Can physical activity attenuate the negative association between sitting time and cognitive function among older adults? A mediation analysis

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Abbreviated title: Sitting time, cognition and MVPA in older adults

Abstract

The purpose of this study was to examine the combined association of sitting time and physical activity with cognitive function and to determine whether moderate-to-vigorous physical activity (MVPA) is a mediator of the association between sitting time and cognitive function in a nationally representative sample of older adults from Chile. Data from 989 older adults (≥65 years old, 61.3% female) from the 2009-2010 Chilean Health Survey were analyzed. Physical activity and sitting time were measured using the Global Physical Activity questionnaire. Cognitive function was assessed using the modified Mini-Mental State levels Examination (mMMSE). Physical activity levels were categorized as "inactive" (<600 metabolic equivalent value minutes per week) or "active" (≥600 metabolic equivalent value minutes per week). Sitting time was categorized as "sedentary", defined as ≥4 h of reported sitting time per day, or "non-sedentary", defined as <4 h. We created the following groups (i) non-sedentary/active; (ii) non-sedentary/inactive; (iii) sedentary/active; and (iv) sedentary/inactive. Hayes's PROCESS macro was used for the simple mediation analysis. Compared with the reference group (individuals classified as non-sedentary/active), older adults who were classified as sedentary/active had elevated odds of cognitive impairment (OR=1.90, [95% CI, 1.84 to 3.85]). However, the odds ratio for cognitive impairment was substantially increased in those classified as sedentary/inactive (OR=4.85 [95% CI, 2.54 to 6.24]) compared with the reference group. MVPA was found to mediate the relationship between sitting time and cognitive function (Indirect Effect=-0.070 [95% CI, -0.012 to -0.004]).

Conclusion: The present findings suggest that, whether overall physical activity is high or low, spending large amounts of time sitting is associated with elevated odds of cognitive impairment and that MVPA slightly weakens the relationship between sitting time and cognitive function.

Key words: cognitive impairment; aging; sedentary behavior; physical inactivity

1. Introduction

The association between age and cognitive decline has been documented [1], however the relation is weak because the declines may reflect quantity more than quality [2]. In this way, very robust inverted-U relations between age and different measures of achievement have been reported in many different domains [2]. Among the factors that contribute to the onset of cognitive decline, age, poor diet, unhealthy lifestyle choices, and mood disorder appear to be key drivers [3]. Efforts are being made to attenuate age-related declines in cognition and its associated health burden, such as a decreased quality of life [4]. In terms of brain function, physical inactivity and poor dietary habits can disrupt cognition, with studies reporting deficits in learning, memory and executive functioning in inactive subjects compared with active individuals [5].

Sedentary behavior is any waking behavior characterized by an energy expenditure ≤1.5 metabolic equivalents while sitting or lying down [6]. Sitting time is an important predictor of healthy aging and a potentially modifiable determinant of health [7]. On this topic, many [8 9] but not all studies have shown that the association of sedentary behaviors and health outcomes is partially independent of levels of physical activity [10 11]. Droga et al. have suggested that sedentary behavior is significantly associated with decreased odds of successful aging among middle-aged and older adults, independent of physical activity [12]. A recent systematic review published by Falck et al. suggests that sedentary behavior earlier in life is a risk factor for cognitive impairment and therefore dementia later in life [8].

Although physical activity has been shown to be positively associated with cognitive function [13] [14] by different several biological mechanisms (e.g., neurogenesis, angiogenesis, attention, memory, and synaptic plasticity) [15], few studies have identified independent associations of physical activity and sitting time with cognitive function. Since levels of physical activity tend to decrease [16] and sitting time tends to increase [17] with aging, an investigation including both independent variables is warranted in this population. On this subject, a recent cross-sectional study suggests that physical activity attenuates the association between sedentariness and cognitive function [18]; however, another prospective study found that a relationship remained evident even after physical activity was adjusted for [9]. Current international strategies for older adults highlight the importance of increased moderate-to-vigorous physical activity (MVPA) for maintaining cognitive health throughout the lifespan [8 19]. For example, physical activity may promote neural resilience by reducing age-related neural inflammation, ultimately helping to preserve cognitive function among older adults [20]. Therefore, it is necessary to elucidate the potential mediating role of MVPA on the effects of sitting time on cognitive function. Our aim, therefore, was to examine the combined association of sitting time and physical activity with cognitive function and to determine whether MVPA is a mediator of the association between sitting time and cognitive function in a nationally representative sample of older adults from Chile. We hypothesize that higher levels of MVPA will mediate the negative effect of sitting time on cognitive function.

2. Methods

2.1. Study population

The 2009-10 Chilean National Health Survey was a representative household survey with a stratified multistage probability sample of 5,416 non-institutionalized participants over 14 years old from the 15 regions in Chile, both urban and rural. The sample size was calculated with a 20% relative sampling error to estimate a national prevalence over 4%. One participant was randomly selected per household, and pregnant female were excluded. The response rate was 85%, with no replacements. Detailed information about the survey has been described elsewhere [21]. In this study, 1,013 older adults (>65 years) were evaluated. Of these respondents, 989 had recorded values for physical activity questionnaire. The study protocol and ethical consent forms were approved by the ethics committee of the Pontificia Universidad Católica de Chile and the Ministry of Health.

2.2. Measurements

Standardized protocols were used, and all investigators (nurses and research technicians) underwent joint training sessions prior to implementation of the survey.

2.2.1. Cognitive function

The modified Mini-Mental State Examination (mMMSE) instrument, which assesses orientation, attention, recent memory and language, was administered [22]. The mMMSE comprises six questions with a maximum total score of 19 points. For example, the question about the orientation became: ‘‘Where are we now?’’. Respondents with scores 13 or less were considered cognitively impaired [23].

2.2.2. Physical activity and sitting time

The Global Physical Activity Questionnaire was conducted via face-to-face interview and assesses sedentary behavior (total time spent sitting, i.e. sitting or reclining at work or at home, getting to and from places, or with friends, but does not include time spent sleeping) and three domains of physical activity (occupational, active-commuting, and recreational). Also, the questionnaire include the following single question: “How much time do you usually spend sitting or lying (reclining) on a normal day?” [24].

2.2.3. Anthropometrics assessment

Height was measured to the nearest 0.1 cm using a portable stadiometer, and weight was measured to the nearest 0.1 kg using a digital scale (Tanita HD-313®) with participants without shoes and in light clothing in their home. Body mass index (BMI) was calculated as [weight/height^2].

2.2.4. Covariates

Socio-demographic data were collected for all participants, including age, sex, education level (primary, secondary or beyond secondary), living alone (yes or no), alcohol intake as assessed by the Alcohol Use Disorders Identification Test (AUDIT) [25], area of residence (urban or rural), tobacco use, and depression in the past year. Past smokers were those who reported that they had smoked > 100 cigarettes in their lifetime but did not currently smoke cigarettes. The Composite International Diagnostic Interview, Short Form (CIDI-SF), was applied to establish a diagnosis of major depressive episode using the Diagnostic and Statistical Manual of Mental Disorders (DSM-

IV) criteria [26]. Finally, the AUDIT test identifies dangerous drinking behaviors through a summary score constructed from questions on drinking behavior including drinking frequency, quantity, and inability to stop drinking.

2.3. Statistical analysis

Statistical normality was tested using both statistical (Kolmogorov–Smirnov test) and graphical procedures (normal probability plots). Due to the skewed distribution, the mMMSE score was log-transformed.

To investigate the combined effects of physical activity and sitting time on mMMSE, physical activity was categorized as "inactive" (<600 metabolic-equivalent value minutes per week) and "active" older adults (≥600 metabolic-equivalent value minutes per week) [24] and sitting time was categorized as "sedentary" and "non-sedentary" and defined as reporting ≥4 h of sitting time per day [27]. From these classification, we created the following groups (i) non-sedentary/active; (ii) non-sedentary/inactive; (iii) sedentary/active; and (iv) sedentary/inactive. ANCOVA models were used to assess mean differences in mMMSE scores among these categories, controlling for age, sex, BMI, social characteristics (educational level and living alone), alcohol and drugs use, tobacco intake, and depression. Pairwise post hoc hypotheses were tested using the Bonferroni correction for multiple comparisons.

Logistic regression models were employed to compare the prevalence of cognitive impairment (i.e. ≤ 13) across combined above-mentioned categories and adjusted by age, sex, BMI, social characteristics (educational level and living alone), alcohol and drugs use, tobacco intake, and depression.

Finally, to examine whether the association between sitting time and cognitive function was mediated by total physical activity, linear regression models were fitted using bootstrapped mediation procedures included in the PROCESS SPSS macro [28]. Data were analyzed using SPSS-

IBM (Software, v.22.0 SPSS Inc., Chicago, IL, USA), and a value of $p < 0.05$ was considered statistically significant.

3. Results

Descriptive characteristics of the study variables are presented in Table 1. Overall, 42.1% spend at least 4 hours or more per day of sitting time and the 37.3% of the older adults were physically inactive.

Figure 1 describes the mMMSE scores in Chilean older adults for each of the joint categories of sitting time and physical activity. Cognitive function (mMMSE score) was lower in sedentary/inactive group than groups categorized as non-sedentary/active ($p < 0.001$), non-sedentary/inactive ($p < 0.001$), and sedentary/active ($p = 0.014$). Also, older adults categorized as sedentary/active have lower mMMSE scores than non-sedentary/active counterparts ($p = 0.020$).

Table 2 shows the odds ratios (ORs) for the prevalence of cognitive impairment across combined categories. The adjusted analysis shows that compare to older adults classified as non-sedentary/active those who were sedentary/active or sedentary/inactive had higher odds for cognitive imparment (OR=1.90, [95% CI 1.84 to 3.85], $p = 0.016$) and OR=4.85, [95% CI 2.54 to 6.24], $p < 0.001$), respectively.

Table 2 near here

We performed a mediation analysis to test whether MVPA acted as mediator variables between cognitive function (dependent variable) and sitting time (independent variable) (Figures 2). As shown in Figure 1, the effect of sitting time on cognitive function was mediated by MVPA. In the first regression step (equation a), sitting time was positively related with the MVPA ($p < 0.001$). In the second step (equation c), the regression coefficient of sitting time on the dependent variable (cognitive function) was negatively associated ($p < 0.001$). In the last regression model, the mediator variable (MVPA) was negatively associated with the dependent variable (equation b) (p <

0.001), but when MVPA was included in the model (equation *c'*), the regression coefficient did remain significant but the relationship was slightly attenuated. Finally, the indirect effect was significant (indirect effect=-0.070 (95% CI, -0.012 to -0.004), confirming the mediation role of MVPA in this model.

4. Discussion

The present study examined the combined association of sitting time and physical activity with cognitive function. Our findings suggest that individuals who are sedentary and active or sedentary and inactive have higher odds of cognitive impairment than their non-sedentary, active counterparts. In addition, we found that MVPA mediates the relationship between sitting time and cognitive function. These results may suggest the importance of restrict sitting time and preferably also increase MVPA to attenuate its negative association with cognitive function. However, these findings could be studied longitudinally.

Increasing age is associated with a decrease in physical activity and cognitive function, and sedentary behavior may be a modifiable risk factor that can reduce the risk of disease and disability among older adults [19]. Increasing physical activity is one promising strategy to promote or maintain cognitive health in later life [29]. Additionally, while evidence suggests that sitting time is associated with cognitive function in older adults [8],in the absence of studies evaluating cardiometabolic factors, the interrelationship among sitting time, physical activity and cognitive function remains unclear [18]. The findings of the present study suggest that sedentary and active or sedentary and inactive older adults had lower cognitive function levels and had higher odds of cognitive impairment than non-sedentary, active individuals. Therefore, our results seem to indicate that even if a person meets the daily physical activity recommendations (i.e., ≥600 metabolic equivalent value minutes per week), one of the key correlates of cognitive health in older adults [18], sitting for ≥4 hours per day is related to cognitive impairment. If we add the effect of physical inactivity to the effect of high levels of sedentary behavior, the odds of having cognitive impairment are doubled.

Therefore, the new physical activity recommendations for the older population, which suggest limiting discretionary sedentary behavior to <2 hours per day and concomitantly engaging in ≥150 minutes per week of MVPA [8], could have a beneficial effect on the maintenance of optimal cognitive function in the elderly.

Several studies have suggested the ability of MVPA to attenuate [30] or even eliminate [10 31] the risks of a variety of health outcomes. Recently, Edwards et al. [18] reported that MVPA is positively associated with cognitive function even among those with prolonged sedentary behavior. In contrast, our mediation analysis reveals that MVPA mediates the relationship between sitting time and cognitive function, slightly weakening this relationship. The mechanisms whereby sitting time may negatively influence cognitive function in older adults are not clear. First, the negative impact of sitting time on cardiovascular disease biomarkers [7], which are related to cognitive function [32], could increase the risk of cognitive impairment in older adults. Second, depression is considered another risk factor that has been associated with compromised cognitive function [33], and sitting time is related to the prevalence of depression[34]. Since some older adults are unable to engage in MVPA owing to fitness reductions [35] or chronic conditions [36], efforts to reduce sitting time should thus be made to avoid potential declines in cognitive function. Also, cognitive function is related with frailty characteristics, such as poor sitting ability, since both diseases share some pathophysiological mechanisms and short-term and mid-term consequences (e.g., hospitalization, incidence of falls, disability, institutionalization, and death). In addition, muscular and central nervous systems share common pathogenic pathways in the evolution of disability, probably underlying the negative association between neuromuscular performance (i.e., strongly associated with sitting ability) or functional abilities and cognitive impairment [37].

There are several strengths and limitations to our investigation. The strengths include the use of a large, nationally representative dataset from a population of older Chilean adults. Additionally, we used the mMMSE questionnaire, which has good test-retest reliability and validity [22], and our adjustments for known confounding variables also make the study findings more valid and reliable.

Of course, our study has several limitations. First, the cross-sectional nature of the study limits our ability to explore whether physical activity was reduced as a result of cognitive decline (loss of independence) or vice versa, with cognitive decline developing as a result of low levels of physical activity. Second, although the mMMSE questionnaire is the most widely used test for determining an individual's cognitive health, it is considered to have an insufficient scope to identify mild forms of cognitive decline [38]. Finally, the use of a self-report measurement to assess sitting time and physical activity may have elicited some degree of recall and desirability bias. However, recent work published by Aguilar-Farias and Leppe [39] suggests that this question has shown fair validity in the Chilean population.

5. Conclusion

The present findings suggest that, whether overall physical activity is high or low, spending large amounts of time sitting is associated with elevated odds of cognitive impairment. Additionally, our mediation analysis reveals that MVPA mediates the relationship between sitting time and cognitive function, slightly weakening this relationship. Therefore, these findings may indicate that in older adults restrict sitting time and increase MVPA is related with cognitive benefits [40]. Finally, taken into account that in most parts of the world we are expected to stay longer at the labor market, it plausible to suggest that the present results will also have relevance for older workers.

Figure captions

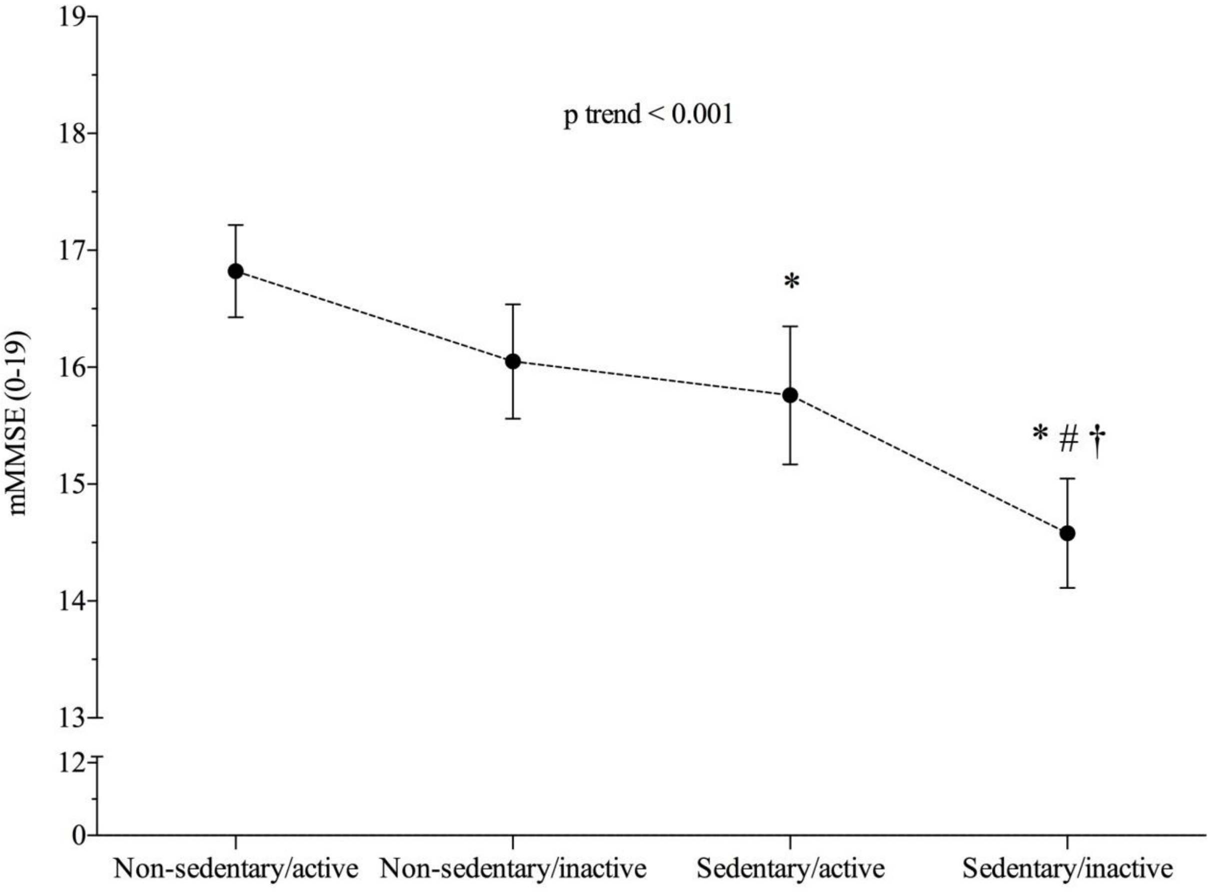

Figure 1. Mean differences in the modified Mini Mental Status Examination scores by sitting time and physical activity categories controlling for potential confounders. * # †, $p < 0.05$ compared to non-sedentary/active group.

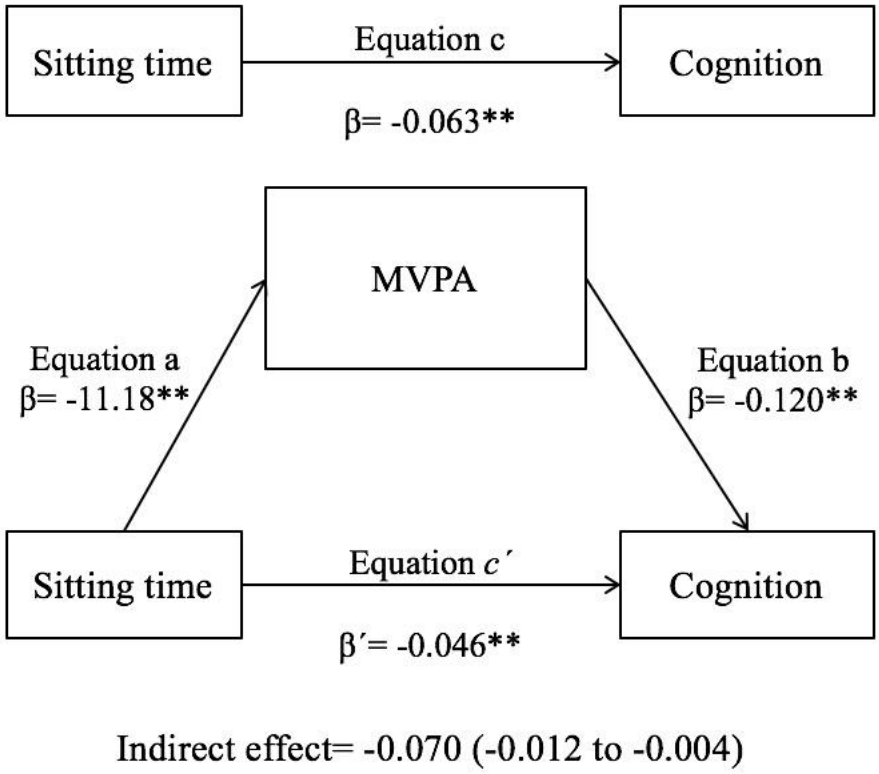

Figure 2. Physical activity mediation models of the relationship between sitting time and cognitive function in older adults, adjusted by age, sex, body mass index, social characteristics (educational level and living alone), alcohol and drugs use, tobacco intake, and depression.

Acknowledgements

We thank all participants for their co-operation and the Chilean Health Ministry and Department of Public Health, The Pontificia Universidad Católica de Chile for designing and conducting the second National Health Survey 2009–2010.

Table 1. Characteristics of the study variables (n = 989)

Age (years)	74.13 (6.95)
Female, n (%)	606 (61.3)
Weight, kg	69.16 (14.72)
Height, m	1.55 (0.09)
Body mass index, kg/m^2	28.37 (5.29)
Cognition function	
mMMSE (0-19)	15.66 (3.83)
Impairment cognition	
mMMSE (≤ 13), n (%)	153 (15.5)
Self-reported physical activity	
MVPA (MET min per day), mean (SD)	63.6 (9.5)
Physical inactivity, n (%)	369 (37.3)
Sitting time, h per day	3.75 (3.34)
Sedentary risk behavior, n (%)§	416 (42.1)
Healthy behavior	
Alcohol use, n (%)#	750 (83.8)
Tobacco use, n (%)†	126 (12.7)
Medication use, n (%)*	734 (81.6)
Depression	
CIDI-SF, n (%)	97 (9.8)
Education	
Up to primary (<8 years), n (%)	576 (58.3)
Up to secondary (<12 years), n (%)	252 (25.5)
Beyond secondary (>12 years), n (%)	66 (6.7)
Living alone, n (%)	278 (27.4)

CIDI-SF, Composite International Diagnostic Interview, Short Form; MET, metabolic-equivalent value; mMMSE, modified Mini Mental Status Examination.
* At least one prescription drug; # Alcohol intake as assessed by the Alcohol Use Disorders Identification Test; † Defined as never having smoked or quit smoking ≥12 months ago; § Risk sedentary behaviour was defined as reporting ≥4 h of sitting time per day

Table 2. Combined effects of sitting time and physical activity on cognitive impairment function according to the modified Mini Mental Status Examination (mMMSE ≤ 13).

	OR	(95% CI)	*p*
Non-sedentary / Active	1.00		
Non-sedentary / Inactive	1.63	0.92 to 4.75	0.084
Sedentary / Active	1.91	1.83 to 3.75	0.011
Sedentary / Inactive	4.65	2.50 to 6.31	<0.001

* Analysis adjusted by age, sex, educational level, body mass index, social characteristics (educational level and living alone), alcohol and drugs use, tobacco intake, and depression.

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