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Association Between Physical Activity Levels and Cognitive Function in Older Adults: A Replication Cohort Analysis Using the Brazilian Longitudinal Study of Aging

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Abstract

Introduction: *Few studies address the complex relationship between physical activity and cognitive function in aging individuals. This topic has gained significant attention in recent years, as cognitive decline poses a substantial public health challenge. There is a lack of research focusing on the effect of physical activity on cognitive function in the Brazilian population.*

Purpose: *Our study aims to replicate the findings of Lautenschlager et al. using a Brazilian cohort from the ELSI study, a comprehensive longitudinal study capturing aging processes and determinants among individuals in Brazil.*

Methods: *In line with the reference study, our analysis focused on individuals aged 50 and older without depression and dementia. The primary outcome was cognitive function, assessed using a summary score obtained from the ELSI study to replicate the ADAS-Cog, as in the original study. Participants were categorized into two groups: those engaging in moderate to vigorous exercise (exercise) and those who did not meet this exercise threshold (no exercise). To evaluate the relationship between exercise and cognitive function, we performed three linear regression models: one without adjustments for covariates, a second model adjusting for sex, education, and race (main model), and a third model with multiple adjustments. A sensitivity analysis using Cohen's D was also conducted.*

Results: *In this study from the ELSI cohort, data from 7,292 individuals were available, and 6,147 met the inclusion criteria for analysis. A total of 935 individuals were excluded due to depression, and 98 were excluded due to dementia. Baseline characteristics were not well balanced between groups. The mean age in the exercise group was 64 years compared to 67 years in the no exercise group, with a higher percentage of males (48% vs. 39%) and a higher education level (12% with university education vs. 6%). In the unadjusted linear regression, there was a positive correlation between exercise and cognitive function (2.19, 95% CI 1.89 - 2.48, p<0.001). In the second model, which emulated the reference trial by including sex, race, and educational status, the positive correlation persisted, though with a lower effect size (1.53, 95% CI 1.25 - 1.82, p<0.001). A third model with additional adjustments was employed to assess the consistency of the association, which was maintained (1.92, 95% CI 1.62 - 2.23, p<0.001).*

Conclusion: *Our study reaffirms the potential benefits of moderate to vigorous exercise on cognitive function in older adults with mild cognitive impairment.*

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Introduction

The association between the level of physical activity and cognitive function has been the subject of much research in recent years. Since cognitive decline is a major public health concern, particularly among older adults, a deeper understanding of associations and risk factors in different study populations is needed. As the population ages, the number of people with cognitive impairment is expected to increase, and finding effective interventions to prevent or slow cognitive decline is a priority for researchers and clinicians.

Physical activity is defined as any energy expenditure resulting from the movement of the musculoskeletal system and its relationship with cognitive function is complex and multifaceted (Cui et al., 2018; Fonte et al., 2019; Gaitán et al., 2021). While there is evidence to suggest that physical activity can positively affect cognitive function, the nature of this relationship is not well understood (Fonte et al., 2019). Some studies have found that physical activity is associated with improved cognitive function (Cui et al., 2018; Fonte et al., 2019; Gaitán et al., 2021; Lautenschlager et al., 2008), by decreasing the risk of cardiovascular diseases as a risk factor for dementia due to the modulation of some neurotrophic factors and improving functional and structural brain changes (Veronese et al., 2023).

The lack of reproducible outcomes in scientific investigations shows the need for replication studies to reinforce the credibility and reliability of scientific discoveries (Bonett, D. G. (2021) and increase awareness of the need for new studies, Held, L. (2020). Such studies are essential, and using large cohort datasets, such as the ELSI-Brazil, they not only confirm or refute previous findings but also enhance the generalizability and reliability of research. Given the importance of this topic, there is a need for replication studies to confirm and extend previous findings.

This research looks into the relationship between exercise and the rate of cognitive decline, specifically focusing on older adults in Brazil. While it's clear that studies replicating previous research are crucial to help us understand if what was found before holds true in different places or among different people. Our main interest lies in seeing how physical activity and cognitive health are connected in the Brazilian population.

Therefore, the primary objective of this study was to reproduce and validate research findings regarding the correlation between physical activity and cognitive function found by N. T. Lautenschlager et al. using the Brazilian Longitudinal Study of Ageing (ELSI - Brazil).

Materials and Methods

Study Design and Population

This study is a cross-sectional design aimed to replicate the findings of the trial titled "Effect of Physical Activity on Cognitive Function in Older Adults at Risk for Alzheimer's Disease: A Randomized Trial" by Lautenschlager et al. Our analysis utilized data from the ELSI cohort, a comprehensive longitudinal study capturing aging processes and determinants among individuals in Brazil, covering essential characteristics, social factors, health conditions, cognitive function, and health services usage.

Reference Study Overview

In the original trial, participants with mild memory impairment were randomly assigned to a 24-week home-based physical activity program or a control group. The primary outcome was the change in the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog), assessed at baseline, 6, 12, and 18 months. Eligible participants were aged ≥50, experienced mild memory issues without dementia, were physically capable of exercising, and provided informed written consent. Exclusion criteria included clinically significant depressive symptoms, excessive alcohol consumption, chronic mental illness, severe medical conditions compromising survival, and limitations in physical activity.

Replication Study Criteria

In our replication study, participants aged ≥50 with memory problems not meeting dementia criteria were included. Patients with dementia and depressive symptoms were excluded. The primary outcome was the difference in the cognitive function between the exercise group and the no-exercise group, assessed using a score based on ELSI dataset parameters (Supplementary), aiming to emulate the ADAS-Cog. The parameters present in the ELSI study were a 10-word list to evaluate immediate and delayed recall, evaluate temporal orientation questions regarding day, month, year, and day of the week were made, semantic verbal fluency was tested with semantic animal fluency, prospective memory tested with writing one´s initials (remember to write one's initials after finishing another test), and semantic memory questions (two questions about common items and two questions about current politics) (Supplement - Table 1). Participants were stratified into "exercise" (moderate to vigorous exercise) and "no exercise" groups. Exercise was measured by a simplified version of the IPAQ (International Physical Activity Questionary) (Matsudo et al., 2012),

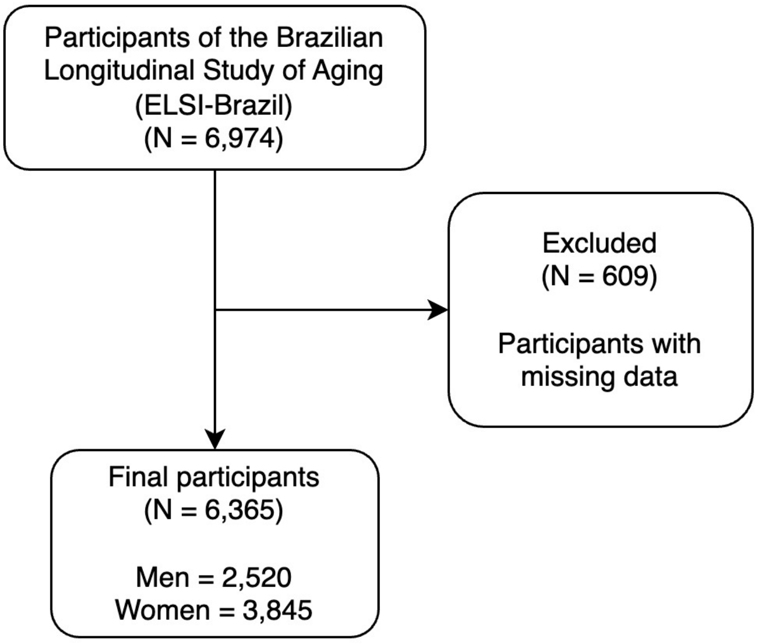

Figure 1: *Baseline characteristics.*

in this questionnaire patients were classified into three groups light, moderate, and vigorous activity based on their answers. The data was evaluated as complete case analysis (CCA) as missing exercise data were considered missing completely at random and excluded.

Statistical Analysis

The data summary employed medians and interquartile ranges and means and standard deviations for non-normal and normal data respectively. Categorical data were presented as frequencies and percentiles. Mean comparisons used t-tests for parametric data and Kruskal-Wallis for non-parametric data; chi-square tests were used for categorical variables.

Main Outcome Analysis

The main outcome was the difference in the summary cognition score between the two groups aforementioned. Three models were used: a simple linear regression with no adjustment, an emulation of the reference study's multivariate model adjusted for sex, race, and education, and an exploratory model adjusted for additional confounders present in the dataset.

Sensitivity Analysis

A sensitivity analysis using Cohen's D to evaluate the strength of the association was performed, it was considered a $d < 0.2$ - very small; $0.2 <= d < 0.5$ - Small; $0.5 <= d < 0.8$ - Medium; $d >= 0.8$ - Large. All analyses were conducted using STATA 18.0 (StataCorp LLC, USA) and RStudio version 4.3.1. Further details on the full model are available in the Supplementary materials.

Results

Sample Characteristics

The ELSI cohort consists of 7292 individuals, however only 6147 patients met the inclusion criteria for the analysis, 935 individuals were excluded because of depression and 98 had dementia. (Figure 1). As shown in Table 1, differences in patient characteristics between groups were observed. In the group of moderate to vigorous exercise, patients had a mean age of 64 years (SD = 8), were younger than the patients in the no-exercise group, and had a higher proportion of males (48%) compared to no-exercise (39%), and had fewer comorbidities. Patients in the exercise group had a higher level of education compared to the other group, 24% had middle school and university in the exercise

		No exercise	Exercise	p-value
		N=3,886	N=2,294	
Age, mean (SD)		67 (10)	64 (8)	<0.001
Men (%)		1,511 (39%)	1,107 (48%)	<0.001
Education (%)	No education	654 (17%)	263 (12%)	<0.001
	Elementary	1,930 (50%)	946 (41%)	
	High School	584 (15%)	503 (22%)	
	Middle School	472 (12%)	285 (12%)	
	University	222 (6%)	283 (12%)	
Retired (%)		2,315 (60%)	1,252 (55%)	<0.001
Alcohol (%)	Never	3,070 (79%)	1,588 (69%)	<0.001
	Less than once a month	356 (9%)	250 (11%)	
	One a month or more	452 (12%)	453 (20%)	
Current Smoke (%)	Yes, daily	444 (11%)	265 (12%)	0.72
	Yes, less than daily	53 (1%)	37 (2%)	
	No	3,389 (87%)	1,992 (87%)	
Past smoke (%)	Yes, daily	702 (18%)	453 (19.7%)	0.17
	Yes, less than daily	103 (2.7%)	68 (3%)	
	No	3,079 (79.2%)	1,770 (51%)	
Race (%)	White	1703 (43.9)	953 (41.7)	0.143
	Black	442 (11.4)	262 (11.5)	
	Brown	1701 (43.9)	1053 (46.0)	
	Yellow	9 (0.2)	10 (0.4)	
	Indigenous	22 (0.6)	10 (0.4)	
Hypertension (%)		2,058 (60%)	1,032 (45%)	<0.001
Diabetes (%)		737 (19%)	326 (5%)	<0.001
Stroke (%)		146 (3.8%)	58 (2.5%)	0.009
Arthritis (%)		845 (21.7%)	360 (15.7%)	<0.001
Cancer (%)		158 (4%)	77 (3.4%)	0.16
CKD (%)		95 (2.4%)	36 (1.6%)	0.021
Parkinson (%)		22 (0.5%)	16 (1%)	0.53
Wheelchair (%)		41 (1%)	8 (0.3%)	0.002
Bed ridden (%)		18 (0.4%)	6 (0.2%)	0.22
Heart disease (%)		312 (8%)	151 (6.6%)	0.037
Lung disease (%)		218 (5.6%)	100 (4.3%)	0.031
BMI, mean (SD)		27.79 (5.74)	27.67 (4.87)	0.37

Table 1: *Baseline characteristics.*

compared to 18% in the no exercise group (Table 1).

Unadjusted and Adjusted Models

Accordingly, we performed three model analyses to try to replicate the result of the previous trial on the effect of exercise on cognitive function (Lautenschlager et al., 2008). First, the unadjusted analysis was performed, and we observed an independent association between exercise in the result of cognitive function. Individuals in the exercise group had a cognitive score that was 2.19 points higher than the other group (p<0.001, 95%-CI 1.89 - 2.48).

The second model emulated the reference trial model, including the variables sex, race, and educational status. It was observed that there was a maintenance of the association between exercise and cognitive function, with the exercise group with a coefficient 1.53 points higher (p<0.001, 95 CI 1.25 - 1.82). However, there was a decrease in the effect size demonstrating that the other covariates are associated with outcome. Another finding from the second model was that education and sex were independently related to cognitive function (Table 3).

To assess the consistency of the results, a third model to adjust for different variables in the dataset was employed. In this model, the association was maintained, with a 1.92 points higher score in the exercise group (p<0.001, CI 95 1.62 - 2.23) (Table 3). The sensitivity analysis was performed using the e-value with Cohen's D with a small effect size in the replication model (Cohen´s D = 0,30).

Discussion

The complex relationship between physical activity and cognitive function in aging individuals has gained significant attention in recent years, as cognitive decline poses a substantial public health challenge. In the current scientific landscape, the replication crisis, marked by a notable lack of reproducible outcomes in scientific investigations, emphasizes the need for replication studies to reinforce the credibility and reliability of scientific discoveries (Bonett, 2021; Held, 2020). Such studies are vital, and by utilizing large cohort datasets, such as the ELSI-Brazil, they not only confirm or refute previous findings but also enhance the generalizability and reliability of research.

The results from this analysis are consistent with the original findings, suggesting a positive correlation between moderate to vigorous exercise and cognitive function in older adults. This aligns with results from other studies (Cui et al., 2018; Fonte et al., 2019; Gaitán et al., 2021; Raichlen et al., 2020; Zhang et al., 2022; Lautenschlager et al., 2008). The correlation persisted after adjusting for various confounders such as demographics and health-related variables, even though the effect size slightly decreased. This suggests that while factors like sex, education, and race do play a role in cognitive function, the beneficial impact of exercise is independent of these factors. In a second model, the original study's multivariate analysis was emulated to account for sex, race, and education, showing a consistent association between exercise and cognitive function. This model also identified education and sex as independent contributors to cognitive function, illustrating the significance of these factors. This is also supported by other results found in the literature (Gonçalves et al., 2023; Castro-Costa et al., 2018). A third model incorporated adjustments for additional variables available in the ELSI dataset. Despite these added confounders, the association between exercise and cognitive function remained intact, with an advantage for the exercise group. This analysis offers further support for the positive relationship between exercise and cognitive function in older adults (Cui et al., 2018; Fonte et al., 2019; Gaitán et al., 2021; Raichlen et al., 2020; Zhang et al., 2022).

One of the strengths of this replication study is the large sample size and the comprehensiveness of the ELSI dataset, which allowed for a detailed analysis of various factors potentially influencing cognitive function. The replication of a previous study's methodology in a different cultural and geographical context adds to the external validity of the findings. However, despite the consistency in our findings with the original study, our research has several limitations. The baseline characteristics between the exercise and no-exercise groups were not well balanced, indicating a potential selection bias. Individuals in the exercise group were on average three years younger, more likely to be male, and exhibited fewer comorbidities. The exercise group also had higher education levels, which could have an independent influence on cognitive function. Additionally, the cross-sectional nature of the study limits the ability to infer causality. Future studies should employ more rigorous participant matching to address imbalances. Moreover, the broad definition of exercise in our study highlights the need for precise definitions in future research, as part of an international collaborative guideline for the prevention of mild cognitive disorders and dementia, which has previously been proposed (Veronese et al., 2023).

Conclusion

This replication study highlights the potential of exercise as a non-pharmacological intervention to sup-

	Coef.	Std. dev.	CI 95%	p-value
Exercise	2.19	0.15	1.89 – 2.48	<0.001

Table 2: *Unadjusted model.*

	Coef.	Std. dev.	CI 95%	p-value
Exercise	1.53	0.15	1.25 – 1.82	<0.001
Female Sex	0.61	0.14	0.33 – 0.88	<0.001
Race				
Black	1.63	0.23	1.18 – 2.09	<0.001
Brown	1.23	0.15	0.94 – 1.52	<0.001
Yellow	-0.84	1.25	-3.28 – 1.60	0.501
Indigenous	2.71	0.96	0.83 – 4.60	0.005
Education				
Elementary	2.03	0.21	1.62-2.44	<0.001
High School	4.87	0.25	4.39 – 5.35	<0.001
Middle School	3.50	0.27	2.97 – 4.02	<0.001
University	5.75	0.31	5.15 – 6.34	<0.001

Legend: Coef = Coefficient; Std. Dev. = Standard Deviation; CI = Confidence interval; Cons. = Constant.

Table 3: *Replication mode.*

	Coef.	Std. dev.	CI 95%	p-value
Exercise*	1.92	0.15	1.62 – 2.23	<0.001

Legend: Coef = Coefficient; Std. Dev. = Standard Deviation; CI = Confidence interval; Cons. = Constant.

Adjusted for chronic kidney disease, heart disease, lung disease, bedridden, wheelchair, arthritis, hearing problems, previous stroke, Parkinson's disease, pain disorders, eyes disease, balance problems (Appendix - Table 2.B).

Table 4: *Explorative mode.*

port cognitive health in older adults. The findings are particularly relevant in the context of aging populations and the increasing prevalence of cognitive impairments. Future research should concentrate on longitudinal studies to better understand a possible causal relationship between physical activity and cognitive function. Moreover, exploring the specific types and intensities of exercise could provide valuable insights to design more effective exercise interventions.

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Conflicts of Interest

The authors declare no conflict of interest.

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