Dementia patients are more sedentary and less physically active than age- and sex-matched cognitively healthy older adults

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Declarations

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ABSTRACT

Aims: To examine physical activity and sedentary behavior characteristics of ambulatory and community dwelling patients with dementia compared to cognitively healthy age-, sex- and weight-matched controls.

Methods: In this cross-sectional study we included community dwelling dementia patients (N=45, age=79.6±5.9 years, MMSE=22.8±3.2) and matched controls (N=49, age=80.0±7.7 years, MMSE=29.0±1.2). Participants wore a wrist accelerometer for seven days to assess sedentary time, sedentary bout duration and time spent in very light, light-to-moderate and moderate-to-vigorous physical activities.

Results: Relative sedentary time and sedentary bout duration was significantly higher in dementia patients compared to controls (median and interquartile range: *57% (49 - 68) vs 55% (47 – 59) and 18.3 (16.4–21.1) minutes vs 16.6 (15.3–18.4) minutes*, P=0.042 and P=0.008 respectively). In addition, dementia patients spent a lower percentage of their waking time in light-to-moderate and moderate-to-vigorous intensity physical activities (20% (15–23) *vs* 22% (18–25) and 5% *(2–10) vs* 10% (5–13), P=0.017 and P=0.001 respectively).

Conclusion: We revealed that dementia patients are more sedentary and perform less physical activity compared to cognitively healthy controls. This may have clinically important consequences, given the observation that sedentary behavior and little physical activity independently predicts all-cause mortality and morbidity.

INTRODUCTION

The incidence and prevalence of dementia is rising [1]. Pharmacological treatment to slow disease progression shows limited benefits on cognitive functioning [2]. Therefore, non-pharmaceutical therapies are needed to attenuate or slow cognitive decline. Engagement in moderate to vigorous physical activity (i.e. exercise) is one of the most important modifiable risk factors for dementia [3]. Moreover, exercise interventions have beneficial effects on cognitive function in older adults with dementia [4]. Interestingly, recent research showed that sedentary behavior (activities requiring low levels of energy expenditure, e.g. sitting and lying), independent of performance of physical activity, is strongly related to negative health outcomes and mortality [5,6]. Moreover, sedentary behavior is associated with lower cognitive performance [7], which stresses the relevance to understand the prevalence and characteristics of sedentary behavior in the context of dementia. Therefore, we aim to objectively determine physical activity and sedentary behavior characteristics of community-dwelling dementia patients compared to cognitive healthy age-, sex- and weight-matched controls. Secondary, we will explore whether increasing age attenuates physical activity and sedentary behavior in dementia.

MATERIALS AND METHODS

Participants and design. In this cross-sectional study persons with a dementia diagnosis, aged >60 years, that were ambulatory and community dwelling were included. Dementia diagnosis was based on comprehensive clinical assessment by a physician, typically including neuropsychological assessment and imaging. We used the mini-mental state examination (MMSE) to indicate severity of cognitive impairment [8]. Baseline measurements of a longitudinal trial examining the effects of exercise on cognitive functioning in dementia were used for the current study [9]. Cognitively healthy controls were age-, sex- and weight-matched to dementia patients and had no history of cognitive impairment (MMSE >24 [8]). All participants were ambulatory and community-dwelling. The study protocol was approved by the local Medical Ethics Committee in accordance with the latest revision of the declaration of Helsinki. Written informed consent was obtained from all participants.

Physical activity monitoring. Directly after screening, physical activity and sedentary behavior were assessed by the Philips Actiwatch 2, a wrist-worn accelerometer validated in middle-aged females [10]. The Philips Actiwatch 2 contains an acceleration-responsive piezoelectric sensor which measures wrist accelerations in three directions every 30 seconds. These wrist accelerations were translated into a number of counts that were used to estimate physical activity and sedentary behavior The accelerometer was worn for seven days on the non-dominant wrist, to provide a reliable estimate of physical activity and sedentary behavior. the [11,12].All participants wore the actiwatch 24 hours per day. The accelerometer was waterproof and participants did not take if off during swimming or taking a shower. Therefore, non-wear time was not expected. Sleep intervals, including daytime naps, were filled in by the participants or their caregivers in a sleep diary.

Data analysis. Data was uploaded using the Philips Actiware 6 software. Data from the first day of testing were excluded from analysis to give participants the opportunity to familiarize with the device. Sleep intervals were manually set by the researcher using the Philips Actiware 6 software[13] and excluded by custom software written in MATLAB R2014b (MathWorks, USA). Hereby only the data of the waking hours remained. Participants were included if they provided at least six valid days (>10 h of waking data). Data was conferred from counts per epoch to counts per minute (CPM). Cut-off points of 145 counts per minute (CPM), 145-274 CPM, 274-597 CPM and >597 CPM were used for sedentary behavior, very light, light-to-moderate and moderate-to-vigorous physical activity respectively [10]. To account for individual differences in waking time, our primary analysis expressed activity levels as a percentage of total (awake) measuring time. Interruptions in sedentary behavior were defined as spending one minute ≥145 CPM after 5 minutes <145 CPM. Prolonged sedentary behavior was defined as spending 30 minutes <145 CPM without one minute above 145 CPM. Duration of average sedentary bout was defined by total time spent sedentary divided by number of interruptions in sedentary behavior.

Statistical analysis. Statistical analyses were performed in IBM SPSS Statistics 20.0 (IBM SPSS; IBM Corp., Armonk, New York, USA). We performed a complete case analysis, including only those

participants that wore the actiwatch for a minimum of 7 days. Chi^2-tests for categorical variables and independent samples t-tests for continuous variables were used to compare dementia patients and controls. Non-parametric tests were used for not normally distributed data (including physical activity and sedentary behavior). To evaluate the impact of age, the same analyses were performed between participants aged <80 years and ≥80 years. All data are presented as median (interquartile range) unless stated otherwise. Level of significance was set at P<0.05.

RESULTS

45 dementia patients (mean±SD age=79.6±5.9 years, MMSE=22.8±3.2) and 49 controls (mean±SD age=80.0±7.7 years, MMSE=29.0±1.2) were included (Figure 1). Sex, BMI, walking aid use and number of comorbidities did not differ between groups (Table 1). MMSE was significantly lower in dementia patients (P<0.001), and dementia patients received significantly more home care (P<0.001). The majority of dementia patients and controls lived independently (93% and 98% respectively).

Total waking time tended to be lower in dementia patients compared to controls (mean±SD 14.9±1.3 h/day *vs* 15.4±1.0 h/day, P=0.053, Table 2). Dementia patients had significantly lower activity counts and spent more hours in categories reflecting lower-intensity activity (Table 2). Relative sedentary time was significantly higher in dementia patients compared to controls (57% (49 - 68) vs 55% (47 – 59), P=0.042, Table 2). In addition, dementia patients spent a lower percentage of their waking time in light-to-moderate and moderate-to-vigorous intensity physical activity (20% (15-23) *vs* 22% (18-25) and 5% (2-10) *vs* 10% (5-13), P=0.017 and P=0.001, respectively). Number of interruptions in sedentary behavior and prolonged sedentary bouts did not differ. Duration of sedentary bouts was significantly longer in dementia patients compared to controls (18.3 (16.4-21.1) minutes vs 16.6 (15.3-18.4) minutes, P=0.008, Table 2).

When comparing younger *versus* older subgroups, older participants showed more walking aid users. Whilst older controls showed significantly less physical activity and more sedentary behavior compared to their younger peers, no such changes were present between dementia patients aged ≥80

years and aged <80 years (Figure 2). More specifically, younger controls had a significantly higher activity counts, lower relative sedentary time, and spent more hours in categories reflecting light-to-moderate and moderate-to-vigorous intensity activity compared to older controls. Since no such differences were present between young and older dementia patients, differences in physical activity and sedentary behavior characteristics between populations was most prominent in the younger groups (see Figure 2).

DISCUSSION

The aim of our study was to objectively investigate physical activity and sedentary behavior characteristics of dementia patients compared to controls, and assess whether age affects this comparison. First, in our relatively large sample we found that dementia patients spent significantly more of their waking hours in a sedentary state and significantly less time in light-to-moderate and moderate-to-vigorous intensity activities. This may have clinically important consequences, given the observation of previous prospective studies that sedentary behavior independently predicts all-cause mortality and morbidity [5,14]. Secondly, we found that older age was associated with a decline in physical activity and increase in sedentary behavior in controls, whilst no such age-related changes were found in dementia patients. Consequently, negligible differences in physical activity and sedentary behavior characteristics were present when comparing older dementia patients and controls.

In line with observations from previous work [15,16], our data confirm that community-dwelling dementia patients spend a large amount of time in sedentary behavior and have low levels of physical activity. We add the novel finding that differences between dementia patients and controls remain when corrected for sleep time. Even though we used an accelerometer validated to measure physical activity and sedentary behavior [10], time spent in moderate-to-vigorous intensity activity seems unusually high in both groups [17]. We have compared our findings to other studies that assessed physical activity and sedentary behavior in older adults with and without dementia, and we note that sedentary behavior ranged from 6.7 to 10.7 hours between studies [15,18,19]. Moreover, percentage of elderly meeting physical activity guidelines (150min/week of moderate-to-vigorous physical activity)

ranged from 27-69% [17,20]. Differences in sedentary behavior and physical activity duration between studies might relate to the use of different types of accelerometers, given that the reported studies used hip-worn accelerometers, wrist-worn accelerometers or questionnaires to estimate physical activity and sedentary behavior [21]. However, this does not invalidate our primary comparison between subjects with dementia and healthy peers. Moreover, this highlights the importance of including a control group to provide valid interpretation of the results.

Our observation raises the question if differences in physical activity and sedentary behavior are simply a consequence of dementia. A decline in executive functioning (i.e. necessary for goal directed behavior such as physical activity) could lead to apathy [22], which is known to lower activity levels in Alzheimer's' patients [23]. However, it is important to realize that lower physical activity and higher sedentary behavior have already been reported in the preclinical stages of dementia [24] and in subjects with mild cognitive impairment) [25]. This might suggest that differences in physical activity and sedentary behavior are causally linked to progression from mild cognitive impairment to later stages of dementia. Future research is necessary to answer this question on cause of effect. Nevertheless, since higher physical activity and lower sedentary behavior are associated with better cognitive performance [7,25], benefits of interventions promoting physical activity and reducing sedentary behavior should be investigated.

In response to our second research question, we found that older age was associated with a decline in physical activity and increase in sedentary behavior in controls. This observation can partly be explained by deterioration of walking and mobility and increased disability with older age [26]. Interestingly, no further decline in physical activity and increase in sedentary behavior was found in dementia patients, despite the age-related increased number of walking aid users. This striking result suggests that cognitive impairment in dementia has a great impact on physical activity and sedentary behavior, and may be more important than the impact of other factors such as deterioration of walking and mobility. An alternative explanation is that a (near) minimum level is achieved in the decline in levels of physical activity and sedentary behavior in community-dwelling subjects [17].

In addition to the duration of sedentary behavior, previous work revealed that the frequency of breaking up sitting (and therefore duration of each sedentary bout) may have clinical relevance. Breaks in sedentary behavior can prevent cardiovascular impairments [5] and plays a role in maintaining glycemic control, which may positively influence brain health [27]. Our study found that the average duration of a sedentary bout was higher in dementia patients compared to controls. This observation suggests that not only reducing sedentary time, but also preventing prolonged sedentary bouts by regularly breaking up sedentary behavior, can be targeted as a lifestyle intervention [28].

Limitations Since we only included community-dwelling patients, our results cannot be generalized to institutionalized dementia patients. Furthermore, dementia patients in our study were enrolled in an exercise trial [9]. Therefore, this group may be more motivated to be physically active. Nonetheless, significant differences in physical activity characteristics were observed. Furthermore, physical activity characteristics were measured by wrist-worn accelerometry, which is associated with limited discriminative capacity between sedentary and very light intensity activities [29]. Consequently, differences between dementia patients and controls might even be more pronounced. Another limitation relates to our accelerometer, which has only been validated in a group of middle-aged females [10] and was unable to correct for potential presence of short (~1-min) periods of non-wear time. Nonetheless, we do not expect this will invalidate our findings of between-group differences in physical activity and sedentary behavior. In addition, using wrist-worn accelerometry may explain the two outliers in the younger dementia patients (Figure 2), which could relate to restless arm movements. Whilst this may affect exploring individual differences in physical activity *versus* sedentary behavior characteristics, significant differences remained present at group level. Furthermore, we did not discriminate between types of sedentary activities. Cognitively challenging sedentary activities, such as reading, might have a protective effect on cognition and are therefore less harmful than passive sedentary activities (e.g. television-viewing) [30]. The final limitation is use of the MMSE as a cognitive screening instrument since this measure, especially in healthy highly educated older adults, has limited discriminative power to detect mild cognitive deficits [31,32]. It is

191 important to indicate that diagnosis of dementia was not made using the MMSE, but included standard
192 clinical procedures (including imaging if required).
193
194 *Clinical relevance.* Knowledge of physical activity characteristics across the entire activity spectrum
195 in dementia is highly relevant given that physical activity is an important factor accelerating
196 development and progression of dementia [3,7]. In addition, a high amount of sedentary behavior and
197 low amount of physical activity are associated with higher mortality and morbidity [5,6]. Even though
198 we found relatively small differences in physical activity characteristics between dementia patients
199 and controls, these may be highly relevant. For example, even very short breaks of light intensity
200 activity (i.e. 2 minutes walking) can already prevent acute metabolic [33] and cardiovascular [5]
201 impairments. This underlines the importance to develop interventions suitable for this vulnerable
202 patient group to safely engage in light intensity activities. However, future research should first
203 explore the role of physical activity and sedentary behavior in the progression and prevention of
204 dementia.
205
206 *Conclusion.* In the current study we objectively demonstrated that dementia patients spend
207 significantly more of their waking hours in sedentary behavior and spend less time in light-to-
208 moderate and moderate-to-vigorous intensity physical activity. Moreover, we found that older age
209 attenuated sedentary behavior and physical activity in controls, whilst this age-related decline is absent
210 in dementia patients. This means that patients with dementia (independent of age) lead a physically
211 inactive lifestyle characterized with significant time spent sedentary.
212 Taken together, these data improve our understanding of physical activity and sedentary behavior
213 characteristics in this highly relevant patient group and implies that targeting sedentary behavior and
214 physical activity may be relevant in dementia patients, especially at a younger age.

215 **FIGURE CAPTIONS**

216 **Fig. 1: Flowchart of participants**

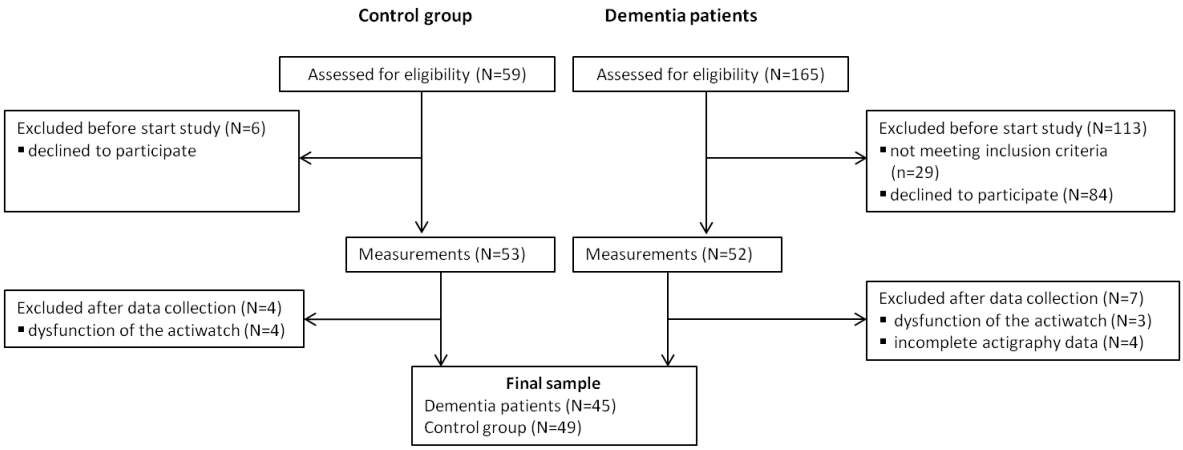

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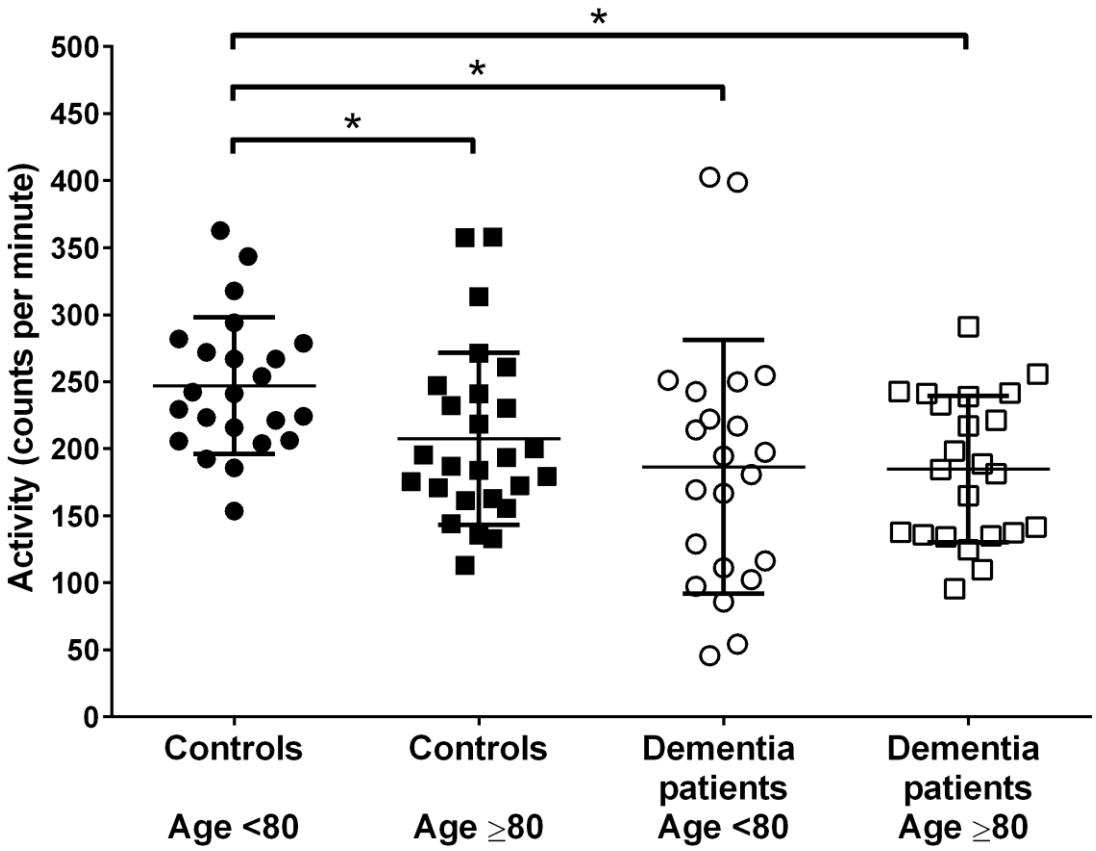
Fig 2: Activity levels of dementia patients and cognitively healthy controls



Activity levels of younger and older age groups. Mean activity score (counts per minute) grouped by age. Controls Age<80 (n=23), Controls Age ≥80 (n=26), Dementia patients Age <80 (n=22), Dementia patients Age ≥80 (n=23). Values represent median ± interquartile range. * Significant difference between: Controls Age <80 and Controls Age ≥80 P=0.044, Controls Age <80 and Dementia patients Age <80 P=0.004, Controls Age <80 and Dementia patients Age ≥ 80 P=0.002.

Table 1. Baseline characteristics

	Control (n=49)	**Dementia (n=45)**	**P-value**
Age (years), *mean ± SD*	80.0 ± 7.7	79.6 ± 5.9	0.744*
Females, *n (%)*	25 (51.0%)	22 (48.9%)	0.836†
Body Mass Index (kg/m²), *mean ± SD*	25.5 (4.0)	26.3 (5.0)	0.411*
Mini Mental State Examination‡, *mean ± SD*	29.0 ± 1.2	22.8 ± 3.2	**<0.001***
Number of walking aid users, *n (%)*	10 (20.4%)	16 (35.6%)	0.101†
Number of home-care receivers, *n (%)*	6 (12.2%)	24 (53.3%)	**<0.001†**
Number of comorbidities§, *mean ± SD*	2.7 ± 1.8	3.3 ± 1.9	0.150*
Residence, *n (%)*			0.629†
- Independent, alone	18 (36.7%)	14 (31.1%)	
- Independent, together	30 (61.2%)	28 (62.2%)	
- Care home	1 (2.0%)	3 (6.7%)	
- Nursing home	0	0	
Dementia type, *n (%)*			
- Alzheimer's disease	n/a	25 (55.6%)	
- Vascular dementia	n/a	2 (4.4%)	
- Alzheimer's Disease/Vascular Dementia (%)	n/a	12 (26.7%)	
- Dementia type not specified (%)	n/a	6 (13.3%)	

*Differences between groups were tested with independent samples t-test; †Differences between groups were tested with Chi-Square Test; ‡ Scores on the Mini-Mental State Examination (MMSE) range from 0 (severe impairment) to 30 (no impairment); §Comorbidites are scored using the Older Persons and Informal Caregivers Survey-Minimum Dataset (TOPICS-MDS) with a theoretical range of 0-17 and a higher score indicates more comorbidities [34]

Table 2: Physical activity and sedentary behavior characteristics

	Control (n=49)	**Dementia (n=45)**	**P-value**
Total waking time (h/day)	15.4 ± 1.0*	14.9 ± 1.3*	0.053†
Counts per minute (day^{-1})	226 ± 61*	186 ± 76*	**0.005†**
Absolute values (h/day)			
Sedentary time	8.1 (7.2 – 9.2)	8.5 (7.2 – 10.0)	0.216
Very light intensity activity	2.2 (1.9 – 2.6)	2.3 (1.7 – 2.9)	0.748
Light-to-moderate intensity activity	3.5 (2.7 – 4.0)	2.7 (2.0 – 3.7)	**0.006**
Moderate-to-vigorous intensity activity	1.5 (0.8 – 2.0)	0.8 (0.4 – 1.5)	**0.001**
Relative values (% of total measuring time)			
% sedentary time	55 (47 – 59)	57 (49 – 68)	**0.042**
% very light intensity activity	15 (12 – 16)	16 (12 – 19)	0.284
% light-to-moderate intensity activity	22 (18 – 25)	20 (15 – 23)	**0.017**
% moderate-to-vigorous intensity activity	10 (5 – 13)	5 (2 – 10)	**0.001**
Sedentary behavior characteristics			
Number of interruptions in sedentary behavior (day^{-1})	28.2 (26.2 – 32.5)	27.2 (24.5 – 31.0)	0.195

Number of 30 minutes prolonged sedentary bouts (day^{-1})	2.0 (0.9 – 3.3)	2.3 (1.0 – 4.1)	0.227
Duration of average sedentary bout (minutes)	16.6 (15.3 – 18.4)	18.3 (16.4 –21.1)	**0.008**

Median and Interquartile range are presented unless reported otherwise. P-values represent Mann-Whitney U test; *Mean ± SD; †Differences between groups were tested with independent samples t-test

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