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Short report

# Associations between activity fragmentation and subjective memory complaints in middle-aged and older adults

Borja del Pozo Cruz [a,b,*], Jesus del Pozo-Cruz [c]

[a] Centre for Active and Healthy Ageing, Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Campusvej 55, 5230 Odense, Denmark
[b] Motivation and Behavior Research Program, Institute for Positive Psychology and Education, Faculty of Health Sciences, Australian Catholic University, North Sydney, New South Wales, Australia
[c] Epidemiology of Physical Activity and Fitness Across the Lifespan Research Group, Departament of Physical Education and Sport, Faculty of Education, University of Seville, Seville, Spain

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ABSTRACT

*Introduction:* Subjective memory complaints (SMC) are often considered a clinical marker of mild cognitive impairment and dementia and could manifest as shortening of activity bouts throughout the day causing daily activity to accumulate in a more fragmented pattern. In the current study we explored the association between activity fragmentation and SMC in middle-aged and older adults.
*Methods:* We used data from 3820 participants in the National Health and Nutrition Examination Survey (2003–2006) with valid accelerometer SMC data. The analyses were conducted in 2020. To calculate activity fragmentation, an active-to-sedentary transition probability was calculated as the number of physical activity bouts (i.e., consecutive minutes registering 100+ counts/min) divided by the total sum of minutes spent in physical activity. A multivariable ordinal logistic regression model was conducted to examine the association between activity fragmentation (scaled) and SMC (yes/no).
*Results:* Higher activity fragmentation was associated with an increased likelihood of self-reported SMC in the study population (Odd Ratio [95% Confidence Interval] = 1.335 [1.067, 1.669]; Average Marginal Effect [95% CI] = 0.029 [0.006, 0.052]; *p*-value = 0.021). This association was independent of total physical activity volume.
*Conclusions:* The findings provide support that studying fragmented activity patterns can be useful in identifying those at risk for SMC, over and above total volume of physical activity. Future longitudinal studies are required to establish causality and the temporal order of the observed association. Nevertheless, activity fragmentation in middle-aged and older adults may reflect pre-clinical signs of future neurodegenerative processes indicating potential targets for modification through intervention.

## 1. Introduction

Dementia is one of the major causes of disability and dependency among older people worldwide (Frankish and Horton, 2017). Subjective memory complaints (SMC) are particularly prevalent among older adults and are often considered a clinical marker of mild cognitive impairment and dementia, even in the absence of objective neurocognitive impairment. Accordingly, targeting people with SMC provides a critical opportunity to establish adequate preventive and intervention strategies to delay the onset of cognitive problems later in life.

Physical activity is considered one of the most promising strategies for promoting healthy cognitive ageing (Wheeler et al., 2020). Previous studies have already established an association between self-reported physical activity and SMC (Fondell et al., 2018; Nemoto et al., 2018; Felez-Nobrega et al., 2020). However, only focusing on the total amount of physical activity may overlook how physical activity accumulates throughout the day, which can be useful for detecting characteristics of accelerated biological ageing—e.g., the capacity of individuals to sustain longer bouts of activity could reflect fatigability and could be an early sign for functional declines. In fact, exploring the patterns of activity accumulation may be informative to evaluating the onset and/or severity of SMC, and subsequent poor cognitive outcomes. Using accelerometer-derived, continuous assessment of minute-by-minute activity as well as sedentary cycles throughout the day, a measure of

* Corresponding author at: Centre for Active and Healthy Ageing, Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Campusvej 55, 5230, Odense, Denmark.
*E-mail address:* bdelpozocruz@health.sdu.dk (B. del Pozo Cruz).

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activity fragmentation (i.e., frequency with which a person transitions into a sedentary state from an active state throughout the day) can be derived to determine how physical activity is accrued (Wanigatunga et al., 2018a). A fragmented pattern of activity has been previously associated with cancer history (Wanigatunga et al., 2018a), fatigue (Palmberg et al., 2020), and all-cause mortality (Wanigatunga et al., 2019). The current study aimed to explore the associations between activity fragmentation and SMC in a population-based US sample of people 45 years and over.

## 2. Methods

The current cross-sectional analysis used data from the 2003–2006 waves of the National Health and Nutrition Examination Survey (NHANES) (Zipf et al., 2013). Participants who were 45 years or over (Felez-Nobrega et al., 2020) with at least 3 days of valid accelerometry data (10 h/day) and available SMC data (n = 3820) were included in the study.

Participants wore accelerometers (AM-7164, ActiGraph, LLC, Fort Walton Beach, Florida) on their waist according to the protocol for 7-consecutive days during waking hours (Leroux et al., 2019; Troiano et al., 2008). Accelerometer data reduction in the current study followed validated procedures (Leroux et al., 2019; Troiano et al., 2008). Using an established cut-point (Leroux et al., 2019; Troiano et al., 2008), accelerometer counts were classified into sedentary (<100 cpm) or otherwise active (100+ counts/min). To calculate activity fragmentation, an active-to-sedentary transition probability was calculated as the number of physical activity bouts (i.e., consecutive minutes registering 100+ counts/min) divided by the total sum of minutes spent in physical activity (Wanigatunga et al., 2018a). We defined SMC as present if participants responded "yes" to the question— "(Are you/is survey participant) limited in any way because of difficulty remembering or because (you/s/he) experience(s) periods of confusion?".

A multivariable ordinal logistic regression model was conducted to examine the association between activity fragmentation and SMC. The results are reported as odds ratio (OR) and associated 95% Confidence Interval (CI). The magnitude of the association is illustrated through the average marginal effect (AME) and associated 95%CI. For additional interpretability of the results, the activity fragmentation index was standardized by subtracting population-level mean and dividing by population-level standard deviation, resulting in a model coefficient that corresponds to one standard deviation change. The model was adjusted for age, sex, race, education level, smoking status (never, former, current), drinking status (former-never drinker, heavy drinker, moderate drinker, non-drinker), body mass index (BMI; kg/m$^2$), mobility difficulty (yes, no), diagnosis of diabetes, coronary heart disease, congestive heart failure, stroke, and cancer, accelerometer wear time and total physical activity volume defined as log-transformed total activity counts per day (Wanigatunga et al., 2018a). A locally weighted scatterplot smoothing curve was used to represent the adjusted estimated probability of SMC associated with activity fragmentation. The analyses were conducted in 2020. All analyses were conducted with R software (version 3.5.1). The alpha was set at 0.05, two-tailed.

## 3. Results

Participant characteristics are shown in Table 1. Participants without SMC were younger and more educated than those with self-reported SMC. Participants who reported SMC had more comorbidities and mobility problems than their counterparts without complaints, including diabetes, heart failure, and stroke. Also, participants with SMC accumulated their physical activity in a more fragmented manner compared with those without SMC. Fig. 1 shows the adjusted estimated probability of reporting SMC associated with activity fragmentation. Results from the logistic regression indicated that an increment of 1SD in activity fragmentation was associated with an increased likelihood of self-reported SMC in the population of the study (OR [95%CI] = 1.335 [1.067, 1.669]; AME [95%CI] = 0.029 [0.006, 0.052]; $p$-value = 0.011) (Table 2).

**Table 1**
Characteristics of the study participants.

| | Total | No SMC | SMC | $p$-Value |
|---|---|---|---|---|
| | n = 3820 | n = 3407 | n = 413 | |
| Age, yrs. | 63.30 (11.11) | 62.90 (11.01) | 66.56 (11.42) | **<0.001** |
| Body Mass Index (kg/m$^2$) | 28.96 (6.04) | 28.92 (5.95) | 29.28 (6.70) | 0.249 |
| Sex: Male (%) | 50.0 | 50.7 | 44.1 | **0.012** |
| Race (%) | | | | 0.144 |
| Black | 20.1 | 19.8 | 23.2 | |
| Mexican American | 18.2 | 17.9 | 20.8 | |
| White | 56.4 | 57.1 | 50.8 | |
| Other | 3.3 | 3.3 | 2.9 | |
| Other Hispanic | 1.9 | 1.9 | 2.2 | |
| Education (%) | | | | **<0.001** |
| Less than high school | 30.5 | 28.7 | 45.3 | |
| High school or equivalent | 25.0 | 24.7 | 27.4 | |
| More than high school | 44.4 | 46.5 | 27.4 | |
| Comorbidity status (%)[a] | | | | |
| Diabetes | 16.4 | 15.3 | 25.7 | **<0.001** |
| Coronary heart disease | 7.4 | 7.2 | 8.4 | 0.307 |
| Congestive heart failure | 5.2 | 4.7 | 9.9 | **<0.001** |
| Stroke | 5.4 | 4.5 | 12.8 | **<0.001** |
| Cancer | 14.0 | 14.1 | 13.7 | 0.840 |
| Smoking status (%) | | | | 0.986 |
| Current | 18.9 | 18.9 | 18.6 | |
| Former | 36.2 | 36.2 | 36.6 | |
| Never | 44.9 | 45.0 | 44.8 | |
| Drinking status (%) | | | | **<0.001** |
| Heavy drinker | 6.3 | 6.5 | 5.1 | |
| Moderate drinker | 48.8 | 50.5 | 34.9 | |
| Non-drinker | 40.0 | 38.4 | 53.3 | |
| Former-never drinker | 4.9 | 4.7 | 6.8 | |
| Mobility problems: yes (%) | 2.9 | 2.5 | 5.7 | **0.007** |
| Valid wear time (min/day) | 879.83 (140.52) | 879.34 (135.98) | 883.84 (173.69) | 0.539 |
| LTAC/day | 10.35 (0.62) | 10.38 (0.61) | 10.16 (0.66) | **<0.001** |
| Fragmentation index/day | 0.29 (0.09) | 0.28 (0.09) | 0.32 (0.10) | **<0.001** |

Data are presented as mean (SD) for continuous measures, and % for categorical measures.
LTAC, log-transformed total activity counts per day.
Bold means statistically significant differences between the groups.
[a] Self-reported history of being diagnosed by a doctor.

## 4. Discussion

Our study provides preliminary, first-time evidence that fragmented activity patterns are associated with an increased probability of SMC in people 45 years and over, independently of total volume of physical activity. This finding supports that looking at fragmented activity patterns can be useful in identifying those at risk for cognitive impairment, even before clinical signs are present. This information may also reveal important insights for the design of tailored physical activity interventions to prevent cognitive declines in middle-aged and older adults.

Previous studies have shown an association between ambulatory capacity and poor cognition and increased brain atrophy (Demnitz et al., 2017). Several mechanisms may account for the observed association in

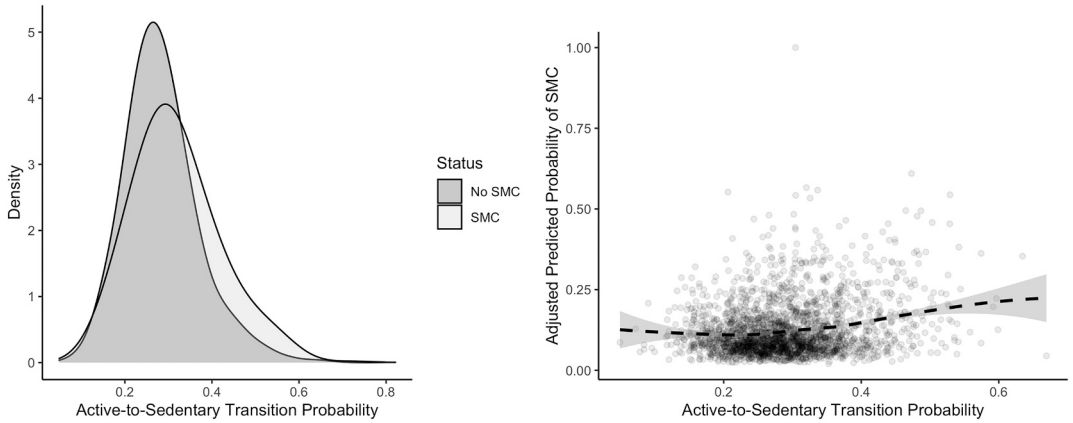


**Fig. 1.** Adjusted estimated probability of subjective memory complaints (SMC) associated with activity fragmentation. The panel on the left represents a density plot of frequencies of active-to-sedentary transition probabilities across SMC status. The panel on the right represents the locally weighted scatterplot smoothing curve of the adjusted estimated (i.e., fitted values) probability of SMC associated with activity fragmentation.

**Table 2**
Association between activity fragmentation and subjective memory complaints.

| | Subjective memory complaints, *yes* | |
|---|---|---|
| | Odd ratio (95% confidence interval) | Average marginal effect (95% confidence interval) |
| Activity fragmentation[a] | 1.335 (1.067 to 1.669) | 0.029 (0.006 to 0.052) |

[a] The activity fragmentation index was standardized by subtracting population-level mean and dividing by population-level standard deviation, resulting in a model coefficient that corresponds to one standard deviation change. The model was adjusted for age, sex, race, education level, smoking status (never, former, current), drinking status (former-never drinker, heavy drinker, moderate drinker, non-drinker), body mass index (BMI; kg/m$^2$), mobility difficulty (yes, no), diagnosis of diabetes, coronary heart disease, congestive heart failure, stroke, and cancer, accelerometer wear time and total physical activity volume defined as log-transformed total activity counts per day.

the current study. Executive functioning seems to lead SMC, which could explain activity fragmentation (i.e., the ability of individuals to initiate and sustain physical activity is highly dependent on performance of executive functioning) (Snitz et al., 2015). The reverse could also be true (i.e., activity fragmentation may precede declines in executive functioning), which reinforces the observed association (Snitz et al., 2015). Moreover, subjective belief systems may transcend specific health domains (Luszcz et al., 2015). Thus, individuals reporting SMC may also have a poor self-perceived physical function which may limit their ability to sustain longer bouts of physical activity, even in the absence of objective physical limitations (Cosentino et al., 2018). Nevertheless, more fragmented patterns of physical activity are associated with lower functional ability and higher perceived physical fatigability (Felez-Nobrega et al., 2020), which may lead to an overall decrease of levels of physical activity (Wanigatunga et al., 2018b) and thereby declines in cognitive health outcomes (Livingston et al., 2020).

Our results should be interpreted in the light of several limitations. Given the cross-sectional design of this study, causality or the temporal associations between activity fragmentation and SMC cannot be established. Accelerometers may not be able to accurately differentiate between sedentary behavior and physical activity, which may have led to behavior misclassification. The instrument used to assess SMC in this study was self-reported and responses may be affected by current life situations rather than reflecting actual memory problems. Nonetheless, our results were robust to multiple covariate adjustments, although residual confounding cannot be ruled out. Furthermore, the NHANES survey assesses specifically for limitations experienced by memory problems and confusion, which may have excluded individuals who felt that their memory problem or confusion did not result in any restriction of activities. Lastly, the item used to assess SMC combined two constructs (i.e., memory and confusion) but only allowed one answer, which limits the ability to examine memory and confusion complaints separately. Strengths of this study include a relatively large sample of older adults with device-assessed physical activity data for 3–7 days, which allowed first-time exploration of minute-by-minute acceleration and utilization of a novel accelerometer metric to the phenotype physical activity accumulation pattern in the study sample. Future studies are warranted to establish the temporal order of the observed relationship.

## 5. Conclusions

In conclusion, we found that more fragmented patterns of activity were associated with higher probabilities of reporting SMC in middle-aged and older adults. Future studies are necessary to understand the underlying mechanisms underpinning the association between activity fragmentation and SMC. Longitudinal studies are warranted to establish causality and the temporal order of the observed association. Nevertheless, activity fragmentation may reflect pre-clinical signs of future neurodegenerative processes indicating potential targets for modification through intervention.

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Conflict of interest BdPC – Original idea; BdPC and JdPC - Conceptualization; BdPC - Data curation; BdPC -Formal analysis; BdPC and JdPC - Investigation; BdPC -Methodology; BdPC - Visualization; BdPC - Writing – original draft; BdPC and JdPC - Writing – review & editing.

## Declaration of competing interest

None to declare.

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The research presented in this paper is that of the authors. BdPC had the original idea, conceptualized the project, conducted the analysis and wrote the first draft of the manuscript. JdPC conceptualized the project, help in drafting the manuscript and critically reviewed the paper. All authors approved the final version of the paper. No financial disclosures were reported by the authors of this paper.

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