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Mid-life physical activity preserves lower extremity function in older adults: Age Gene/Environment Susceptibility (AGES) - Reykjavik Study

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Abstract

OBJECTIVES—To examine the long-term association between mid-life physical activity (PA) and lower extremity function (LEF) in late-life.

DESIGN—A longitudinal study with an average of 25 years of follow up.

PARTICIPANTS—A large community-based population of 4753 men and women (mean age 76±6 yrs) residing in Reykjavik, Iceland.

MEASUREMENTS—On the basis of weekly hours of regular PA reported at the mid-life examination, participants were classified as “Active” and “Inactive”. Measures of LEF in late-life included gait speed from 6m walk (meter per second, m/s), Timed Up and Go (TUG, second), and Knee Extension (KE) strength (kg) tests. Linear regression analysis was used to examine the association.

RESULTS—Participants who were active in mid-life had significantly better LEF (faster gait speed,, $\beta = 0.05$, $p \leq 0.001$; faster TUG time, $\beta = -0.53$, $p \leq 0.001$; stronger KE strength, $\beta = 1.3$, $p \leq 0.001$) in late-life compared with those who were not active in mid-life, after adjusting for socio-demographic and cardiovascular risk factors. After adjustment for cognitive function in late life (speed of processing, memory, and executive function), participants who were active in mid-life still had significantly faster gait speed ($\beta = 0.04$, $p \leq 0.001$), faster TUG time ($\beta = -0.34$, $p \leq 0.001$), and greater KE strength ($\beta = 0.87$, $p \leq 0.001$) in old age compared with those who were not active in mid-life.

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CONCLUSION—Regular PA reported in mid-life is associated with better performance of LEF in later life, even after controlling for late life cognitive function.

Keywords

mid-life physical activity; mobility; aging; cognitive function; lower extremity function

INTRODUCTION

Mobility is critical for maintaining physical independence of older people, and regular PA participation in early life is associated with mobility in old age [1, 2]. Lower extremity function (LEF) is the main indicator of mobility which is often used as a clinical screening tool [3, 4]. LEF is generally assessed by measuring walking capacity [5] and leg strength [6, 7]. Mobility is also strongly related to cognitive ability [8] which is associated with both LEF [8-10] and PA participation in older population [11]. Having both low levels of PA and cognitive function are associated with reduced mobility in old age [12]. However, it is unclear whether the effects of midlife PA on LEF are independent of the effects on cognition. The long-term association between mid-life PA and late-life LEF with adequate control for more details of cognitive performance would extend the current knowledge of the association.

The aim of the current study was to examine the long-term association between mid-life PA and LEF in late-life among older people adjusting for confounders from mid-life and late-life. The AGES-Reykjavik Study assessed various specific domains of cognitive function at the late-life examination on average 25 years later, which allows us to evaluate if this relationship is independent of cognitive function with full adjustment for multiple mid-life and late-life confounders. In a secondary analysis, we further investigate the association in a population free of dementia adjusting for confounders from mid-life and late-life, as well as measures of various domains of cognitive function.

METHODS

Study Population

Age Gene/Environment Susceptibility (AGES) - Reykjavik Study—The Reykjavik Study (RS) was initiated in 1967 by the Icelandic Heart Association to study cardiovascular disease and associated risk factors. The cohort included men and women born in 1907–1935, living in Reykjavik. The details of RS have been published previously [13]. Surviving members of the RS cohort were re-invited in 2002 to participate in the AGES-Reykjavik Study. Re-examination included a structured survey instrument, cognitive testing, brain MRI, and physical performance tests. All participants signed an informed consent. Details on the AGES-Reykjavik Study have been described elsewhere [14].

Mid-life Leisure Time Physical Activity

At the mid-life RS examination, interviewers asked participants two questions about leisure time PA, 1) if they regularly participated in sports or exercise and 2), how many hours per week they participated in sports or exercise separately in the winter and summer (1=none, 2=5 hours or less, and 3=more than 5 hours). Two categories of mid-life PA were defined:

1) Active = reported any PA hours during summer or winter, and 2) Inactive = reported no PA hours in both winter and summer.

LEF performance test

LEF was assessed in late-life as part of the AGES-Reykjavik Study using the 6 meter walk test [15], the timed up and go test [16], and knee extension strength [3, 17], similar to the assessments of LEF that have been used in other epidemiological and clinical studies [5]. Each test is described below.

Gait speed (6 meter walk)—Gait speed was assessed in meters in second from a 6 meter walking test at usual speed [6]. This test is reliable when performed in a standardized fashion, and well tolerated by older people [15]. The average time of two trials was used in the analysis.

Timed Up and Go (TUG)—The Timed Up and Go [16] measures the time taken to stand up from a sitting position, walk 3 meters, turn around, walk back to the chair, and sit down. It is a useful screening test for balance problems among older people [18] and is used as a predictor of decline in activities of daily living (ADL) [16]. When taking the test, participants had their own footwear on and a cane or walker was allowed if necessary. Those who could not rise from the chair (height = 45.5 cm) by themselves or walk were excluded from the test. The time of the first complete trial was used in the analysis.

Knee Extension Strength (KES)—Lower extremity strength was measured as maximum isometric strength of knee extension using an adjustable and computerized dynamometer on a fixed chair (Good Strength, Metitur, Palokka. Finland) [19]. KES was measured at a fixed knee angle of 60 degrees from full extension toward flexion during which the ankle was fastened to a strain-gauge transducer by a belt. The right leg was measured in two trials of knee extensions, each lasting 4 seconds, with a 30 second rest in between. Participants who had surgery on their leg or hand, or had any ischemic heart conditions in the past 2 months were excluded from the tests. Highest maximum force was used in the analysis.

Cognitive Function and Dementia

All participants were administered a battery of cognitive tests [20] once at the baseline visit. Composite scores were constructed for speed of processing (SP), memory (MEM), and executive function (EF) based on a theoretical grouping of tests, similar to other population-based studies [20]. Details have been described in a previous study [21]. A consensus diagnosis of dementia was made according to international guidelines, Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition (DSM-IV) [22], by a geriatrician, neurologist, neuropsychologist and a neuroradiologist.

Covariates

Several demographic and health factors were controlled for in subsequent analyses. Measures obtained from the mid-life RS examination included education, blood pressure (BP, mmHG), height (cm), weight (kg), serum cholesterol (mmol/L), and smoking status (never/previous/current). Education was categorized into 4 levels (elementary school, high school, undergraduate, more than undergraduate education). BP was measured in a semi-recumbent position using mercury sphygmomanometer and a cuff of appropriate size on the right arm after subjects had rested for several minutes. Body mass index (BMI) was calculated with weight in kilogram divided by height in squared meters. Serum cholesterol level was measured from a blood sample drawn at the in-person examination in a fasting/ thirsting state.

Variables collected at the late-life AGES-Reykjavik Study were also included in the analysis as covariates. Diabetes was defined as self-reported doctor's diagnosis, late-life medication use, or fasting glucose level ≥7.0 mmol/L. Coronary events included both those identified in an on-going surveillance system or self-reported history of myocardial infarction, coronary bypass surgery, heart bypass surgery, angioplasty or other coronary artery diseases. Self-reported doctor's diagnosis of stroke was assessed via questionnaire. Global cognitive function was examined using Mini-Mental State Examination (MMSE). High levels of depressive symptoms was classified as a score of ≥ 6 on the 15-item Geriatric Depression Scale (GDS) [23].

Analytical Sample

Of the total study cohort (n=5764), 797 subjects (317 men and 480 women) were excluded because of missing data on the LEF tests, and 214 (110 men and 104 women) subjects with diagnosed dementia were excluded because dementia is significantly associated with low LEF [9, 24]. The final study population was 4753 participants (2011 men and 2742 women). Participants included in the analysis were significantly younger (mean late-life age 76.5 ± 5.5 years), and generally healthier (data not shown) compared with excluded population (n = 1011, mean age 80.5 ± 6.4 years). From the final study cohort, 4359 subjects with complete cognitive data were selected for the secondary analysis to examine the association adjusting for various aspects of cognitive function.

Statistical Analysis

We used descriptive statistics to examine sociodemographic and health characteristics according to the mid-life PA category. General linear regression models were used for continuous variables, and chi-square (χ^2) tests were used for categorical variables to compare subject characteristics. The difference in performance of gait speed, TUG, and KE strength tests of LEF by the mid-life PA level was examined by linear regression analysis, adjusting for confounders. The first model was adjusted for age, sex, and education. A second model was further adjusted for mid-life covariates (cholesterol level, systolic BP, smoking, and BMI), and a third model was further adjusted for late-life covariates (diabetes, history of coronary events, high depressive symptoms, and self-reported strokes). The final (4^{th}) model was additionally adjusted for MMSE score.

Secondary analyses were conducted for the sub-population of 4359 people who had complete cognitive subscale data. All models from original analyses were repeated in the secondary analyses, but the final model was adjusted for the cognitive subscales instead of

MMSE. Statistical analyses were performed using the STATA software, version 10 (Statacorp, Texas, USA).

RESULTS

Compared with the inactive group, the active group had slightly younger age, a shorter average follow-up time, higher education level, higher MMSE scores, and were less likely to have ever smoked (all p's <0.05, Table 1).

After adjusting for age, gender, and education (Model 1, Table 2), the active group had 0.055 m/s faster gait speed, completed TUG test 0.6 second faster, and had 1.5 kg greater KES compared the inactive group (all p's < 0.001). After adjusting for risk factors from both mid-life (model 2) and current life (model 3), the results remained similar with model 1. With additional adjustment for MMSE in model 4, all LEF tests were still significantly associated with mid-life PA level (Table 2) with attenuations up to 11%. After the full adjustment, compared with the inactive group, the active group had 0.049 m/s faster gait speed (95% Confidence Interval (CI): 0.038, 0.059, P < 0.001), completed TUG test 0.53 seconds faster (CI: −0.71 ~ −0.36, P < 0.001), and had 1.34 kg greater KES (CI: 0.83 ~ 1.86, P < 0.001).

The secondary analysis was performed in sub-population with complete domain specific cognitive data. The results from the first three models in the secondary analysis were similar with the original analysis. In the final model (model 4, Table 3), after adjusting for detailed cognitive function of SP, MEM and EF, the coefficients of three LEF performance tests were attenuated by up to 41%, but remained significant. Compared with the inactive group, the active group had 0.037 m/s higher gait speed (95% CI: 0.026, 0.048, P < 0.001), completed TUG test 0.34 seconds faster (CI: −0.52 ~ −0.16, P < 0.001), and had 0.87 kg greater KES (CI: 0.34 ~ 1.42, P < 0.001).

DISCUSSION

Participants who were active at mid-life had significantly better LEF indicated by faster gait speed, faster time to complete timed up and go test, and stronger knee extension strength compared with those who were inactive at mid-life. The association remained strong even after adjusting for various confounders from mid-life and late-life including cognitive function. Our longitudinal data are unique with regard to assessment of the association between an unbiased report of mid-life PA and LEF as ascertained a mean of twenty-five years later. Further, the association was controlled with subscales of cognitive function in a secondary analysis. The current study contributes strong evidence of a long-term association between PA and LEF with insights into how this association might be affected by the development of cognitive difficulty.

Our study has several strengths. First, data was from a large and well-described population-based cohort initially representative of the population of an urban center, and our study follow-up time was an average interval of 26-years. Second, weekly hours of PA were recorded at the time of mid-life examination. Third, the late-life examination included objective LEF performance tests. Finally, we investigated the effect of various domains of cognitive function on the association between mid-life PA and late-life LEF in a secondary analysis. Our study also has some limitations. Although we used a standardized PA questionnaire, it only included limited number of items related to sports and exercise, and did not include items for housework and related activities. Additionally, the study was limited by the lack of LEF performance data at mid-life, and also the study population could only include those who were still alive when the AGES-Reykjavik Study was initiated.

Evidence suggests that people who participated in a regular exercise program improved walking capacity compared with sedentary people [1, 25, 26]. The performance of LEF (Gait, TUG, and KES) measured in our study represents mobility, which is an important element of independence among older adults. Although the magnitude was small, all LEF performance tests were significantly associated with mid-life PA level where the size of the effects in the active group compared with the inactive group were equivalent to 4.7, 3.5, and 2.6 years of age in gait speed, TUG, and, KES respectively (original analysis). That is, an active person had a gait speed comparable to, on average, someone 4.7 years younger than an inactive person. Our results are in agreement with previous reports about the effect of cognitive function on LEF [10, 27]. However, the effect of adjusting for various aspects of cognitive function on the association between LEF and mid-life PA was much larger in the secondary analysis (up to 41 % attenuation) compared with the effect shown after adjusting for MMSE (up to 11 % attenuation). It suggests that the effect of cognitive function on LEF could be much stronger than is previously reported. When we investigated the effect of each cognitive domain (SP, MEM, and EF), SP had the strongest effect on the association in all three LEF performances (data not shown). A previous study using the same cohort reported a similar trend showing that SP had the strongest association with mid-life PA[11].

Several mechanisms may contribute to our findings. The first possible hypothesis is that those who were active in mid-life were more likely to continue exercising during the interval years. In the AGES-Reykjavik Study, the active group reported a greater number of PA hours in all life span periods compared with the inactive group. The results after adjusting for current PA level in the final model were still highly significant (attenuation up to 27% in the original analysis and 34% in the secondary analysis) except knee strength in the secondary analysis (data not shown). Second, there is a direct physiological effect of regular PA on muscle and joint strength as well as on overall cardiovascular health [28]. It is clear that people who engage in regular PA have greater muscle strength compared with sedentary people [28]. Furthermore, there are other suggested benefits of regular PA such as improved aerobic capacity which helps in the prevention of cardiovascular disease [29], and preservation of cognitive function [11]. Third, regular mid-life PA may have been influenced by self-efficacy, which may be associated with engagement in other social activities that involve PA in daily life [30]. However, our study did not have information about social activities in mid-life, so we could not test this hypothesis.

CONCLUSION

Men and women who participated in regular PA during mid-life had better performance of LEF, a key function in maintenance of independence for older adults, 25 years later. Our data suggest that being active in mid-life is associated with better mobility in old age.

Promoting regular PA among middle aged adults would help preserve mobility and delay disability in later life.

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Sponsor's Role: None.

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Table 1

Demographic and Health Characteristics by Level of Mid-life Physical Activity (n = 4753)

	Mid-life PA (n=4753)				
	Inactive Group (n=3275)		Active Group (n=1478)		
Variable	**Mean**	**SD**	**Mean**	**SD**	**P (age adj.)**
Follow-up time, mean (± SD), y	25.5	(4.0)	24.4	(4.5)	<.001
Female no. (%)	1912	(58.4)	830	(56.2)	.138
Elementary education, primary only, no. (%)	837	(25.6)	221	(15.0)	<.001
Mid-life Examination					
Age, mean (± SD), y	50.9	(6.5)	51.7	(7.2)	
Body mass index, mean (± SD)	25.2	(3.6)	25.1	(3.1)	.385
Systolic blood pressure, mean (± SD), mmHg	131.0	(19.0)	130.2	(18.2)	.269
Cholesterol, mean (± SD), mmol/l	6.4	(1.1)	6.3	(1.1)	.748
Midlife never smoked, no. (%)	1281	(39.2)	619	(41.9)	.053
Current Examination					
Age, mean (± SD), y	76.4	(5.5)	76.0	(5.4)	
Body mass index, mean (± SD)	27.2	(4.5)	26.9	(4.2)	.063
Systolic blood pressure, mean (± SD), mmHg	142.6	(20.2)	141.7	(20.0)	.224
Cholesterol, mean (± SD), mmol/L	5.7	(1.2)	5.6	(1.2)	.111
MMSE, mean (± SD)	26.7	(2.7)	27.2	(2.6)	<.001
Diabetes, no. (%)	399	(12.2)	163	(11.0)	.251
Coronary event, no. (%)	469	(14.3)	217	(14.7)	.832
Self reported stroke, no. (%)	186	(5.7)	89	(6.0)	.731
High depressive symptoms[#], no. (%)	219	(6.7)	75	(5.1)	.083
Never smoked, no. (%)	1310	(40.9)	660	(45.6)	.002
PA hours/week in the past 12 month, mean (± SD)	1.0	(2.0)	1.8	(2.5)	<.001
Lower Extremity Function					
Gait speed, mean (± SD), meter/sec	0.9	(0.2)	1.0	(0.2)	<.001
Timed up and go, mean (± SD), sec	12.5	(3.3)	11.8	(3.0)	<.001
Knee extension, mean (± SD), kg	32.0	(11.6)	34.1	(12.2)	<.001

Abbreviations: PA = physical activity, MMSE = mini mental state examination, SD = standard deviation, no = number, sec = second

[#]15-item Geriatric Depression Scale score ≥6

Table 2

Association of Lower Extremity Function and Midlife PA Among Dementia Free Population

Adjusted mean differences of lower extremity function scores by mid-life PA levels				
Population (n=4753)	**Active Group (n=1478) versus Inactive Group (n= 3275)**			
Lower Extremity Function	**β coefficient (95% Confidence Interval)**			***P*-value**
Gait Speed	Model 1	0.055*	(0.044 ~ 0.066)	<.0001
	Model 2	0.053*	(0.042 ~ 0.064)	<.0001
	Model 3	0.053*	(0.042 ~ 0.064)	<.0001
	Model 4	0.049*	(0.038 ~ 0.059)	<.0001
Timed Up and Go	Model 1	−0.62*	(−0.80 ~ −0.44)	<.0001
	Model 2	−0.59*	(−0.77 ~ −0.41)	<.0001
	Model 3	−0.59*	(−0.77 ~ −0.41)	<.0001
	Model 4	−0.53*	(−0.71 ~ −0.36)	<.0001
Knee Extension	Model 1	1.50*	(0.98 ~ 2.02)	<.0001
	Model 2	1.51*	(0.99 ~ 2.03)	<.0001
	Model 3	1.50*	(0.98 ~ 2.02)	<.0001
	Model 4	1.34*	(0.83 ~ 1.86)	<.0001

Model 1 = adjusted for age, sex and education

Model 2 = + midlife covariates: BMI, systolic blood pressure, cholesterol, and smoking

Model 3 = + late-life covariates: diabetes, coronary event, high depressive symptoms, smoking, and self reported stroke

Model 4 = + MMSE score

Abbreviations: PA, physical activity; MMSE, mini mental state examination

Table 3

Secondary Analysis For an Association of Lower Extremity Function and Mid-life PA among Population with Details of Cognitive Function

Adjusted mean differences of lower extremity function by mid-life PA levels				
Population (n=4359)	**Active (n=1364) versus Not Active (n=2995)**			
Lower Extremity Function	**β coefficient (95% Confidence Interval)**			***P*-value**
Gait Speed	Model 1	0.054*	(0.042 ~ 0.065)	<.0001
	Model 2	0.052*	(0.041 ~ 0.063)	<.0001
	Model 3	0.052*	(0.041 ~ 0.063)	<.0001
	Model 4	0.037*	(0.026 ~ 0.048)	<.0001
Timed Up and Go	Model 1	−0.59*	(−0.78 ~ −0.40)	<.0001
	Model 2	−0.57*	(−0.76 ~ −0.39)	<.0001
	Model 3	−0.58*	(−0.76 ~ −0.39)	<.0001
	Model 4	−0.34*	(−0.52 ~ −0.16)	.006
Knee Extension	Model 1	1.44*	(0.89 ~ 1.98)	<.0001
	Model 2	1.43*	(0.89 ~ 1.98)	<.0001
	Model 3	1.43*	(0.89 ~ 1.98)	<.0001
	Model 4	0.87[#]	(0.34 ~ 1.42)	.001

Model 1 = adjusted for age, sex and education

Model 2 = + midlife covariates: BMI, systolic blood pressure, cholesterol, and smoking

Model 3 = + late-life covariates: diabetes, coronary event, high depressive symptoms, smoking, and self reported stroke

Model 4 = + cognitive composite scores of speed of processing, memory, and executive function

Abbreviations: PA, physical activity