Early-onset dementia: With exercise in mind

Hooghiemstra, A.M.

2014

PART I

Cross-sectional studies in patients with early-onset dementia

CHAPTER 2

The level of physical activity and executive functioning in early-onset dementia

ASTRID M. HOOGHIEMSTRA[1,2], LAURA H.P. EGGERMONT[1], PHILIP SCHELTENS[2], WIESJE M. VAN DER FLIER[2,3], PIETER JELLE VUIJK[1], ERIK J.A. SCHERDER[1]

Affiliations

[1] Department of Clinical Neuropsychology, VU University, Amsterdam, the Netherlands

[2] Alzheimer Center & Department of Neurology, VU University Medical Center, Neuroscience Capus Amsterdam, Amsterdam, the Netherlands

[3] Department of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, the Netherlands

Submitted

Abstract

Background: Physical activity is associated with cognitive functioning, in particular with executive functioning (EF). Patients with early-onset dementia (EOD) are prone to executive dysfunctioning, but are still physically capable to perform physical activity. The relationship between physical activity and EF has never been studied in patients with EOD exclusively. The aim of the present study was to investigate the relationship between the level of everyday physical activity and EF in patients with EOD.

Methods: Participants were 61 patients with EOD (mean age 61.9 years; 32.8% female, 75.4% diagnosed with Alzheimer's disease). The level of physical activity was assessed using pedometers and the Physical Activity Scale for the Elderly (PASE). Measures of EF were the Trail Making Test, Stroop Color Word Test, Digit Span backwards and category fluency. Hierarchical multiple linear regression analysis was used to investigate relationships between measures of EF and measures of physical activity.

Results: A trend towards a positive relationship between category fluency and mean steps per day (pedometer) was found (β=.27, p=.06). No other relationships were found between measures of EF and measures of physical activity.

Conclusion: The relationship between EF and the level of physical activity was inconsistent.

Introduction

It is well known that participating in regular physical activity has several health benefits, such as reduced mortality, and the prevention and management of diabetes mellitus, hypertension, and obesity.[1] Over the last few decades, the relationship between cognitive functioning and physical activity has become a research focus. This is triggered by the aging of the population,[2] which results in an increasing incidence of age-related disorders, such as dementia.[3] The relationship between cognitive functioning and physical activity has been investigated using various study designs: prospective observational studies show that middle-aged and older persons with physically active lifestyles have a lower risk of cognitive decline and dementia years later, compared to persons with physically inactive lifestyles;[4] cross-sectional studies show that higher self-reported levels of physical activity in older adults are associated with better performance on cognitive tasks;[5] and intervention trials reveal that those participating in an aerobic exercise program show improved performance on cognitive tasks, in comparison with a control group.[6] When examining the entire body of literature focusing on physical activity and cognitive functioning, it attracts notice that most studies are performed in cognitively intact adults of middle and older age. Studies, especially intervention trials, in persons with dementia are performed less and show less equivocal results.[2] These mixed results are mainly caused by methodological limitations and heterogeneity in study designs.[7] To date, no studies that focus on physical activity are performed in patients with early-onset dementia (EOD) exclusively. Patients with EOD are prone to disturbances in executive functioning (EF).[8] EF comprises higher-order cognitive functions, including planning, set-shifting, and inhibition,[9] functions that have been found to be related to physical activity in cognitively intact elderly people.[5] Also, patients with EOD have better physical functioning compared to older patients with dementia,[10] and hence are physically more capable to perform physical activity. This combination makes patients with EOD an interesting population for studies that focus on physical activity and cognitive functioning, in particular EF. Therefore, the aim of the present study is to investigate the relationship between the level of everyday physical activity and EF in patients with EOD.

Methods

DESIGN

The present study made use of a cross-sectional design. Procedures and ethical matters of the study were approved by the medical ethics committee of the VU University Medical Center (VUmc). We obtained written informed consent of each participant and his/her caregiver.

PARTICIPANTS

Study participants were 61 community dwelling patients with EOD, who were recruited in order to participate in an intervention trial.[11] Patients were recruited primarily from the Amsterdam Dementia Cohort of the VUmc Alzheimer Center in Amsterdam, the Netherlands. Diagnoses were based on a multidisciplinary consensus team conference, according to established clinical criteria; detailed descriptions of the diagnostic procedures and the recruitment process are provided elsewhere.[11]

Inclusion criteria were: 1) diagnosis of EOD (onset of symptoms < 66 years); 2) mild to moderate stage of dementia (Mini-Mental State Examination (MMSE)[12] score between 16 and 30; 3) presence of a primary caregiver. *Exclusion criteria* were: 1) wheelchair-bound; 2) diagnosis of a neurodegenerative disease that primarily results in motor impairments, e.g. Parkinson's disease; 3) diagnosis of serious cardiovascular disease, e.g. heart failure; 4) history of substance abuse; 5) a head injury involving loss of consciousness greater than 15 minutes in the medical history; 6) history of severe psychiatric illness, e.g. schizophrenia; 7) severe visual problems; 8) severe hearing problems; 9) insufficient mastery of the Dutch language.

Confounders. In view of possible confounding effects, the following variables were considered: age, gender, level of education, diagnosis of EOD, current comorbidities, and depressive symptoms. The level of education was scored according to the system of Verhage, ranging from 1 (less than 6 years of primary education) to 7 (academic degree).[13] Subsequently, patients were classified as having received low (Verhage score 1 through 3), medium (Verhage score 4 and 5) or high (Verhage score 6 and 7) education. Comorbidities considered were: cardiovascular comorbidities, such as hypertension, cardiac arrhythmia, and thrombosis; psychiatric comorbidities, such as anxiety; locomotor comorbidities, such as rheumatism, fractured hip, problems with limbs and, osteoporosis; and respiratory comorbidities, such as asthma and Chronic Obstructive Pulmonary Disease (COPD). For each participant we added the number of comorbidities in each category. Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression scale (CESD)[14].

MATERIAL AND PROCEDURE

EF was assessed during a neuropsychological examination at the participants' homes. Examiners were Master students Clinical Neuropsychology, who were thoroughly trained by a skilled neuropsychologist. Strict protocols were followed for test administration and scoring in order to minimize variation in test administration. The total neuropsychological examination took approximately 2 hours. Following the neuropsychological examination a pedometer was provided (for a detailed description see below).

EXECUTIVE FUNCTIONING

The *Trail Making Test* (TMT)[15] is a measure for mental speed and mental flexibility, which is a component of EF. In part A (TMTA) the participant is asked to connect numbers in ascending order. In the more complex part B (TMTB) the participant is asked to connect numbers and letters alternately, i.e. 1-A-2-B-etc. The outcome measure used was the number of seconds needed to complete part A and B. An interference score was calculated by dividing the seconds needed to complete part B by the seconds needed for part A.

The *Stroop Color Word Test-short version* (SCWT-sv)[16] is an abbreviated version of the Stroop Color Word Test. The first card consists of words printed in black ink: blue, red yellow and green. In the SCWT-sv, the participant is asked to read aloud as many words as possible in 45 seconds. The second card consists of colored blocks. The participant is asked to name as many blocks in 45 seconds. On the final card the names of the words are printed in an incongruent color, e.g. the word yellow printed in blue ink. The participant is required to name the color of the ink of as many words as possible in 45 seconds. In order to do this the participant needs to inhibit an automatic response, i.e. reading. An interference score was calculated by subtracting the number of correct responses on the second card from the number of correct responses on the third card. This interference score is a measure of inhibition, which is part of EF.

Category fluency is a subtest of the Groningen Intelligence Test.[17] In this test the participant is asked to name as many words as possible in a semantic category in 60 seconds. The categories used were animals and occupations. The outcome measure was based on the total number of correctly generated items in each category. Category fluency performance relies on semantic memory and set shifting abilities,[18] the latter being a component of EF. In the present study animal naming and occupation naming were combined into one category fluency factor, by calculating the average score between the two variables, after the Cronbach's alpha showed acceptable reliability.

Digit span backwards (digit span BW)[19] gives a measure for working memory, which is part of EF. The examiner read aloud series of numbers with increasing length to the sequence. The participant was asked to repeat the sequence in reversed order. The number of correct reversed sequences was used as the outcome measure (range 0-21).

PHYSICAL ACTIVITY

Physical activity was assessed using *pedometers* (OMRON Walking Style II, OMRON Healthcare CO. Ltd. Kyoto, Japan). The pedometer was worn for 7 days consecutively. The participant reported the number of steps in a diary every night before bedtime. When needed patients with EOD were assisted by their primary caregiver. The outcome measure used was the mean number of steps per day. A gradual classification of level of physical activity for healthy adults, based on the daily step count, has been proposed.[20] Based on this classification we divided the EOD group in a relatively physically active group (≥ 5.000 steps per day) and a relatively physically inactive group (< 5.000 steps per day), in order to make comparisons in demographic variables between groups.

The level of everyday physical activity was also assessed with the Dutch version of the *Physical Activity Scale for the Elderly* (PASE)[21]. This brief questionnaire is designed to assess physical activity in the last week. Items on sitting; walking; cycling; light, moderate, and vigorous sport and recreation; and muscle strengthening were recorded as never, seldom (1–2 days/week), sometimes (3–4 days/week), and often (5–7 days/week). Duration was categorized as less than 1 hour, 1–2 hours, 2–4 hours, or more than 4 hours. Housework (light and heavy), lawn work/yard care, home repair, outdoor gardening, and caring for others were recorded as yes/no. Paid or unpaid work was recorded in total hours per week and classified into four categories of intensity of physical activity. The total PASE score was computed by multiplying the amount of time spent in each activity or participation (yes/no) in an activity by the item weights and then summing all items. The total PASE score ranges from 0 to 400, with higher scores reflecting higher levels of physical activity. We administered the PASE in an interview in order to increase the comprehension of the questions.

STATISTICAL ANALYSIS

DATA EXPLORATION

Cases with missing values on EF tasks, due to an inability to complete the task or due to an early abortion of the examination, were excluded from the analyses. In the pedometer data, individuals with more than 2 days missing were excluded from the analyses and for persons with 1 or 2 days missing a corrected mean number of steps per day was calculated, by adding the values of the days that were completed and dividing this value by the number of days that were recorded.

Reliability analysis (Cronbach's Alpha) was used to examine the category fluency factor. A Cronbach's alpha of .80 or higher is indicative of a good internal consistency.[22] Normality was considered using Shapiro-Wilk tests, with transformations applied subsequently when appropriate.

DATA ANALYSIS

Participant characteristics of physically active and physically inactive patients with EOD were considered using independent sample *t*-tests, Mann-Whitney *U* tests, and χ^2-tests.

To examine the relationship between the EF measures and the measures of physical activity, hierarchical multiple linear regression analysis with the enter method was used. Dependent variables were the scores on the EF measures; independent variables were mean steps per day (pedometer) and PASE total score (each in separate analysis). Confounders considered were age, gender, educational level, diagnosis, cardiovascular-, psychiatric-, locomotor-, respiratory comorbidities, and depressive symptoms. Confounders were added in the model when they correlated with one of the dependent variables (Table 2, p. 37). Two regression models were built: First, in the unadjusted model the relationship between the EF measures and the measures of physical activity was examined (model 1). In the adjusted model confounders were added (model 2). In all regression analyses probability for entry was set at .05 and for removal at .10. Statistical significance was set at $p < .05$ for all analyses performed. For statistical analyses, SPSS version 20.0 (IBM for Windows, Armonk, New York, USA) was used.

Results

DATA EXPLORATION

In 24 patients with EOD TMTB scores were missing, due to lack of time or inability to alternate letters and numbers (n = 20) or because the examination was aborted early (n = 4). We considered these missing values extensive and not random, hence we decided to leave TMT B out of the analyses.
Eleven patients did not perform SCWT-sv, five patients did not perform category fluency, four patients did not perform digit span BW, and four patients did not complete the CESD, because the examination was aborted early.
These cases were left out of the analyses. In the pedometer data, 7 patients had more than 2 days missing and were excluded from analyses. For 4 patients a corrected mean number steps per day was calculated.
Reliability analysis showed a good reliability for the category fluency factor (Cronbach's Alpha = .82).

PARTICIPANT CHARACTERISTICS

An overview of the group characteristics is given in Table 1 (p. 36). No significant differences between the physically active and the physically inactive EOD group were found.

RELATIONSHIPS BETWEEN EF AND PHYSICAL ACTIVITY

Confounders were added into the regression model when they correlated with one of the EF measures (see Table 2, p. 37), and included age, gender, educational level (for digit span BW), and depressive symptoms (for SCWT-sv). An overview of the regression coefficients (*B*), standard errors (*SE*), 95% confidence intervals (*95% CI*), standardized regression coefficients (*Beta*) and the proportions explained variance, is given in Tables 3a and 3b (p. 38/39). The unadjusted models (model 1), predicting SCWT-sv and digit span BW by mean steps per day and PASE total score, were not significant. The adjusted models (model 2), predicting SCWT-sv and digit span BW, were significant. However, the regression coefficients of mean steps per day and the PASE total score were not significant, meaning that SCWT-sv and digit span BW performance was not associated with the level of physical activity while controlling for confounders. For statistics and details on the predictors see Table 3a and 3b. A trend was found ($F(1,47) = 3.70$, $p = .06$, Table 3a) towards a positive association between category fluency and mean steps per day, explaining 7.3% of the variance. In the regression model with the PASE total score as main predictor, the model was not significant (Table 3b).

Discussion

This study considered the level of physical activity in relation to EF in patients with EOD. Main results showed a trend towards a positive relationship between category fluency and mean steps per day. No other relationships were found between the measures of EF and measures of physical activity.

Support for a relationship between category fluency and physical activity stems from exercise intervention studies that have found causal relationships between aerobic exercise and category fluency performance; these positive effects are reported in cognitively intact older adults,[23] older persons with mild cognitive impairments,[24] and older persons with dementia.[25] A better performance on the category fluency test implies a better ability of semantic memory and set shifting.[18] Set shifting is the ability to switch rapidly between mental sets.[26] With respect to category fluency these mental sets are semantic categories, such as farm animals and zoo animals.[18] No studies provide an explanation why category fluency performance appears to be sensitive to differences in the level of physical activity. Although category fluency is considered a measure of set-shifting, it also relies on semantic and episodic memory.[27] Whether this explains the sensitivity of category fluency performance to differences in physical activity level could be explored in future studies. The found trend for a relationship between the daily step count and category fluency is interesting, since step count can be modifiable, for instance by means of pedometers in combination with exercise counseling.[28] Also, set shifting is an important function in daily life. Set shifting is needed to organize complex activities, modify plans, and make decisions based on complex information.[26]

We did not observe an association between category fluency performance and the PASE total score. This is in contrast to a previous study that did report this relationship in cognitively intact older adults.[5] Neither did we find relationships between the other EF tasks and the measures of physical activity. This is in contrast to what we expected and to findings of cross-sectional and intervention studies performed in healthy older adults.[6] This discrepancy might be explained by several factors. First, perhaps this study did not have enough power to find associations. Also, in contrast to cognitively intact people, patients with EOD have more pronounced EF disorders, which might have led to a restricted range in scores on the EF tasks. The restricted range in scores may lead to an underestimation of a relationship (type II error). Another explanation may be found in the way physical activity was measured. In the pedometer data, we did not consider the intensity of the ambulatory activities, which seems to be related to cognition in particular.[29] More specifically, the ambulatory activity in the present study might have been performed at a low intensity, resulting in limited associations. Concerning the PASE questionnaire, weights are assigned according to the level of physical strain of the physical activities. This provides a self-report measure of intensity, meaning that persons may have under- or overestimated the true intensity of the physical activities performed. In future studies, gait speed could be included as an objective measure of intensity of ambulatory activity; A gait speed of at least a 100 steps per minute is considered a moderate level of physical activity.[30]

Regarding the TMT, due to the substantial missing data on TMTB, we decided to leave TMTB out of the analyses. The missing values were caused by the difficulty of the task. Several persons were not capable to alternate the letters and numbers in ascending order. It might be that this task is less suitable for evaluation in studies focusing on EOD. In clinical settings the TMT is valuable, because observations of why a person was not capable to perform the test are very informative. These qualitative observations are difficult to incorporate in research.

This is the first study that related EF to the level of physical activity in patients with EOD. A strength of this study is that diagnoses of EOD were based on strict guidelines and were reached through multidisciplinary consensus. Further, physical activity was measured both subjectively and objectively. Most studies addressing the level of physical activity only use self-report questionnaires.[6] Questionnaires may be subject to limited reliability and validity.[6] Some limitations have to be considered when interpreting the results. First, the present study is cross-sectional in nature, precluding inferences on causation. Second, cognitive testing was performed at participants' homes, limiting standardized testing conditions. We attempted to limit this variability through the use of detailed testing protocols. Third, missing values were substantial, which may have biased the results. Finally, our results cannot be generalized to severely affected patients with EOD. The present population was mild to moderately affected and recruited in order to participate in an intervention study, which could have led to a more active population. The results may be generalized to patients with EOD that are mild to moderately affected and community-dwelling.

In conclusion, the relationship between EF and the level of physical activity was inconsistent. Only the relationship between better category fluency performance and a higher daily step count showed a trend. Future studies may replicate the previous findings, taking the intensity of physical activity in mind.

ACKNOWLEDGEMENTS

We are grateful to all participants of this study. The authors would like to acknowledge the contribution of the Master students who were responsible for collecting the data: Bente van der Lelij, Karlijn de Cleen, Aura George, Nikki de Rooy, Leonie Franken, Britt Elstrodt, Sarah de Vos, and Muriel Romijn.

Research of the VUmc Alzheimer Center is part of the neurodegeneration research program of the Neuroscience Campus Amsterdam. The VUmc Alzheimer Center is supported by Alzheimer Nederland and Stichting VUmc fonds.

References

1.
Reiner M, Niermann C, Jekauc D, Woll A. Long-term health benefits of physical activity - a systematic review of longitudinal studies. ***BMC Public Health***. 2013;13(1):813.

2.
Lautenschlager NT, Cox K, Kurz AF. Physical activity and mild cognitive impairment and Alzheimer's disease. ***Curr Neurol Neurosci.*** 2010;10(5):352–358.

3.
Brookmeyer R, Johnson E, Ziegler-Graham K, Arrighi HM. Forecasting the global burden of Alzheimer's disease. ***Alzheimers Dement***. 2007;3:186–191.

4.
Lautenschlager NT, Cox K, Cyarto E V. The influence of exercise on brain aging and dementia. ***Biochim Biophys Acta.*** 2012;1822(3):474–481.

5.
Eggermont LHP, Milberg WP, Lipsitz LA, Scherder EJA, Leveille SG. Physical activity and executive function in aging: the MOBILIZE Boston Study. ***J Am Geriatr Soc.*** 2009;57(10):1750–1756.

6.
Brown BM, Peiffer JJ, Martins RN. Multiple effects of physical activity on molecular and cognitive signs of brain aging: can exercise slow neurodegeneration and delay Alzheimer's disease? ***Mol Psychiatry.*** 2013;18:864–874.

7.
Farina N, Rusted J, Tabet N. The effect of exercise interventions on cognitive outcome in Alzheimer's disease: a systematic review. ***Int Psychogeriatrics.*** 2014;26(1):9–18.

8.
Smits LL, Pijnenburg YAL, Koedam ELGE, et al. Early Onset Alzheimer's Disease is Associated with a Distinct Neuropsychological Profile. ***J Alzheimers Dis***. 2012;30:101–108.

9.
Elliott R. Executive functions and their disorders. ***Brit Med Bull.*** 2003;65:49–59.

10.
Seltzer B, Sherwin I. A comparison of clinical features in early-onset and late-onset primary degenerative dementia - one entity or two. ***Arch Neurol***. 1983;40(3):143–146.

11.
Hooghiemstra AM, Eggermont LHP, Scheltens P, et al. Study protocol: EXERcise and cognition in sedentary adults with early-ONset dementia (EXERCISE-ON). ***BMC Neurol.*** 2012;12(1):75

12.
Folstein MF, Folstein SE, Mchugh PR. Mini-Mental State - Practical Method for Grading Cognitive State of Patients for Clinician. ***J Psychiatr Res.*** 1975;12(3):189–198.

13.
Verhage F. ***Intelligence and Age: Study With Dutch People Aged 12-77*** [in Dutch]. Assen: Van Gorcum; 1964.

14.
Radloff LS. The CESD Scale: A Self-Report Depression Scale for Research in the General Population. ***Appl Psychol Meas.*** 1977;1(3):385–401.

15.
Reitan RM. The Relation of the Trail Making Test to Organic Brain Damage. ***J Consult Psychol.*** 1955;19(5):393–394.

16.
Macleod CM. Half A Century of Research on the Stroop Effect - An Integrative Review. ***Psychol Bull.*** 1991;109(2):163–203.

17.
Luteijn F, van der Ploeg FAE. ***Handleiding Groninger Intelligentie Test (Manual Groningen Intelligence Test)***. Lisse, The Netherlands: Swets & Zeitlinger; 1983.

18.
Troyer AK, Moscovitch M, Winocur G. Clustering and switching as two components of verbal fluency: evidence from younger and older healthy adults. ***Neuropsychology.*** 1997;11(1):138–146.

19.
Lindeboom J, Matto D. Digit series and Knox cubes as concentration tests for elderly subjects. ***Tijdschr Gerontol Geriatr.*** 1994;25:63–68.

20.
Tudor-Locke C, Craig CL, Brown WJ, et al. How Many Steps/day are Enough? For Adults. ***Int J Behav Nutr Phys Act.*** 2011;8:79.

21.
Schuit AJ, Schouten EG, Westerterp KR, Saris WHM. Validity of the physical activity scale for the elderly (PASE): According to energy expenditure assessed by the doubly labeled water method. ***J Clin Epidemiol.*** 1997;50(5):541–546.

22.
Bland J, Altman D. Statistics notes: Cronbach's alpha. ***BMJ***. 1997;314:572.

23.
Stones MJ, Dawe D. Acute exercise facilitates semantically cued memory in nursing home residents. ***J Am Geriatr Soc.*** 1993;41(5):531–534.

24.
Baker LD, Frank LL, Foster-Schubert K, et al. Effects of Aerobic Exercise on Mild Cognitive Impairment. ***Arch Neurol***. 2010;67(1):71–79.

25.
Van de Winckel A, Feys H, De Weerdt W, Dom R. Cognitive and behavioural effects of music-based exercises in patients with dementia. ***Clin Rehabil.*** 2004;18(3):253–260.

26.
Rohlf H, Jucksch V, Gawrilow C, et al. Set shifting and working memory in adults with attention-deficit/hyperactivity disorder. ***J Neural Transm.*** 2012;119(1):95–106.

27.
Greenberg D, Keane M, Ryan L, Verfaellie M. Impaired category fluency in medial temporal lobe amnesia: The role of episodic memory. ***J Neurosci.*** 2009;29(35):10900–10908.

28.
De Blok BMJ, de Greef MHG, ten Hacken NHT, Sprenger SR, Postema K, Wempe JB. The effects of a lifestyle physical activity counseling program with feedback of a pedometer during pulmonary rehabilitation in patients with COPD: A pilot study. ***Patient Educ Couns.*** 2006;61(1):48–55.

29.
Angevaren M, Vanhees L, Wendel-Vos W, et al. Intensity, but not duration, of physical activities is related to cognitive function. ***Eur J Cardiovasc Prev Rehabil.*** 2007;14(6):825–830.

30.
Marshall SJ, Levy SS, Tudor-Locke CE, et al. Translating physical activity recommendations into a pedometer-based step goal: 3000 steps in 30 minutes. ***Am J Prev Med.*** 2009;36(5):410–415.

Table 1. Participant characteristics of physically active and physically inactive patients with EOD

	Physically active (n = 34)[d]	**Physically inactive** (n = 20)[d]	p
Age, *M (SD)*	60.8 (5.2)	63.4 (4.2)	.06[a]
Gender, male, *n (%)*	25 (73.5)	11 (55.0)	.16[b]
Level of education, *n (%)*			.55[b]
Low	1 (2.9)	2 (10.0)	
Medium	15 (44.1)	8 (40.0)	
High	18 (52.9)	11 (50.0)	
MMSE, *Median (range)*	24 (16-30)	25 (18-29)	.80[c]
Diagnosis, *n (%)*			.07[b]
AD	30 (88.2)	12 (60.0)	
VaD	1 (2.9)	4 (20.0)	
DLB	2 (5.9)	3 (15.0)	
FTD	1 (2.9)	0 (-)	
Dementia NOS	0 (-)	1 (5.0)	
Comorbidities, *n (%)*			
Cardiovascular	8 (23.5)	4 (20.0)	.76[b]
Psychiatry	3 (8.8)	2 (10.0)	.89[b]
Locomotion	3 (8.8)	1 (5.0)	.60[b]
Respiration	1 (2.9)	0 (-)	.44[b]

Notes:
[a] Independent samples *t*-tests.
[b] χ^2–test.
[c] Mann-Whitney *U* test.
[d] Total sample size is 54 due to 7 missing values on the pedometer.
[e] Categorization of education (low, medium, high) is based on Verhage's education classification.[13]
Abbreviations: AD = Alzheimer's disease; DLB = dementia with lewy bodies; Dementia NOS = dementia not otherwise specified; EOD = early-onset dementia; FTD = frontotemporal dementia; MMSE = Mini-Mental State Examination; VaD = vascular dementia.

Table 2. Pearson correlations between EF measures and possible confounding factors

	SCWT-sv (*n* = 50)	Digit span BW (*n* = 57)	Category Fluency (*n* = 56)
	r	*r*	*r*
Age	-.09	**.32***	.06
Gender	.10	**-.33***	-.16
Level of education	-.07	**.32***	.06
Diagnosis	.17	.08	-.02
Cardiovascular comorbidities	.13	-.13	-.11
Psychiatric comorbidities	.16	-.17	-.12
Locomotor comorbidities	-.13	.05	.16
Respiratory comorbidities	-.06	.02	.00
Depressive symptoms	**.41****	.00	.06

Notes:
Sample sizes vary due to missing values on the EF measures.
**$p < .01$; *$p < .05$.
Abbreviations: Digit span BW = Digit Span backwards; SCWT-sv = Stroop Color Word Test short version.

Table 3a. Hierarchical multiple linear regression analysis (enter method) showing associations between EF measures and mean steps per day

		SCWT-sv (*n* = 42)			Digit span BW (*n* = 50)			Category fluency (*n* = 49)		
		B (SE)	*95% CI*	*Beta*	*B (SE)*	*95% CI*	*Beta*	*B (SE)*	*95% CI*	*Beta*
Mean steps per day	M 1	-0.02 (0.09)	-0.20-0.17	-.03	0.00 (0.00)	-0.01-0.01	.07	0.06 (0.03)*	-0.00-0.13	.27
	M 2	0.01 (0.08)	-0.15-0.17	.01	0.00 (0.00)	.0.00-0.01	.13	-	-	-
Age	M 2				0.05 (0.02)***	0.02-0.08	.45			
Gender	M 2				-0.26 (0.15)	-0.56-0.05	-.21			
Educational level	M 2				0.19 (0.07)***	0.06–0.33	.37			
Depressive symptoms	M 2	0.93 (.27)***	0.40-1.47	.49						
R^2	M 1	.00			.01			.07*		
	M 2	.24***			.35***			-		
F	M 1	0.04			0.27			3.70*		
	M 2	6.20***			5.95 ***			-		

Notes:
M 1 represents the unadjusted regression coefficients for mean steps per day (pedometer).
M 2 represents regression coefficients for mean steps per day adjusted for confounding factors, and the regression coefficients of the confounding factors.
Sample sizes vary due to missing values on the EF and physical activity measures.
***$p < .01$; **$p < .05$; *$p < .10$.
Abbreviations: Digit span BW = Digit Span backwards; SCWT = Stroop Color Word Test short version.

Table 3b. Hierarchical multiple linear regression analysis (enter method) showing associations between EF measures and PASE total score

		SCWT-sv (*n* = 49)			**Digit span BW** (*n* = 57)			**Category fluency** (*n* = 55)		
		B (SE)	*95% CI*	*Beta*	*B (SE)*	*95% CI*	*Beta*	*B (SE)*	*95% CI*	*Beta*
PASE total score	M 1	0.00 (0.03)	-0.05-0.06	.02	0.00 (0.00)	-0.00-0.00	.07	0.01 (0.01)	-0.01-0.03	.11
	M 2	0.01 (0.02)	-0.04-0.05	.03	0.00 (0.00)	-0.00-0.00	.01	-	-	-
Age	M 2				0.05 (0.01)***	0.02-0.08	.39			
Gender	M 2				-0.23 (0.15)	-0.53-0.08	-.19			
Educational level	M 2				0.18 (0.06)***	0.05–0.30	.37			
Depressive symptoms	M 2	0.70 (0.23)***	0.24-1.15	.41						
R^2	M 1	.00			.00			.01		
	M 2	.17**			.31***			-		
F	M 1	0.01			0.24			0.68		
	M 2	4.76**			5.75***			-		

Notes:
M 1 represents the unadjusted regression coefficients for PASE total score.
M 2 represents regression coefficients for PASE total score adjusted for confounding factors, and the regression coefficients of the confounding factors.
Sample sizes vary due to missing values on the EF and physical activity measures.
***$p < .01$; **$p < .05$; *$p < .10$.
Abbreviations: Digit span BW = Digit Span backwards; SCWT = Stroop Color Word Test short version.