amount and proportion of time spent in PA of varying intensity. Secondly, this is one of the first studies to examine the association between objectively measured PA and cognitive function in a diverse population, providing more detailed analysis for older white and black women and men. Finally, we were able to explore the relationship of accelerometer-derived PA and sedentary behavior within specific domains of memory and executive function in addition to odds of impairment in global cognitive status.

The findings of this study were also subject to limitations. First, our study was an attempt to characterize the participant's habitual PA by accelerometers. A limitation to using accelerometers is the type of PA activity and upper body movements are not captured. Second, as a cross-sectional analysis, causality cannot be inferred. Third, because of the potential for unaccounted confounding factors and random errors or noise in the dataset, our results should be interpreted with caution. Lastly, due to the excessive skewness of MVPA (min/wk) and MVPA% as continuous variables, we were unable to identify a precise threshold for reducing the risk of cognitive impairment or the degree of risk reduction associated with a relatively minor increase in daily or weekly MVPA. It is possible a MVPA level higher than that exhibited by those in quartile 3 (11.1 min/day) and less than that observed for quartile 4 (36.9 min/day) is adequate to reduce the risk of cognitive decline in older adults. Further studies are well warranted in this arena to help refine PA guidelines.

In summary, higher levels of objectively measured MVPA% were independently associated with lower prevalence of cognitive impairment and better performance in memory

and executive function for both white and black older adults. In addition, there was a dose-response relationship between MVPA% and cognitive function in older adults, with the highest level of MVPA% associated with higher cognitive function. The amount of MVPA associated with lower prevalence of cognitive impairment is consistent with meeting U.S. PA guidelines. Neither LPA% nor ST% was associated with any measures of cognitive function in this cohort warranting further investigation.

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Author Contributions:

Zhu W., Hooker S.P.: design of the study, analysis of data, drafting and revising the manuscript; Howard V.J., Wadley V.G., Hutto B.: conception and design of the study, interpretation of data, revising the manuscript; Blair, S.N., Vena, J.E., Colabianchi, N., Rhodes, D.: conception and design of the study, revising the manuscript.

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Table 1. Characteristics of Participants by Level of Moderate to Vigorous Physical Activity (% or mean ± SD , N = 7,098)

Variable	Quartile[a] 1	Quartile 2	Quartile 3	Quartile 4	Total
Women, n (%)	1164 (65.7)	1026 (57.8)	904 (51.0)	750 (42.1)[b]	3844 (54.2)
African American, n (%)	749 (42.3)	611 (34.4)	495 (28.0)	379 (21.3)[b]	2234 (31.5)
Stroke-belt, n (%)	991 (56.0)	1001 (56.4)	989 (55.8)	913 (51.3)[b]	3894 (54.9)
Education, n (%)					
Less than high school	203 (11.5)	111 (6.3)	85 (4.8)	48 (2.7)	447 (6.3)
High school graduate	544 (30.7)	445 (25.1)	366 (20.7)	263 (14.8)	1618 (22.8)
Some college	486 (27.4)	561 (31.6)	469 (26.5)	385 (21.6)	1901 (26.8)
College graduate and above	538 (30.4)	659 (37.1)	851 (48.1)	1084 (60.9)[b]	3132 (44.1)
Smoking, n (%)	255	219	165	112	751

	(14.4)	(12.3)	(9.3)	(6.3)[b]	(10.6)
Hypertension, n (%)	1224 (69.1)	987 (55.6)	831 (46.9)	657 (36.9)[b]	3699 (52.1)
Diabetes, n (%)	454 (25.6)	308 (17.3)	215 (12.1)	162 (9.1)[b]	1139 (16.1)
Age (yr)	75.2±8.1	70.9±7.7	68.1±7.8	66.3±7.7[b]	70.1±8.5
Body Mass Index (kg*m^{-2})	30.1±6.4	29.3±5.8	28.3±5.3	26.9±4.6[b]	28.6±5.7
Systolic blood pressure (mmHg)	130.1±16.3	126.4±15.5	124.4±14.7	121.5±14.3[b]	125.6±15.6
Diastolic blood pressure (mmHg)	76.4±9.6	76.3±9.5	76.3±9.0	75.8±8.8[b]	76.2±9.2

[a] Denotes the quartiles of the proportion of total time spent in moderate to vigorous physical activity.

[b] Denotes significant difference among quartiles (P<0.001), tested by Analysis of Variance (continuous variables) or Chi-square tests (categorical variables)

Table 2. Physical Activity and Cognitive Function by Level of Moderate to Vigorous Physical Activity (% or mean ± SD， N = 7,098 unless otherwise noted)

Variable	**Quartile[a] 1**	**Quartile 2**	**Quartile 3**	**Quartile 4**	**Total**
Compliance (days with valid wear)	6.4±0.9	6.6±0.8	6.6±0.7	6.7±0.7[i]	6.6±0.8
Total wearing time (min/day)	868.3±117.0	885.4±104.1	897.8±99.7	910.1±92.9[i]	890.4±104.9
MVPA[b] (min/day)	0.4±0.4	3.3±1.5	11.1±3.8	36.9±19.5[i]	12.9±17.5
Light PA (min/day)	117.0±58.	181.9±60.	213.8±68.	235.0±69.	186.9±78.

	3	7	3	7[i]	4
Sedentary time (min/day)	750.9±119.5	700.2±108.5	672.9±105.9	638.3±107.1[i]	690.5±117.8
MVPA%[b,c]	0.05±0.05	0.37±0.15	1.23±0.39	4.05±2.10[i]	1.42±1.91
LPA%[d]	13.6±6.6	20.7±6.9	24.0±7.5	26.0±7.7[i]	21.1±8.6
ST%[e]	86.4±6.6	78.9±6.9	74.8±7.5	69.9±8.1[i]	77.5±9.5
Cognitive impairment[f] , n **(%)**	134 (7.6)	103 (5.8)	70 (4.0)	52 (2.9)[i]	359 (5.1)
Letter fluency score (n=3,405)	10.3±4.3	11.2±4.5	11.4±4.5	12.3±4.8[i]	11.3±4.6
Animal fluency score (n=4,353)	14.9±5.1	16.7±5.0	17.6±5.6	19.4±5.7[i]	17.1±5.6
Word list learning sum score[g] (n=3,847)	16.4±5.1	17.7±5.1	18.9±4.8	19.5±4.5[i]	18.1±5.0
MoCA[h] recall and orientation (n=5,160)	9.6±1.6	10.0±1.3	10.1±1.2	10.2±1.2[i]	10.0±1.4

[a] Denotes the quartiles of the proportion of total time spent in moderate to vigorous physical activity.

[b] MVPA refers to moderate to vigorous physical activity.

[c] Denotes the proportion of total wear time spent in moderate to vigorous physical activity.

[d] Denotes the proportion of total wear time spent in light physical activity.

[e] Denotes the proportion of total wear time spent in sedentary behavior.

[f] Cognitive impairment is defined as a score of 4 or fewer correct responses in six-item screener. The score ranges from 1 to 6, consisting of a 3-item recall and 3-item temporal orientation.

[g] WLL is from the Consortium to Establish a Registry for Alzheimer's Disease battery (0-30).

[h] MoCA refers to Montreal Cognitive Assessment, including a 5-word delayed memory recall test (0-5), and
6-item orientation test (0-6).

[i] Denotes significant difference among quartiles (P<0.001), tested by Analysis of Variance (continuous variables) or Chi-square tests (categorical variables)

Table 3. Multivariable Odds Ratios for Prevalence of Cognitive Impairment by Level of **Moderate to Vigorous Physical Activity (MVPA)**

		Model 1[a]		Model 2[b]		Model 3[c]	
		O.R.	95.0% C.I.	O.R.	95.0% C.I.	O.R.	95.0% C.I.
MVPA%[d]	Q1(low)[e]	Ref.		Ref.		Ref.	
	Q2	0.76	0.58-0.99	0.99	0.75-1.31	0.97	0.71-1.31
	Q3	0.52	0.39-0.70	0.78	0.56-1.07	0.74	0.51-1.07
	Q4(high)	0.37	0.27-0.51	0.64	0.44-0.93	0.63	0.43-0.93
Weekly MVPA[f] (min)	<150min	Ref.		Ref.		Ref.	
	≥150min	0.43	0.31-0.61	0.63	0.44-0.89	0.64	0.44-0.91

[a] Unadjusted regression model.

[b] Adjusted by age, sex, race, region of residence, and education.

[c] Adjusted by age, sex, race, region of residence, education, proportion of time spent in sedentary behavior, body mass index, hypertension, smoking and diabetes.

[d] Denotes the proportion of total time spent in moderate to vigorous physical activity.

[e] Denotes the quartiles of the proportions of total time spent in moderate to vigorous physical activity. Q1 refers the lowest quartile, and Q4 refers the highest quartile.

[f] The U.S. Physical Activity Guidelines recommended older adults perform ≥150 minutes of moderate to vigorous physical activity per week.[24]

Table 4. Linear Regression Model Indicating the Association of Moderate to Vigorous Physical Activity with Z-scores of Expanded Cognitive Battery Tests

	Model 1[a]			Model 2[b]			Model 3[c]		
	Beta	SE	P	Beta	SE	P	Beta	SE	P

Average overall cognitive z-score[e] (N=5188)	Q1(low)[d]									
	Q2	0.32	0.03	<0.001	0.13	0.03	<0.001	0.15	0.03	<0.001
	Q3	0.46	0.03	<0.001	0.19	0.03	<0.001	0.16	0.03	<0.001
	Q4(high)	0.63	0.03	<0.001	0.27	0.03	<0.001	0.23	0.03	<0.001
Executive function z-score[f] (N=4441)	Q1(low)[d]									
	Q2	0.30	0.04	<0.001	0.13	0.03	<0.001	0.11	0.03	0.003
	Q3	0.46	0.04	<0.001	0.17	0.03	<0.001	0.13	0.04	0.001
	Q4(high)	0.71	0.04	<0.001	0.29	0.04	<0.001	0.25	0.04	<0.001
Memory z-score[g] (N=5178)	Q1(low)[d]									
	Q2	0.32	0.03	<0.001	0.20	0.03	<0.001	0.19	0.03	<0.001
	Q3	0.46	0.03	<0.001	0.21	0.03	<0.001	0.19	0.04	<0.001
	Q4(high)	0.63	0.03	<0.001	0.26	0.04	<0.001	0.24	0.04	<0.001

[a] Unadjusted regression model.

[b] Adjusted by age, sex, race, region of residence and education.

[c] Adjusted by age, sex, race, region of residence, education, proportion of time spent in sedentary behavior, body mass index, hypertension, smoking and diabetes.

[d] Denotes the quartiles of the proportion of total time spent in moderate to vigorous physical activity. Q1 refers the lowest quartile, and Q4 refers the highest quartile.

[e] Average cognitive z-score refers to the average of mean executive score and mean memory score.

[f] Executive z-score refers to the average of standardized scores of letter fluency and animal fluency tests. For participants with only one executive test, the mean score would be the result of that test.

[g] Memory z-score refers to the average of standardized scores of word list learning and MoCA recall and orientation tests. For participants with only one executive test, the mean score would be the result of that test. MoCA refers to Montreal Cognitive Assessment, including a 5-word delayed memory recall test, and a 6-item orientation test.Table 5. Adjusted[a] Z-scores (Mean ± SE) of Cognitive Battery Tests and Prevalence of Cognitive Impairment by Levels of Moderate to Vigorous Physical Activity and Race/Sex.

Variable	Race/Sex	Quartile[f] 1	Quartile 2	Quartile 3	Quartile 4	P-value
Average overall cognitive z-score[b] (N=5,188)	Black Male	-0.70±0.05	-0.49±0.05	-0.35±0.05	-0.40±0.06	<0.001[g]
	Black Female	-0.35±0.04	-0.21±0.04	-0.27±0.05	-0.15±0.06	0.30
	White Male	-0.44±0.04	-0.28±0.04	-0.22±0.03	-0.14±0.03	<0.001[g]
	White Female	-0.08±0.03	0.06±0.03	0.01±0.04	0.08±0.04	0.06
Executive function z-score[c] (N=4,441)	Black Male	-0.56±0.07	-0.38±0.07	-0.35±0.07	-0.32±0.08	0.50
	Black Female	-0.48±0.05	-0.42±0.05	-0.49±0.06	-0.39±0.08	0.99
	White Male	-0.32±0.05	-0.18±0.0	-0.08±0.0	0.01±0.04	<0.001[h]

			5	4		
	White Female	-0.13±0.04	-0.03±0.04	-0.02±0.05	0.14±0.05	<0.001[g]
Memory z-score[d] (N=5,178)	Black Male	-0.74±0.07	-0.48±0.06	-0.32±0.07	-0.38±0.07	<0.001[g]
	Black Female	-0.23±0.04	-0.03±0.05	-0.10±0.06	0.01±0.08	0.27
	White Male	-0.52±0.05	-0.32±0.04	-0.26±0.04	-0.20±0.04	<0.001[g]
	White Female	-0.02±0.04	0.14±0.04	0.05±0.04	0.08±0.05	0.14

[a] Adjusted by age, region, education, proportion of time spent in sedentary behavior, body mass index, hypertension, smoking and diabetes.

[b] Average cognitive z-score refers to the average of mean executive score or/and mean memory score. The reference of the z-score is the mean and standard deviation of the total sample.

[c] Executive z-score refers to the average of standardized scores of letter fluency and animal fluency tests. For participants with only one executive test, the mean score would be the result of that test. The reference of the z-score is the mean and standard deviation of the total sample.

[d] Memory z-score refers to the average of standardized scores of word list learning and MoCA recall and orientation tests. For participants with only one executive test, the mean score would be the result of that test. The reference of the z-score is the mean and standard deviation of the total sample. MoCA refers to Montreal Cognitive Assessment, including a 5-word delayed memory recall test, and a 6-item orientation test.

[e] Cognitive impairment is defined as a score of 4 or fewer correct responses in six-item screener. The score ranges from 1 to 6, consisting of a 3-item recall and 3-item temporal orientation.

[f] Denotes the quartiles of the proportion of total time spent in moderate to vigorous physical activity.

[g] Denotes significant difference (P<0.05) between Quartile 1 and 3, and Quartile 1 and 4.

[h] Denotes significant difference (P<0.05) between Quartile 1 and 3.