

Physical Activity in Late Middle- to Older-Aged People and Dementia, Cognitive, and Physical Function Two Decades Later

Jerry Öhlin^a Annika Toots^b Håkan Littbrand^a Patrik Wennberg^c
Birgitta Olofsson^d Yngve Gustafson^a Carl Hörnsten^a Ursula Werneke^e
Peter Nordström^a Johan Niklasson^f Stefan Söderberg^g

^aDepartment of Community Medicine and Rehabilitation, Geriatric Medicine, Umeå University, Umeå, Sweden; ^bDepartment of Community Medicine and Rehabilitation, Occupational Therapy, Umeå University, Umeå, Sweden; ^cDepartment of Public Health and Clinical Medicine, Family Medicine, Umeå University, Umeå, Sweden; ^dDepartment of Nursing, Umeå University, Umeå, Sweden; ^eDepartment of Clinical Sciences, Division of Psychiatry, Sunderby Research Unit, Umeå University, Umeå, Sweden; ^fDepartment of Community Medicine and Rehabilitation, Geriatric Medicine, Sunderby Research Unit, Umeå University, Umeå, Sweden; ^gDepartment of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden

Keywords

Cognitive function · Dementia · Gait speed · Physical activity · Very old people

Abstract

Introduction: Low physical activity (PA) is a potential risk factor for dementia and cognitive impairment. However, few studies have focused on very old people (aged ≥ 80 years), the age group with highest prevalence of dementia. The aim was to investigate if PA associated with subsequent dementia, cognitive function, and gait speed (GS), in very old people. **Methods:** A population-based survey was conducted in 1999 and followed-up between 2016 and 2019 in participants ≥ 80 years. Altogether 541 individuals (56.2% women), 64.9 ± 4.2 years of age at baseline participated. Self-rated baseline PA was categorized into low, medium, or high. Cognitive function was assessed with the Mini-Mental State Examination (MMSE), executive function with the Frontal Assessment Battery (FAB), and GS (in meters/second) was measured over 2.4 m at follow-up. **Results:** During a mean of 19.0 ± 1.1 years, 175 (32.3%) developed dementia. Low or

medium PA compared to high PA did not associate with subsequent dementia, and PA did not associate with future cognitive function (MMSE). PA associated with executive function (FAB) (unstandardized beta [95% confidence interval]) (0.67 [0.07–1.27]), but not after adjustments. PA associated with subsequent GS in the unadjusted model and after adjustment for age, sex, smoking, and education (0.06 [0.02–0.09], and 0.04 [0.01–0.08], respectively), but not after adding adjustment for hypertension, obesity, and glucose intolerance. **Conclusion:** No support was found for the hypothesis that low PA is a potential risk factor for dementia in very high age. However, PA and executive function were associated in unadjusted analyses which indicate that PA may be important for at least one aspect of cognitive function. The association between PA and GS around 2 decades later seems attenuated by cardiometabolic risk factors. Future investigations regarding PA, dementia, and cognitive decline may consider cardiometabolic risk factors such as hypertension, obesity, and glucose intolerance, and include repeated measures of PA over the life course.

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Introduction

Dementia disorders are a leading cause of disability in older people [1]; hence, prevention is important. Up to a third of dementia cases may be delayed or prevented with management of risk factors, e.g., smoking, diabetes, obesity, and low physical activity (PA) [2]. Low PA is associated with cardiovascular events [3]. However, results are conflicting regarding the association between PA and cognitive function and dementia over decades; some found an association [4, 5], while others did not [6, 7]. In addition, low PA associated with lower gait speed (GS) several years later [8]. GS is a measure of physical function shown to predict numerous health outcomes in older people, such as disability [9], dementia [10], and mortality [11].

As low PA may be a modifiable risk factor for dementia, clarifying if PA associated with cognition among very old people (aged ≥ 80 years) is important, since it is the age group with the highest dementia prevalence. Despite dementia increasing exponentially with age [12], few studies have investigated the association between PA and future dementia in very old people. In addition, as low PA may indicate subclinical dementia [7], more studies of very old people with long enough follow-up time to avoid reverse causality are needed. This study tested the hypothesis that PA associated with subsequent dementia development, cognitive function, and GS, in very old people.

Method

Setting and Study Design

The WHO project Multinational Monitoring of Trends and Determinants of Cardiovascular Disease (MONICA) was initiated in 1984 to survey cardiovascular risk factors and events in a large number of populations worldwide [13]. In 2016, SilverMONICA, an extension of the Northern Sweden MONICA study [14], was initiated. Eligible for SilverMONICA were individuals that participated in the 1999 MONICA survey and at least in one previous survey (1986, 1990, 1994), living in the study area and aged ≥ 80 years. Eligible participants were contacted by letter and phone, and signed informed consent. If cognitive impairment was suspected, relatives were informed and consulted. Medical professionals (physiotherapists, nurses, physicians) trained in the study protocol collected data through interviews and assessments in participants' homes. Diagnoses and disorders were validated by the review of medical records by experienced geriatricians.

Measurements and Outcomes

Physical Activity

Previous years' leisure-time PA was measured in 1999 using a questionnaire adapted to older populations with reduced physical function leading to relatively low PA levels [15]. The six levels were

(i) hardly any PA, (ii) mostly sitting, sometimes a walk or similar, (iii) light physical exercise at least 2 h a week, such as walking or biking (also to and from work or school), fishing, dancing, etc., (iv) moderate exercise 1–2 h a week, such as jogging, tennis, swimming, badminton, gymnastics, (v) moderate exercise at least 3 h a week, such as jogging, tennis, swimming, badminton, gymnastics, (vi) hard or very hard physical exercise or competition, regularly and several times per week with great physical effort, such as running, soccer, swimming. The distribution of the original six-item PA scale was from lowest to highest (n (%)): 16 (3.0), 64 (12.1) 357 (67.2), 41 (7.7), 42 (7.9), and 11 (2.0). PA was categorized as *low* if rated 1–2, *medium* if rated 3, and *high* if rated 4, 5, or 6.

Dementia

Dementia diagnosis information was collected during the surveys between 2016 and 2019. The diagnoses were validated by experienced geriatricians according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, Text Revision (DSM-IV-TR) [16] and fifth edition [17] aided by interviews and assessments, medical history including brain imaging when available, and prescribed medication.

Cognitive Function

Cognitive function was measured with the Mini-Mental State Examination (MMSE). The MMSE is a commonly used screening instrument measuring attention, orientation in time and space, calculation, language, short-term memory, and visuospatial function [18], with good reliability and validity [19]. To measure executive function, the Frontal Assessment Battery (FAB) was used. The FAB measures abstract reasoning, mental flexibility and motor programming, sensitivity to interference, inhibition, and autonomy, with good reliability and validity [20].

Gait Speed

Self-paced GS over 2.4 m was measured using a stopwatch and started when participants began walking from behind a first marking on the floor and ended when their first foot passed the second marking. The test was conducted twice, and mean GS was calculated (meters/second).

Covariates

Education was dichotomized into < 8 or ≥ 8 years. Smoking status was defined as smoker or non-smoker (including previous smokers). Glucose intolerance was dichotomized as (i) diabetes, impaired glucose tolerance, impaired fasting glucose, or (ii) normal glucose tolerance, using WHO guidelines [21]. Blood pressure (BP) was coded as hypertension (systolic BP ≥ 140 mm Hg and/or diastolic BP ≥ 90 mm Hg and/or using antihypertensive medication) or normotension. Body mass index was calculated as weight/height², and obesity was defined as body mass index ≥ 30 .

Statistical Analyses

Student's t test and χ^2 test were used to assess differences in age, sex, and education between participants and nonparticipants (declined, deceased, moved, no information). Logistic regression analyses were performed with PA as exposure and dementia diagnosis as outcome. Logistic regression analyses were performed unadjusted, adjusted for age, sex, education, and smoking in model A, and adding hypertension, obesity and glucose intolerance in model B. Linear regression models were used to estimate the as-

Table 1. Baseline characteristics at the 1999 survey for the total sample and stratified according to subsequent dementia development

	N = 541	No dementia n = 366	Dementia n = 175
Age 1999, years	64.9±4.2 64 [59–78]	64.6±4.1 64 [59–77]	65.6±4.3 65 [59–78]
Follow-up, years	19.0±1.1 19 [17–20]	19.0±1.1 19 [17–20]	18.9±1.1 19 [17–20]
Women	304 (56.2)	206 (56.3)	98 (56.0)
Lives alone, n = 539	98 (18.2)	66 (18.1)	32 (18.4)
<8 years education	257 (47.5)	155 (42.3)	102 (58.3)
Smoking, n = 539	40 (7.4)	25 (6.8)	15 (8.6)
Myocardial infarction, n = 536	26 (4.9)	20 (5.5)	6 (3.5)
Hypertension	361 (66.7)	239 (65.3)	122 (69.7)
Glucose intolerance, n = 266	89 (33.5)	52 (28.4)	37 (44.6)
BMI, n = 540	27.1±4.1	27.0±4.0	27.4±4.3
Obese (BMI ≥30)	115 (21.3)	77 (21.1)	38 (21.7)
Systolic BP, mm Hg	146.1±21.3	145.0±21.1	148.4±21.4
Diastolic BP, mm Hg	82.9±10.9	82.8±10.9	83.0±10.9
Low PA ^a	80 (15.1)	47 (13.0)	33 (19.5)
Medium PA ^a	357 (67.2)	248 (68.5)	109 (64.5)
High PA ^a	94 (17.7)	67 (18.5)	27 (16.0)

Data presented as mean ± SD, n (%) or median [range]. BMI, body mass index; BP, blood pressure; PA, physical activity. ^an = 531.

sociation between PA and MMSE, FAB, and GS. These were performed unadjusted, and then adjusted for potential confounders; age, sex, education and smoking in Model A, and adding potential mediators; hypertension, obesity and glucose intolerance in model B. Multicollinearity measures were within limits (Spearman's $Rho > 0.5$, $p < 0.05$), and tolerance and VIF were under 0.1 and 10, respectively. The distribution of the age variable was assessed with histograms and deemed appropriate, and there were no influential outliers. Dummy variables were constructed for covariates with > 2 categories and missing data (diabetes and smoking in particular) was treated as separate category and omitted from the presentation. Additional linear and logistic regressions analyses according to retirement status and education and in the total sample with the original six-level PA scale were conducted. Analyses were performed with SPSS (ver.24 for Windows; IBM Corporation, Armonk, NY, USA), tests were two tailed, and p values < 0.05 were considered statistically significant.

Results

Altogether 541 (67.5%) of 802 eligible individuals were participated (Fig. 1). Compared to nonparticipants, participants were younger at baseline (66.1 ± 4.6 vs. 64.9 ± 4.2 , $p = 0.03$) and had more years of education (8.0 ± 2.7 vs. 9.2 ± 3.6 , $p < 0.001$) with no difference in sex distribution ($p = 0.3$). Over a mean of 19 ± 1.1 years of follow-up, 175 (32%) participants developed dementia. Participants who developed dementia were on average 65.6 years of age and 58% had < 8 years of education,

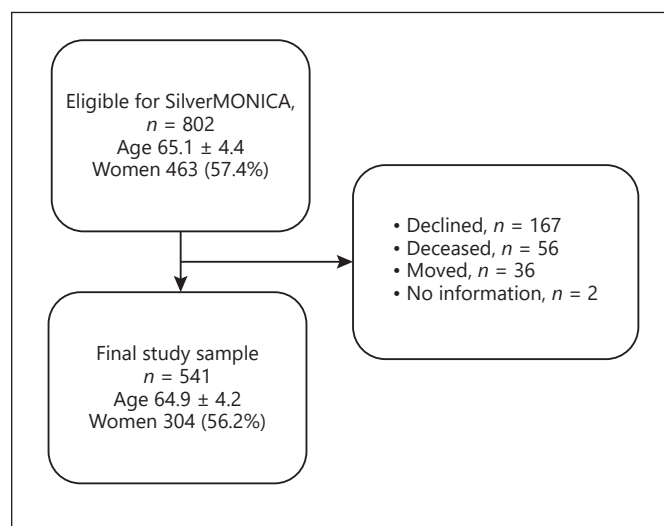


Fig. 1. Flowchart of inclusion procedure.

whereas those that did not develop dementia were 64.6 years of age and 42% had < 8 years of education (Table 1). In the low PA group, 62% had < 8 years of education, while the corresponding proportions were 45% and 40%, in the medium and high group, respectively (Table 2). Characteristics at 1999 and 2016–2019, and 2016–2019 according to dementia development, are described in online supplementary Tables 1 and 2, respec-

Table 2. Baseline characteristics at the 1999 survey according to level of PA

	Low, <i>n</i> = 80	Medium, <i>n</i> = 357	High, <i>n</i> = 94
Age 1999, years	64.8±4.5 64 [59–77]	64.9±4.2 64 [59–78]	64.8±4.2 64 [59–77]
Follow-up, years	19.0±1.1 19 [17–20]	18.9±1.1 19 [17–20]	19.0±1.0 19 [17–20]
Women	51 (63.8)	204 (57.1)	45 (47.9)
Lives alone, <i>n</i> = 539	18 (22.5)	61 (17.1)	16 (17.0)
<8 years education	50 (62.5)	162 (45.4)	38 (40.4)
Smoking, <i>n</i> = 539	13 (16.3)	22 (6.2)	5 (5.3)
Myocardial infarction, <i>n</i> = 536	4 (5.0)	16 (4.5)	6 (6.4)
Hypertension	55 (68.8)	245 (68.6)	56 (59.6)
Glucose intolerance, <i>n</i> = 266	20 (55.6)	60 (31.7)	6 (16.7)
BMI, <i>n</i> = 540	28.5±4.6	27.2±4.0	25.7±3.3
Obese (BMI ≥30)	31 (38.8)	74 (20.7)	7 (7.4)
Systolic BP, mm Hg	148.2±22.6	147.1±21.9	141.5±17.5
Diastolic BP, mm Hg	84.1±12.3	83.1±10.9	81.0±9.6

Data presented as mean ± SD, *n* (%) or median [range]. BMI, body mass index; BP, blood pressure.

Table 3. Odds ratios for dementia in high age according to PA categories

PA	<i>n</i>	Unadjusted		Model A		Model B	
		OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
High	94	1		1		1	
Medium	357	1.09 (0.66–1.80)	0.73	1.06 (0.64–1.76)	0.82	1.02 (0.61–1.70)	0.95
Low	80	1.74 (0.93–3.27)	0.08	1.53 (0.80–2.94)	0.20	1.48 (0.75–2.91)	0.25
<i>p</i> trend	531	0.76 (0.55–1.04)	0.09	0.81 (0.58–1.13)	0.21	0.82 (0.58–1.16)	0.27

Model A: Age, sex, education, smoking. Model B added glucose intolerance, hypertension, obesity. *p* trend, PA, category treated as continuous variable; OR, odds ratio; 95% CI: 95% confidence interval.

tively (see www.karger.com/doi/10.1159/000523726 for all online suppl. material). PA and dementia did not associate in any model (Table 3). PA and MMSE were not associated in unadjusted or adjusted models (Table 4). PA associated with FAB in the unadjusted model (unstandardized beta [95% confidence interval]) (0.67 [0.07–1.27]), but not after adjustments (0.47 [–0.11–1.04]). PA associated with GS in the unadjusted model and the model adjusted for age, sex, smoking, and education (0.06 [0.02–0.09], and 0.04 [0.01–0.08], respectively) but not in the fully adjusted model (0.02 [–0.01–0.06]). The additional analyses showed no influence of retirement status, education, or using the original 6-level PA scale (data not shown).

Discussion

This study found no association between PA and dementia development, irrespective of adjustments. While PA did not associate with cognitive function measured by MMSE, it is associated with executive function measured by the FAB, albeit only in unadjusted analyses. PA associated with GS but not when also adjusting for hypertension, glucose intolerance, and obesity.

Tan et al. [22] found PA and dementia development to associate when comparing the lowest with the higher quintiles (Q1 vs. Q2–Q5), indicating a threshold of PA to protect against dementia. This could explain why we found no association between PA and dementia development, considering the PA recommendations for older

Table 4. Associations between PA and cognitive function, executive function, and GS

	<i>n</i>	Unadjusted		Model A		Model B	
		β (95% CI)	r^2 (<i>p</i>)	β (95% CI)	r^2 (<i>p</i>)	β (95% CI)	r^2 (<i>p</i>)
Cognitive function (MMSE)	462	0.52 (−0.36 to 1.41)	0.001 (0.2)	0.25 (−0.63 to 1.13)	0.060 (0.6)	0.15 (−0.75 to 1.06)	0.072 (0.7)
Executive function (FAB)	458	0.67 (0.07 to 1.27)	0.008 (0.03)	0.47 (−0.11 to 1.04)	0.109 (0.1)	0.49 (−0.11 to 1.09)	0.105 (0.1)
GS	437	0.06 (0.02 to 0.09)	0.019 (0.002)	0.04 (0.01 to 0.08)	0.144 (0.02)	0.02 (−0.01 to 0.06)	0.186 (0.2)

Model A: age, sex, education, smoking. Model B added glucose intolerance, hypertension, obesity. β , unstandardized beta; 95% CI, 95% confidence interval; r^2 , adjusted coefficient of determination; MMSE, Mini-Mental State Examination; FAB, Frontal Assessment Battery.

people of 150–300 min of MVPA per week [23], but only 17% of our participants achieved even 60–120 min of MVPA per week. Another possible contribution to the discrepancy is that our study only included leisure-time PA, while Tan et al. [22] also included occupational PA. It may be advisable to include both leisure and occupational PA as the latter may have a detrimental effect on general health [24].

Sabia et al. [7] reported no neuroprotective effect of PA over 27 years of follow-up. Nevertheless, PA started to decline up to 9 years before dementia diagnosis and was interpreted as a preclinical sign of dementia. However, other studies have found PA to associate with dementia over two decades later in participants approximately 10 years younger at follow-up than our sample [4, 5, 25]. Therefore, there may be a need for repeated measures of PA to better explain its impact on dementia development. Also, we measured leisure-time PA only since the majority of our sample was retired at baseline. Finally, our PA questionnaire had items combining frequency, intensity, time, and type. To analyze the influence of PA on dementia, it may be important to have these as separate items.

The dementia prevalence of 32% at 84.7 years is comparable to previous studies in northern Sweden [26] but higher than studies from other parts; Qiu et al. [27] found a prevalence of 18.9% in participants aged 84.7 in Stockholm, southern Sweden, and Wimo et al. [28] a prevalence of 13.3% at 83.8 years in Nordanstig, central Sweden. This geographical gradient of dementia prevalence in Sweden has been described previously [29].

While PA was not associated with cognitive function measured with the MMSE, it associated with executive function measured with the FAB in the unadjusted model. A meta-analysis of prospective studies found that ten out of 15 included studies showed a protective effect of PA on cognition, and participants were generally younger at baseline and followed for a shorter period than our

sample [30]. Therefore, PA levels before middle age (45–65 years) may influence dementia development, but its effect at very high age is uncertain. Participants with better executive function may also be able to maintain higher PA levels throughout life, as executive function involves inhibition of actions [20].

The positive association between baseline PA and GS suggest that compared to participants in their 60s with lower PA, those with higher PA had better physical function and overall health in their 80s. The association between PA and GS was robust for adjusting factors until cardiometabolic risk factors were added, with mediatory influence being one possible explanation, i.e., PA may lead to decreased cardiometabolic risk factor burden which protects against decline in physical function. This is in line with an observational study of PA and subsequent GS 8 years later, where the authors proposed that the positive association was mainly mediated by body composition (lean-to-fat mass ratio) [31]. However, PA has also been found to associate with GS irrespective of adjustments [8]. Given the association between PA and GS, and the latter associate with mortality [11], risk of falls [32], and dementia [10], monitoring PA has important clinical implications.

A strength of this study is the validation of diagnoses by experienced geriatricians, since dementia is generally underdiagnosed. Another is the 20-year follow-up. However, we could not control for cognition at baseline. Although the MMSE is a commonly used screening test, it has shown ceiling and training effects [33] and does not capture executive functions that are often affected in dementia. Therefore, the FAB was included. PA was measured by self-report, which may increase misclassification bias, and PA was only measured once, hence PA levels before or after were unknown. Finally, The PA scale may not be sufficiently sensitive to capture enough variation in PA to show an association with dementia, as the majority (67.2%) scored 3 on the original six-item scale.

In conclusion, this study found no support for the hypothesis that low PA up to two decades earlier is a potential risk factor for dementia in very high age. However, PA and executive function were associated in unadjusted analyses which indicate that PA may be important for at least one aspect of cognitive function.

PA may lead to decreased cardiometabolic risk factor burden which can reduce decline in physical function. Future investigations regarding PA, dementia and cognitive decline should consider cardiometabolic risk factors such as hypertension, obesity and glucose intolerance, and include repeated PA measures over the life course.

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Statement of Ethics

This study was performed in accordance with the World Medical Association Declaration of Helsinki. This study protocol was reviewed and approved by the Swedish Ethical Review Authority, approval number Dnr O 29-2015. All participants gave written informed consent. If cognitive impairment was suspected, relatives were informed and consulted.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

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Author Contributions

J.Ö.: Conception, data acquisition, analysis, interpretation, drafting and revising the manuscript and agreed to be accountable for the work. A.T., H.L., P.W., B.O., Y.G., C.H., U.W., P.N., J.N., and S.S.: Conception, data interpretation, revising and final approval of the manuscript, and agreed to be accountable for the work.

Data Availability Statement

The data that support the findings of this study cannot be shared publicly because of the European General Data Protection Regulation. Data are available from the University Director of Umeå University (contact hans.wiklund@umu.se) for researchers who meet the criteria for access to confidential data.

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